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HEALTH IN THE GLOBAL CONTEXT

CHALLENGES, POLICIES, AND PRACTICES

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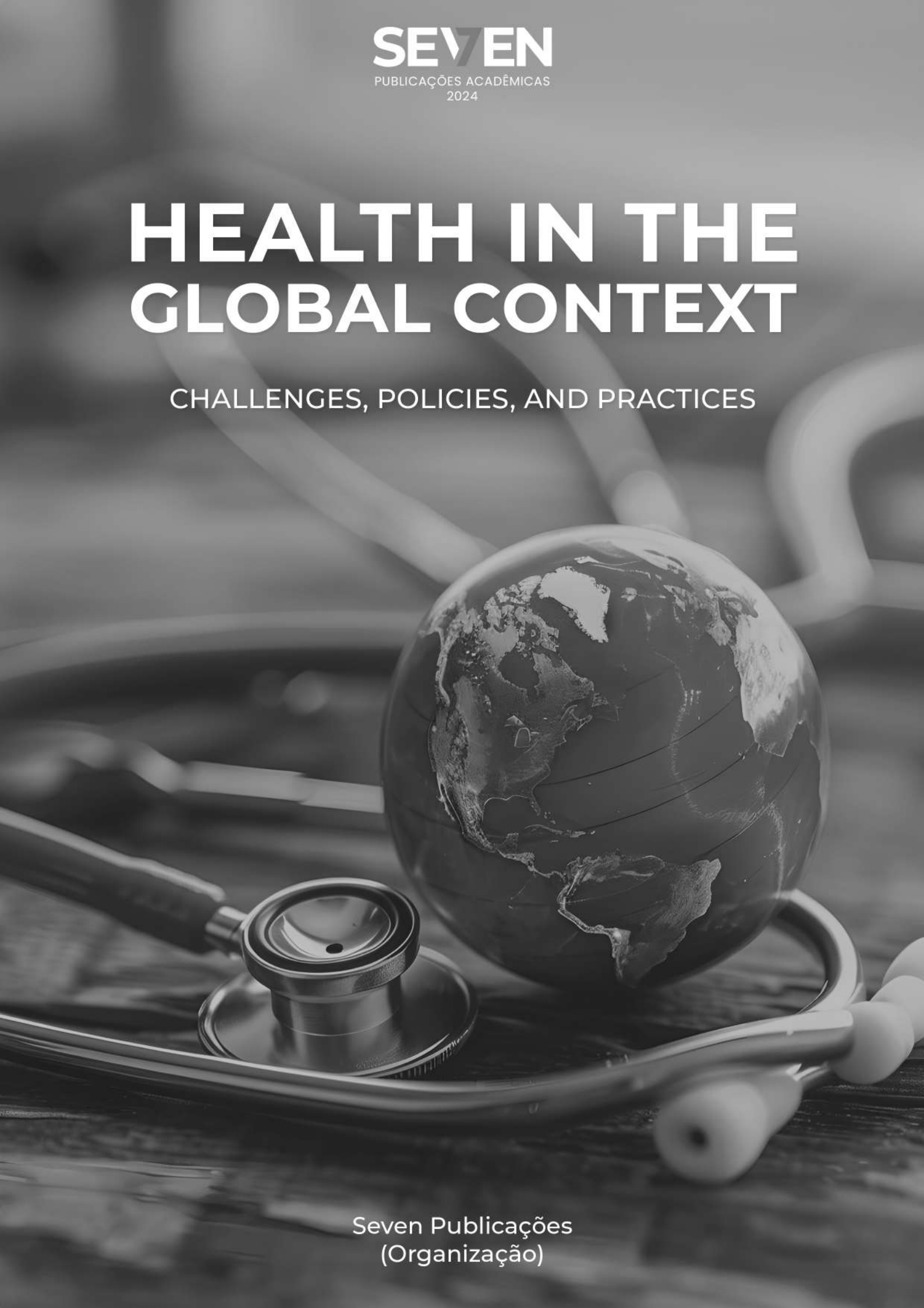

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Amanda Suélen Monteiro
Ana Beatriz Ramalho Leite Silva
Ana Flávia Souto Fonseca Sarni
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SUMMARY

SETTING UP AND EVALUATING AN AERATION SYSTEM WITH ARTIFICIALLY COOLED AIR

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Felipe de Oliveira Dourado[1], Ivano Alessandro Devilla[2] and Antônio Cruvinel Borges Neto[3]

ABSTRACT

The aeration system is used to preserve the quality of the stored grains, with the main objective of cooling the grain mass. Despite being the most widespread system for preserving stored grains, aeration has limitations such as dependence on local climatic conditions. Therefore, the cooling system can be an alternative technology to replace conventional aeration. The objective of this work was to design, construct and evaluate an artificially cooled grain aeration system. A prototype silo with dimensions of 0.9 m in diameter and 3 m in height, with a perforated bottom, was built, and an artificially cooled aeration system was adapted, in which the vortex tube coupled to the side of the plenum was used to blow the cold air. In the recording of temperature and interstitial moisture data of the grains; and the temperature and humidity of the environment, SHT75 sensors were used that were placed in the center of the prototype silo. The vortex tube was activated 15 minutes before turning on the fan, so that the temperature of the air blown by the fan in the silo was lower than the temperature of the ambient air. The artificially cooled system was activated daily at 7 pm and turned off at 8 am. In the evaluation period, the air temperature did not present major variations, ranging from 20.97 to 26.56ºC, on the other hand, the relative humidity of the air suffered large oscillations from 81.13 to 34.78%. The evaluation time was 26 days and the average temperature recorded at the end of the experiment was 24.02ºC. The artificially cooled aeration system worked correctly, reducing the temperature of the aeration air, but only with one compressor it showed low efficiency.

Keywords: Vortex tube. Arduino. Grain storage. Temperature. *Zea mays*.

[1] MSc. in Agricultural Engineering
State University of Goiás
Anápolis,Goiás,Brazil
E-mail: felipedouradoeng@outook.com
[2] Post-doctorate in Agricultural Engineering
Federal University of Viçosa
Anápolis,Goiás,Brazil
E-mail: devilla@ueg.br
[3] MSc in Agricultural Engineering
State University of Goiás
Anápolis,Goiás,Brazil
E-mail: antonio.cruvinel@ueg.br

INTRODUCTION

Food production in Brazil, especially grains such as corn, wheat, soybeans, and barley, had high growth rates, resulting from modernization and agricultural technologies (BARONI et al., 2017).

The grains produced, after going through the cleaning and drying processes, are stored so that they can be used later. Storage is a process that is based on gathering and storing a certain volume of product for a prolonged period, in order to preserve the quality and primary characteristics of the grains, avoiding fungi, pests and excessive moisture (MOHAPATRA et al., 2017; NEME and MOHAMMED, 2017; MUTUNGI et al., 2019)

Temperature and relative humidity are the main factors that can interfere with grain quality during the storage period (BORÉM et al., 2019). The reduction in grain temperature slows down the speed of biochemical and metabolic reactions (PARAGINSKI et al., 2014). According to Ziegler et al. (2016), for grains stored at a temperature of 15 ºC, there is a purge effect, controlling insect infestation.

Aeration is the most widespread and used preventive control method in the preservation of stored grains. This method consists of the forced passage of ambient air through the grain mass, in such a way as to modify the intergranular microclimate, creating unfavorable conditions for the development of organisms that influence the preservation of grain quality (LOPES AND STEIDLE, 2019). Another technique used to maintain the quality of the stored grains is artificial cooling, which consists of reducing the temperature inside warehouses and/or vertical silos. Cooling allows air exchanges between the environment and the interior of the grain mass, and cold air is blown into the silo, which remains in operation until the desired temperature of the grain mass.

Reducing the temperature to refrigeration levels can be a promising technology in maintaining the quality of the grains, delaying the development of insects, pests and the microflora present, regardless of the climatic conditions of the region (Demito and Afonso, 2009). Rigueira et al. (2009) pointed out that storing production in systems where the temperature is reduced is an effective and economical technique for long periods.

In this context, the objective was to build an artificial cooling system for grains stored in metal silos.

MATERIAL AND METHODS

LOCATION AND DESCRIPTION OF THE STUDY AREA

The study was developed at the Laboratory of Drying and Storage of Plant Products, located at the Central Campus of Exact and Technological Sciences Henrique Santilo, of the State University of Goiás, in Anápolis-GO.

CHARACTERIZATION OF THE EQUIPMENT THAT MAKES UP THE ARTIFICIAL COOLING SYSTEM

Prototype Silo

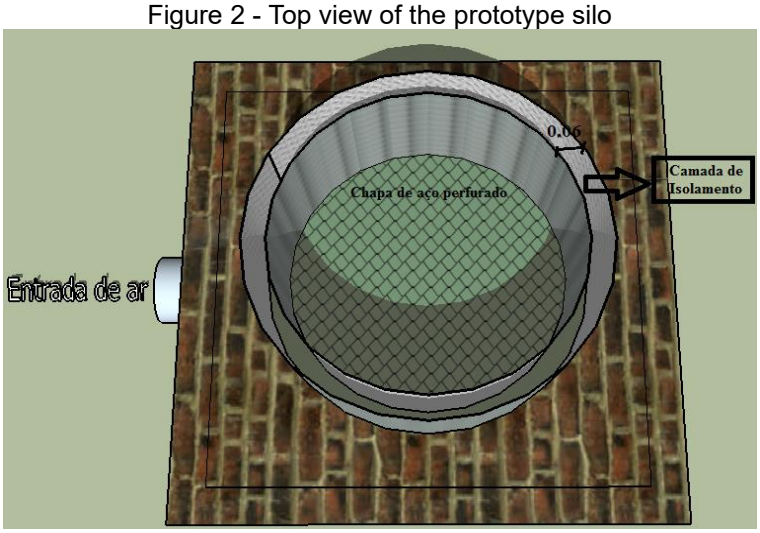
A cylindrical metal silo was used, with dimensions of 0.9 m in diameter and 3 m in height, with capacity to store 1500 kg of corn grains, with a specific weight of 750 kg $^{m-3}$. A masonry plannum was built to allow air to enter the silo, with dimensions of 1.2 m in diameter and 0.3 m in height, as illustrated in Figure 1.

On the external surface of the silo, thermal insulation was inserted, consisting of a layer of glass wool, 0.06 m thick (Figure 2), in order to minimize the heating of the grains from the conditions of the environment outside the silo. In the lower part of the silo, perforated steel plates with sieves with a diameter of 0.006 m were installed to allow the passage of air through the grain mass, Figure 2.

Figure 1 - Prototype silo used to evaluate the artificial cooling system

Source: AUTHOR

Figure 2 - Top view of the prototype silo



Source: ANTUNES (2016)

Fan

A radial blade centrifugal fan, built in sheet metal, was used, Figure 3. The air flow rate provided by the fan was 6 m^3 min^{-1} and the static pressure was 35 mmCA m^{-1}. The high-speed 1 hp three-phase motor was used to drive the radial blades.

Figure 3 - Centrifugal fan with radial blades used to blow air into the silo

Source: AUTHOR

Frequency Inverter

The PowerFlex4 frequency inverter, Figure 4, was used to regulate the rotation of the fan rotor, aiming to achieve an aeration air flow of 0.15 m^3 min^{-1}, so the frequency used in the inverter was 7.2 hertz.

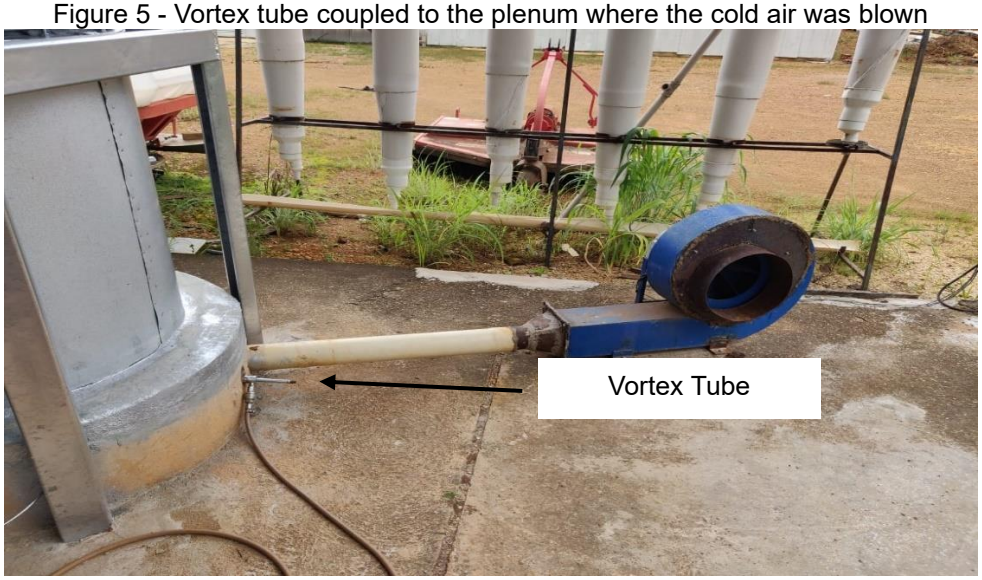
Figure 4 - Frequency inverter used to regulate the rotation of the fan rotor

Source: AUTHOR

Vortex Tube

The small vortex tube of the EXAIR brand, model 3230, was used to provide artificial cooling. The air temperatures generated by the vortex tube were from -1 to 56 ºC, and with a maximum flow rate of 0.6 $m^{3}min^{-1}$. These temperature variations depend on the size of the pipe and the power of the compressor used. The vortex tube was coupled to the side of the silo plenum as shown in Figure 5, where the cold air was blown away.

Figure 5 - Vortex tube coupled to the plenum where the cold air was blown



Source: AUTHOR.

Compressor

A Pressure compressor, Figure 6, was used, with the following characteristics: operating pressure: Maximum 175 lbf $^{in-2}$ (12.07 bar); reservoir volume: 250 L; flow rate: 20 pcm (0.6 $m^{3}/^{min-1}$); and motor power: 5 hp three-phase.

Figure 6 - Compressor used to supply compressed air to the vortex tube

Source: AUTHOR.

PRELIMINARY PROCEDURE FOR ARTIFICIALLY COOLED AERATION

In the artificially cooled aeration system, the vortex tube was activated 15 minutes before turning on the fan, so that the temperature of the air blown by the fan in the silo was lower than the temperature of the ambient air. After the plenum cooling period, the artificially cooled aeration system fan was activated. The system was turned on daily at 7 p.m., and turned off at 8 a.m

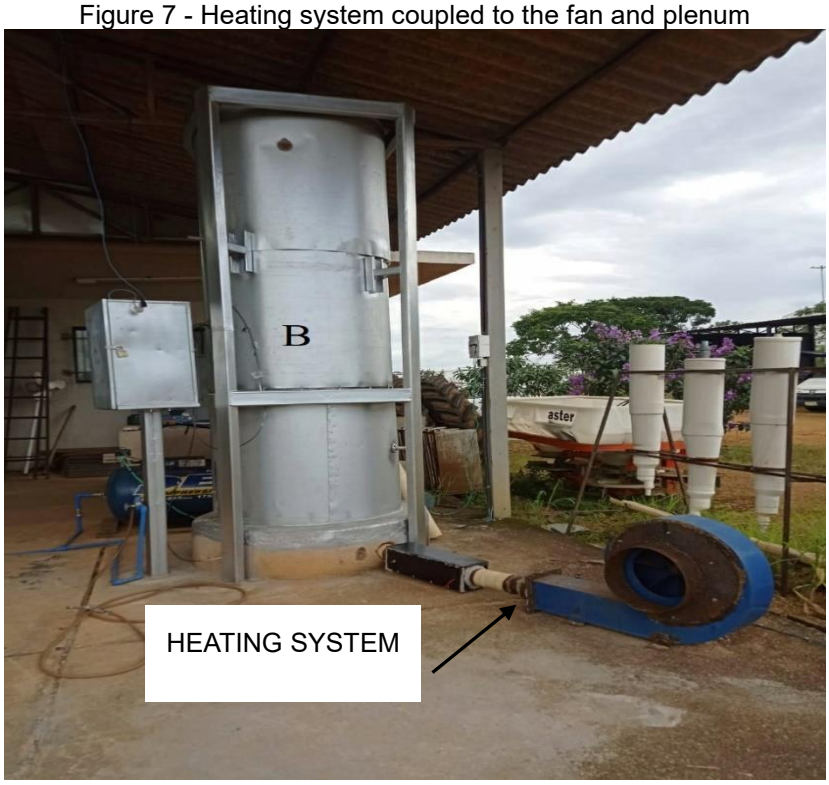
HEATING SYSTEM

An air heating device was developed to heat the stored grains to a temperature of 30 ºC. Grain heating is necessary to simulate the real condition of the grain outlet temperature of a commercial dryer (LAWRENCE and MAIER, 2011).

The device for heating the grain mass was built with metallic material, with dimensions of 0.5 x 0.16 x 0.15 m. Inside the device, two resistors (type U) were placed, with dimensions of 0.45 x 0.06 m and powers of 2 and 1 Kw.

The heating system was coupled to the fan and the planum of the silo, Figure 7. The tests with artificially cooled aeration began when the entire grain mass had reached 30 ºC. To monitor the heating process, a temperature sensor was installed inside the planum.

Figure 7 - Heating system coupled to the fan and plenum



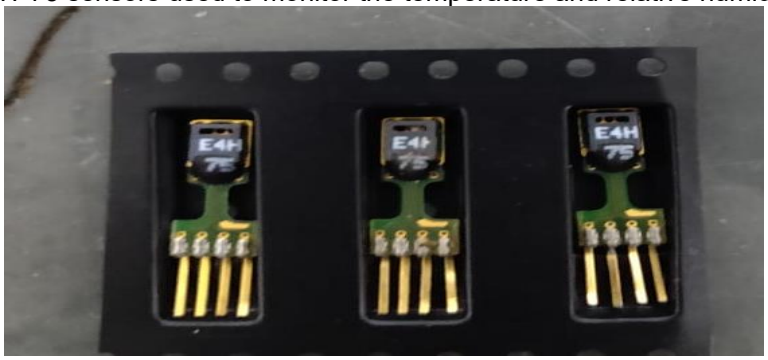
Source: AUTHOR

CHARACTERIZATION OF THE CONTROL OF THE AERATION SYSTEM

Sensors

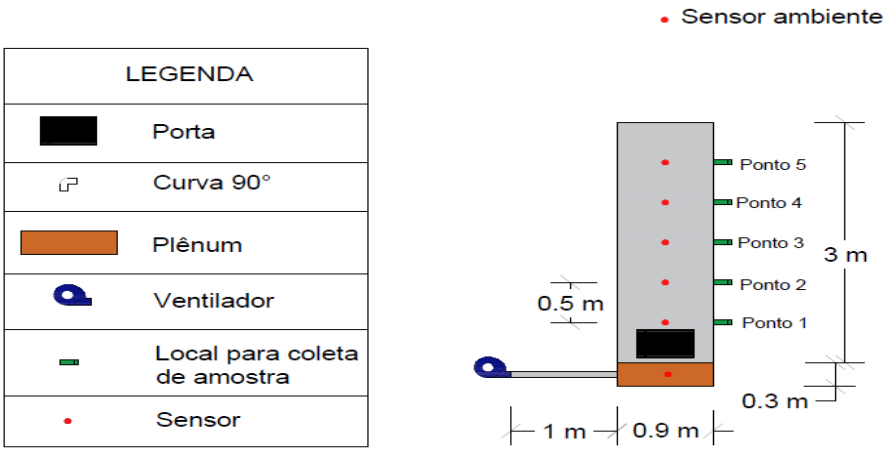
The sensor selected to monitor interstitial air temperature and humidity was the SHT 75 model, Figure 8, of the Sensirion family. The temperature reading range is from -40 to 123.8 ºC with an accuracy of 0.4 ºC. Relative humidity can vary from 0 to 100% with an accuracy of 1.8%. A total of 7 sensors were used, which were distributed: 5 sensors in the silo, spaced 0.5m apart in the grain mass; 1 sensor on the plenum; and 1 for environmental parameters, positioned in a place outside the grain mass, Figure 9.

Figure 8 - SHT 75 sensors used to monitor the temperature and relative humidity of the silo



Source: AUTHOR

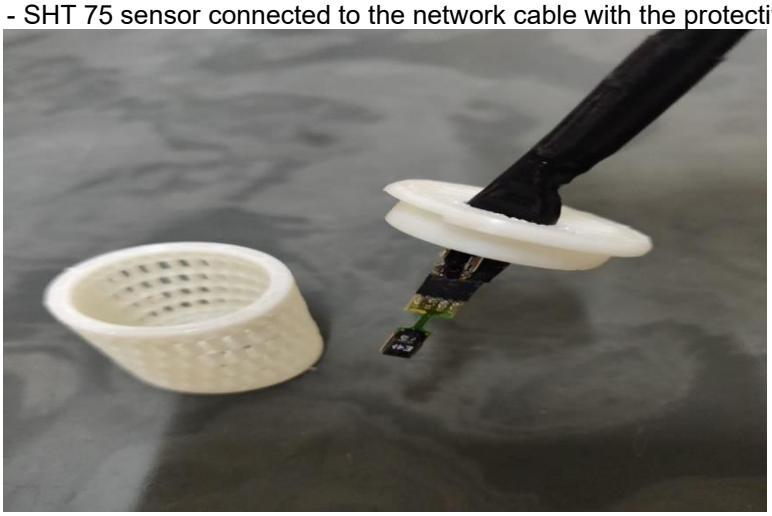
Figure 9 - Schematic of the prototype silo with the sensors arranged in the center



Source: AUTHOR

All sensors were connected to a Cat5 network cable, eight ways and shielded to prevent electromagnetic interference. In order for the sensors not to be in direct contact with the corn, a protection device, Figure 10, was plotted on a 3D printer. The device had the following dimensions: 0.035 m high and 0.03 m in diameter, with rectangular screens 0.001 m high and 0.0005 m wide, and with a lid of 0.03 m in diameter.

Figure 10 - SHT 75 sensor connected to the network cable with the protective device



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Arduino Microcontroller

The Arduino microcontroller was used, because its programming is simple, easy to acquire and met the hardware requirements for the execution of the project. The microcontroller is responsible for intermediating in the system, where it receives information on the temperature and relative humidity parameters and sends it to a microcomputer that presents the information to the user

The Arduino model chosen was the UNO, Figure 11 which has a serial communication channel, 13 digital input and output ports, 6 analog ports and an ATMEGA 328P processor. 1 Arduino board was used for the silo and one for the environmental parameters.

Figure 11 - Arduino Uno used in data acquisition

Source: AUTHOR

Xbee Modules

The Xbee modules were used for wireless communication with the Arduino board installed in the silo. The Xbee module model chosen was S2,

Figure 12, with a communication frequency of 2.4GHZ. Two modules were used, one connected to the Arduino and the other in the microcomputer used to store the data.

Figure 12 - Xbee communication module used in Arduino

Source: AUTHOR

DATA ACQUISITION SYSTEM

In the data acquisition system, the algorithm was developed using the standard libraries, made available by the Arduino software (MCROBERTS, 2011). To present in real time the values of temperature, relative humidity, another system was developed based on

the PHP programming language, where the data was collected and stored every ten minutes.

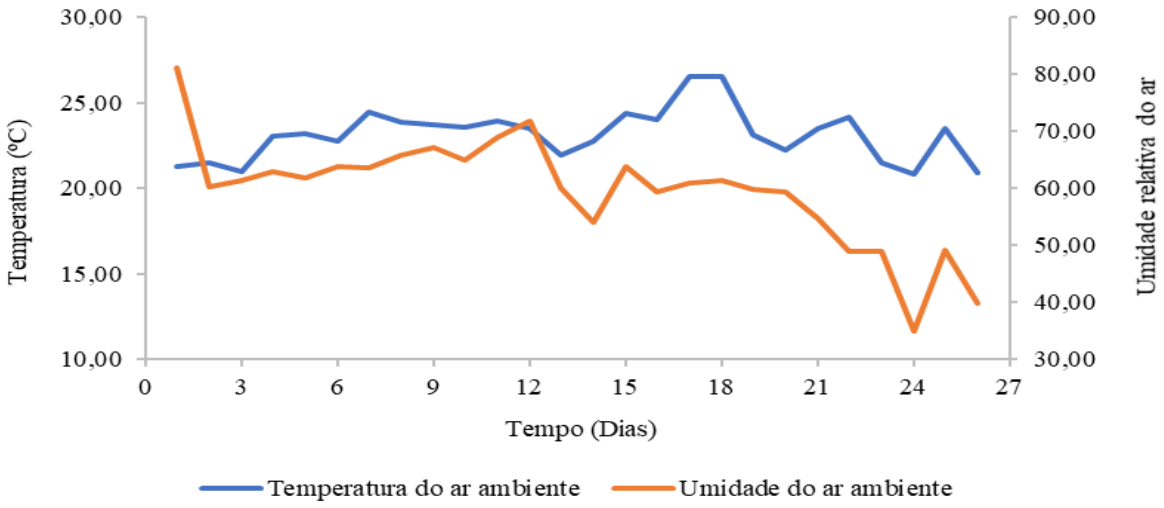
RESULTS AND DISCUSSION

AMBIENT TEMPERATURE AND AIR CONDITIONS DURING ASSESSMENTS

The temperature and relative humidity conditions during the evaluation period (January 14 to February 9, 2021) of the artificially cooled aeration system portray the transition from the rainy season to the dry season, characteristic of the city of Anápolis-GO.

It was noted that during the period of evaluation of the system the air temperature did not suffer major variations, Figure 13, ranging from 20.97 to 26.56 ºC. On the other hand, the data collected on the relative humidity of the air during the 26 days of evaluation varied from 81.13 to 34.78 %, following the characteristic period of the region. According to Lopes et al. (2015), these oscillations in the relative humidity of the air show that the stored grains need efficient control in the aeration process.

Figure 13 - Daily average temperature and relative humidity

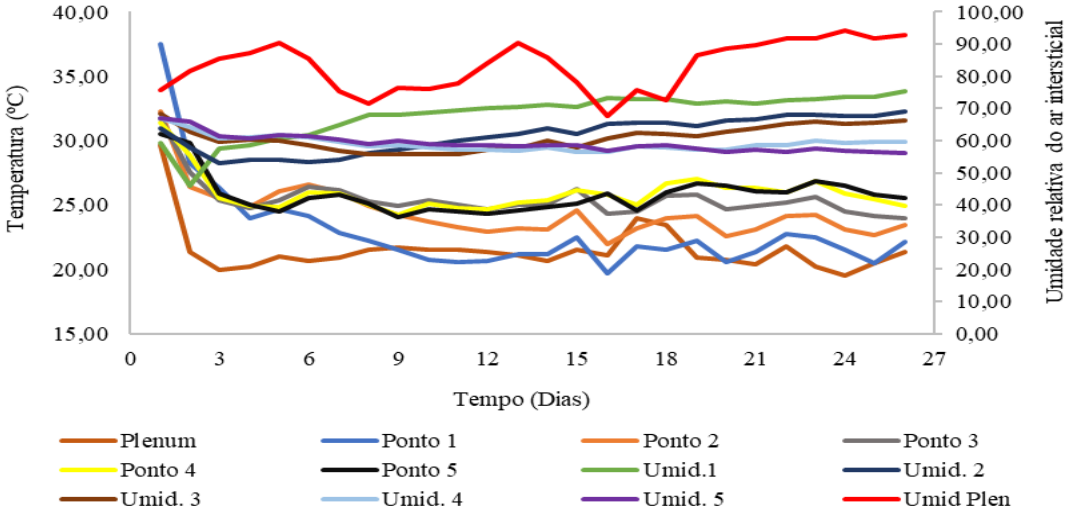


Source: AUTHOR

COOLING FRONT

The temperature variation of the grains stored during the evaluation period of the artificially cooled aeration system, at the 5 points of the silo, is represented in Figure 14.

Figure 14 - Variation in temperature and humidity of the interstitial air of the grain mass at points (1, 2, 3, 4, 5 and Plenum)



Source: AUTHOR.

The average temperature of the grain mass was higher than expected, and was due to the action of insects. According to Antunes et al. (2011), insects provide a warmth in the grain mass, by increasing the metabolic activity and respiration rate of the stored grains.

When there is a reduction in temperature in the grain mass, it can be said that the aeration was satisfactory; And when the temperature of the whole silo is reduced, it can be inferred that the cooling front has reached the top silo. According to Figure 14, it is possible to notice the cooling front, the temperature reduction in the grain mass occurred in the vertical direction, in the upward direction in the silo. The cooling in the grain mass was more intense at points 1 and 2. From point 3 onwards, the process of temperature reduction was slower. It was noted that during the evaluation process of the artificially cooled aeration system, the lowest temperatures recorded were at points 1 and 2, of 19.66 and 21.92 ºC respectively.

It was found that in points 3, 4 and 5 the lowest temperatures were recorded on the last day of evaluation, 23.98; 24.94 and 25.54 ºC, respectively. According to Quirino et al. (2013), the upper layers of the silos are more influenced by the storage environment than the lower layers, thus taking longer for their cooling.

Regarding the temperature of the plenum, it was noted that when activating the vortex tube, the temperature difference between the plenum and the ambient air temperature was 4 ºC, and when turning on the fan, this difference reduced to 2 ºC. This increase in temperature was generated due to the higher temperature of the ambient air, which was inflated in the plenum.

In order for the vortex tube to work efficiently, the air inlet pressure must be 7 bar constantly. Whang et al (2009) used the inlet pressure of 7 bar and obtained the best

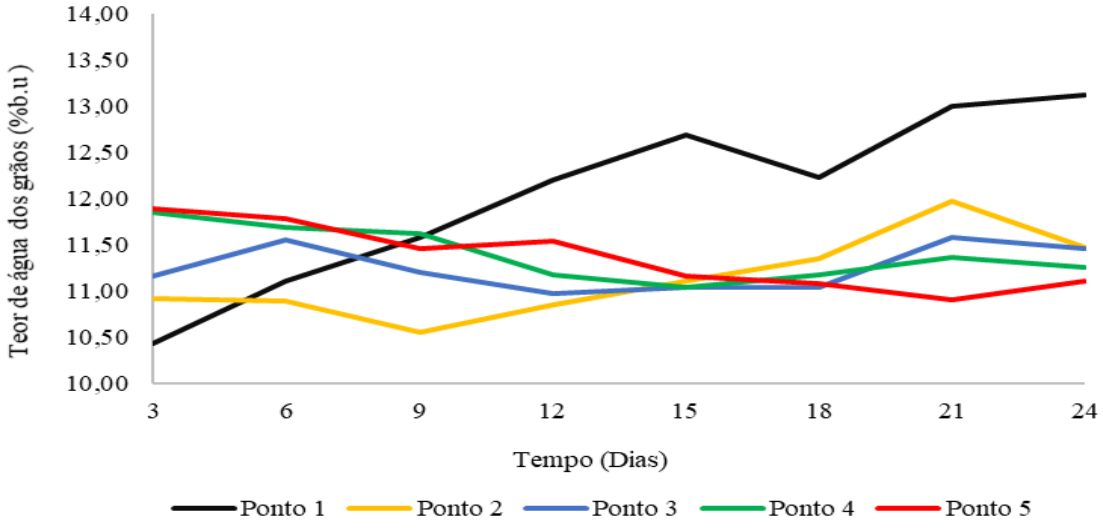
cooling effect. In the tests to start the evaluations of the systems, two compressors were used, connected in parallel, which maintained the inlet pressure at 7 bar. But on the first day of the experiment, one of the compressors broke down. Thus, during the remaining days of the experiment, the artificially cooled aeration system worked only with a compressor, which maintained the inlet pressure of 4 bar, reducing the efficiency of the system.

In the relative humidity of the interstitial air, it is noted that in point 1, there was a reduction from 59.28% to 45.95% from the first to the second day of evaluation. The reduction in the relative humidity of the interstitial air was promoted by heating the grain mass before starting the evaluation of the system. It is observed that the temperature on the first day of evaluation at point 1 of the silo is higher than the other points, causing air drying.

WATER CONTENT OF GRAINS

The evolution of the water content in % b.u in the grain mass is shown in Figure 15 for the five monitored points. The variation of the water content in the grain mass occurred throughout the evaluation period due to the hygroscopicity of the grains. The variation occurred until the grains reached the water content of equilibrium with the environment. It was observed that this variation occurred both by the interference of external factors, such as the relative humidity of the air and temperature of the aeration air and by the humidity of the interstitial air of the plenum.

Figure 15 - Variation of the water content in % b.u of the grain mass at points (1, 2, 3, 4, 5) in the silo



Source: AUTHOR

The initial average water content of the grain mass was 11.25±0.63 % b.u. It was verified that at all points, the water content of the grains remained below 12% b.u., ensuring

good storage. According to Coradi and Lemes (2019), the physicochemical and microbiological qualities are directly linked to the water content of the grains, so the lower the quality of the stored grains. In addition, Bessa et al. (2015) concluded that grains stored for six and eight months should be kept with a water content of 10 to 12 % b.u.

It was noted that in the grain layer of point 1, there was greater drying in relation to the others, which can be explained by the heating done before starting the evaluation of the aeration systems.

It was also found that the grains in point 1 suffered an increase in water content that exceeded the recommended limit for safe storage, which according to Chigoverah and Mvumi (2016) is up to 12.5% b.u for corn grains in non-hermetic storage. The final water content of the grains at point 1 was 13.12±0.02 % b.u. It is verified that this variation in the water content of the grains at point 1 occurred due to the migration of moisture from the interstitial air from the plenum to the grain mass and by the infestation of insects that were in higher concentration at this point. Authors such as Antunes et al. (2011) and Pinto et al. (2002) observed that insect infestation results in an increase in the water content of stored grains by 3.6 percentage points in 90 days of storage; This increase is due to the metabolism of the insects and the respiration of the grains.

In point 2, it was noted that from the sixth day to the ninth day of the experiment the water content of the grains decreased. On the twelfth day, the grains reached hygroscopic equilibrium. However, on the last day of evaluation, the moisture content of the grains rose to 11.47±0.14 % b.u.

In points 3 and 4, it was observed that the water content of the grains entered equilibrium on the twelfth day and increased on the twenty-first day. In the last evaluation, the water content was 11.45±0.11 for point 3 and 11.26±0.26 % b.u for point 4. However, for point 5, the grains had a water content close to 12% b.u and ended the experiment with 11.72 % b.u.

It was found that the grain mass at points 2, 3, 4 and 5 remained with water content below 12.5 % b.u., which is the safe moisture for the storage of corn grains.

CONCLUSION

According to the results obtained and the conditions in which this work was developed, it can be concluded that:

1. The average temperature at the end of the silo evaluation was 24.02 ºC.

2. The artificially cooled aeration system using the vortex tube as a tool for cooling the air worked correctly, lowering the temperature of the aeration air, but only with a compressor it proved to have low efficiency.
3. The computer system for the acquisition of temperature and relative humidity data in grain storage, using Arduino, collected the data efficiently.
4. As future works, it is proposed to use two compressors that could maintain an air inlet pressure of 7 bar constantly, so that the proposed system is efficient. Investigate the use of a screw compressor in the efficiency of the cooling system. Another point to be improved would be automation in the activation of the aeration system.

REFERENCES

1. ANTUNES, L. E. G., VIEBRANTZ, P. C., GOTTARDI, R., & DIONELLO, R. (2011). Características físico-químicas de grãos de milho atacados por *Sitophilus zeamais* durante o armazenamento. *Revista Brasileira de Engenharia Agrícola e Ambiental*, *15*(6), 615-620.

2. BARONI, G. D., BENEDETI, P. H., & SEIDEL, D. J. (2017). Cenários prospectivos da produção e armazenagem de grãos no Brasil. *Revista Thema*, *14*(4), 55-64.

3. BESSA, J. F. V., DONADON, J. R., RESENDE, O., ALVES, R. M. V., SALES, J. D. E. F., & COSTA, L. M. (2015). Armazenamento do crambe em diferentes embalagens e ambientes: Parte I - Qualidade fisiológica. *Revista Brasileira de Engenharia Agrícola e Ambiental*, *19*(3), 224-230.

4. BORÉM, F. M., RIBEIRO, F. C., FIGUEIREDO, L. P., GIOMO, G. S., SIQUEIRA, C., & DIAS, C. A. (2019). Sensory analysis and fatty acid profile of specialty coffees stored in different packages. *Journal of Food Science and Technology*, *56*(9), 4101–4109.

5. BURKOT, R. C. (2014). A qualidade desejada na secagem e armazenagem de grãos em uma cooperativa no município de Ponta Grossa – PR. *Revista de Gestão e Organizações Cooperativas*, *1*, 39–50.

6. BRASIL. Ministério da Agricultura e Reforma Agrária. (2009). *Regras para análise de sementes*. Brasília, DF: 399 p.

7. CHIGOVERAH, A. A., & MVUMI, B. M. (2016). Efficacy of metal silos and hermetic bags against stored-maize insect pests under simulated smallholder farmer conditions. *Journal of Stored Products Research*, *69*, 179-189.

8. COMPANHIA NACIONAL DE ABASTECIMENTO – CONAB. Capacidades estáticas de armazéns cadastrados por U.F. Disponível em: <http://www.conab.gov.br>. Acesso em 20 dezembro 2023.

9. COMPANHIA NACIONAL DE ABASTECIMENTO - CONAB. Acompanhamento da safra brasileira: Grãos, Safra 2023/24 – 7º levantamento. Disponível em: <https://www.conab.gov.br/info-agro/safras/graos>. Acesso em 10 maio 2024.

10. CORADI, P. C., & LEMES, A. F. C. (2018). Silo-secador-aerador experimental para armazenagem de grãos de soja. *Revista Brasileira de Engenharia Agrícola e Ambiental*, *22*(4), 279-285.

11. DEMITO, A., & AFONSO, A. D. L. (2009). Qualidade das sementes de soja resfriadas artificialmente. *Engenharia na Agricultura*, *17*(4), 7-14.

12. HAMMER, O., HARPER, D. A. T., & RYAN, P. D. (2001). Past: Paleontological statistics software packaged for education and data analysis (Version 1.94b). *Palaeontologia Electronica*, *4*(1), 1–9.

13. INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA – IBGE. Pesquisa de Estoques – 1º semestre de 2023. Disponível em: <https://agenciadenoticias.ibge.gov.br/media/com_mediaibge/arquivos/a689f28e65e55fe7c7ef82a33394c097.pdf>. Acesso em 16 janeiro 2024.

14. LAWRENCE, J., & MAIER, D. E. (2011). Aeration strategy simulations for wheat storage in the sub-tropical region of north India. *Transaction of the ASABE*, *54*, 1395-1405.

15. LOPES, D. C., NETO, A. J. S., & JÚNIOR, R. V. (2015). Comparison of equilibrium models for grain aeration. *Journal of Stored Products Research*, *60*, 11-18.

16. LOPES, D. C., & STEIDLE, N. A. J. (2019). Effects of climate change on the aeration of stored beans in Minas Gerais State, Brazil. *Biosystems Engineering*, *188*, 155-164.

17. LUIZ, M. R. (2012). *Estudo teórico e experimental de secagem de tomate (Lycopersicon esculentum)* (Tese de doutorado). Universidade Federal da Paraíba, João Pessoa.

18. CROBERTS, M. (2011). *Arduino Básico*. São Paulo: Novatec.

19. MOHAPATRA, D., KUMAR, S., KOTWALIWALE, N., & SINGH, K. K. (2017). Critical factors responsible for fungi growth in stored food grains and non-chemical approaches for their control. *Industrial Crops and Products*, *108*, 162-182.

20. MUTUNGI, C., MUTHONI, F., BEKUNDA, M., GASPAR, A., KABULA, E., & ABASS, A. (2019). Physical quality of maize grain harvested and stored by smallholder farmers in the Northern Highlands of Tanzania: Effects of harvesting and pre-storage handling practices in two marginally contrasting agro-locations. *Journal of Stored Products Research*, *84*, 101517.

21. NEME, K., & MOHAMMED, A. (2017). Mycotoxin occurrence in grains and the role of postharvest management as mitigation strategies: A review. *Food Control*, *78*, 412-425.

22. OLIVEIRA, V. R., RIBEIRO, N. D., MAZIERO, S. M., FILHO, A. C., & JOST, E. (2011). Qualidade para o cozimento e composição nutricional de genótipos de feijão com e sem armazenamento sob refrigeração. *Ciência Rural*, *41*(5), 746-752.

23. PARAGINSKI, R. T., VANIER, N. L., BERRIOS, J. J., OLIVEIRA, M., & ELIAS, M. C. (2014). Physicochemical and pasting properties of maize as affected by storage temperature. *Journal of Stored Products Research*, *49*, 209-214.

24. PATWARI, A. U., HABIB, M. A., CHOWDHURY, S. I., & AKRAM, R. H. (2015). Thermal investigation of vortex generated green coolant on surface texture for drilling process. *Procedia Engineering*, *105*, 808-813.

25. PARK, C. E., KIM, Y. S., PARK, K. J., & KIM, B. K. (2012). Changes in physicochemical characteristics of rice during storage at different temperatures. *Journal of Stored Products Research*, *48*, 25-29.

26. PINTO, U. M., FARONI, L. R. D. A., ALVES, W. M., & SILVA, A. A. L. (2002). Influência da densidade populacional de *Sitophilus zeamais* (Motsch.) sobre a qualidade do trigo destinado à panificação. *Acta Scientiarum*, *24*, 1407-1412.

27. QUIRINO, J. R., MELO, A. P. CAMPOS, VELOSO, V. R. S., ALBERNAZ, K. C., & PEREIRA, J. M. (2013). Resfriamento artificial na conservação da qualidade comercial de grãos de milho armazenados. *Bragantia*, *72*(4), 378-386.

28. RIGUEIRA, R. J. A., LACERDA FILHO, A. F., & VOLK, M. B. S. (2009). Avaliação da qualidade do feijão armazenado em ambiente refrigerado. *Alimentos e Nutrição*, *20*(4), 649-655.

29. SECCHIAROLI, A., RICCI, R., MONTELPARE, S., & D'ALESSANDRO, V. (2009). Numerical simulation of turbulent flow in a Ranque–Hilsch vortex tube. *International Journal of Heat and Mass Transfer*, *52*(24), 5496–5511.

30. SILVA, K. P. (2017). *Efeitos de resfriamento artificial e tempo de armazenamento sobre a qualidade tecnológica e fisiológica de grãos de trigo* (Dissertação de mestrado). Universidade de Passo Fundo, Passo Fundo.

31. ZIEGLER, V., MARINI, L. J., FERREIRA, F. D., BERTINETTI, I. A., SILVA, W. S. V., GOEBEL, J. T. S., & OLIVEIRA, M. (2016). Effects of temperature and moisture during semi-hermetic storage on the quality evaluation parameters of soybean grain and oil. *Semina: Ciências Agrárias*, *37*(1), 131-144.

32. WHANG, Z., TONG, M., & YUAG, R. (2009). Experimental study on channel characteristics and refrigerating effect in vortex tubes. *Journal of Chongqing University*, *32*(8), 971-975.

CANNABIS *SATIVA* L. IN THE UNIFIED HEALTH SYSTEM

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Mary Anne Medeiros Bandeira[1], Nilton Luz Net Junior[2], Júlio César Oliveira Peixe[3], Vivian Saldanha Dalla[4], Helene Frangakis de Amorim[5], Maria Eliane Barreto da Silva[6], Jaqueline Guimarães de Carvalho[7], Roger Remy Dresch[8] and Ely Eduardo Saranz Camargo[9]

ABSTRACT

The use of medicinal plants is as old as the history of humanity, however, with the advancement of technology there was an inertia in the use of plants, that the popular movement caused a real uproar in the race for the increasing use of medicinal plants. In this way, the development of integrative and complementary practices gradually began. Although integrative practices are implemented in the Unified Health System (SUS), it is still not a reality throughout the country, many resistances, lack of information and incentives, make it not a practice offered to the entire Brazilian population. Primary Health Care must be exercised with managerial practices, democratic assistance with popular participation, with this thought the Family Health Program emerged in 1994 and in 2006, it became the Family Health Strategy. In 2010, the Ministry of Health published ordinance 886 that established the Living Pharmacy, which, like its creator, Prof. Francisco José de Abreu Matos, would be an impulse for the Health Secretariats of Brazilian municipalities, however, it is verified that it has not yet become a reality. Currently, the demand for the use of *Cannabis sativa*, the Unified Health System seeks, in a way, a way to meet the needs of Cannabis prescribers. In RDC 18 of 2013, which provides for Good Handling Practices for Medicinal Plants and in PL 399/2015, which provides for the safety and storage of *Cannabis sativa*, several mechanisms have emerged for the insertion of the species in Living Pharmacies. Many advances have been observed in this fight, however, the Ministry of Agriculture, Livestock and Supply must be involved to discuss the insertion of *Cannabis sativa* in family farming.

Keywords: Medicinal Plant. *Cannabis sativa*. Family Farming. Living Pharmacy.

[1] Profa. Dr. Researcher at the Federal University of Ceará. President of ABFV - CE
[2] Master, head of the Living Pharmacy of the Federal District. Technical Director of ABFV - DF
[3] Pharmacist Responsible for the Farmácia Viva de Maracanaú. Treasurer Director of ABFV - CE
[4] Pharmacist Director of the Dalla Institute. Secretary Director of ABFV - SC
[5] Master, coordinator of the Technical Group of the Living Pharmacy of the CRF RJ. Fiscal Council Member of ABFV - RJ
[6] Pharmacist Responsible for the Farmácia Viva de Brejo da Madre de Deus. Fiscal Councilor of ABFV - PE
[7] Specialist Pharmacist. Technical Consultant and Fiscal Councilor of ABFV - MG
[8] Prof. Dr. Researcher and Technical Director of ABFV – RS
[9] Prof. Dr. Researcher at the Estácio University Center of Ji-Paraná. Vice-President of ABFV - RO

INTRODUCTION

PHYTOTHERAPY IN THE UNIFIED HEALTH SYSTEM (SUS)

With the impetus given by popular movements, reports from numerous national and international conferences and the recommendations of the World Health Organization (WHO), there was the insertion of practices related to the use of medicinal plants and herbal medicines in the public health scenario in Brazil, especially Primary Health Care services.

This gradual inclusion of integrative and complementary practices, initially with community experiences and non-governmental organizations, at the municipal and state levels and later in public health systems, has been promoted by the WHO since 1970 and several countries have developed public policies to integrate these practices into Primary Health Care, as is the case of Brazil with the National Policy of Integrative and Complementary Practices.

Despite the importance of traditional medicine, it is verified that the use of medicinal plants and herbal medicines in public health services, even those included in PHC, is not yet a national reality. This data can be justified by the scarcity of scientific studies on native species or the lack of systematization of research already carried out.

Primary Health Care (PHC) can be characterized by a set of health actions, in the individual and collective fields, including diagnosis, treatment, promotion, protection, rehabilitation, and health maintenance. It must be developed through the use of democratic and participatory management and care practices, with teamwork, directed to specific populations, in well-defined territories, for which health responsibility is given. Its practice considers the subject in his individuality and in his sociocultural reality and seeks to reduce damages that may impair his ability to live in the healthiest way possible.

Inserted in Primary Health Care, the Family Health Program (PSF) was created in 1994 by the Ministry of Health, with the objective of reorganizing care practices, focusing on the family understood and perceived based on its physical and social environment. Based on this conception, the FHP teams have an expanded understanding of health with practices that go beyond the curative perspective, expanding health promotion, prevention and rehabilitation. In this model of care, there is the assumption of valuing health practices that go beyond biomedical practices.

In 2006, the government launched Ordinance No. 648, of March 28, 2006, which changed the status of the PSF from a program to a permanent strategy of Primary Health Care, becoming known as the Family Health Strategy, since the program has a fixed time and the strategy is permanent and continuous.

The multiprofessional teams (doctor, nurse, dentist, nursing technician or assistant, oral health technician or assistant, and community health agents – CHA) that work in the ESF enable comprehensive and multidisciplinary care for the enrolled population. These teams are responsible for monitoring the health situation of a certain number of people and families who live or work in the territory close to the health unit, allowing the establishment of bonds, commitment and co-responsibility between the health professionals who work in the FHS and the population.

The Living Pharmacy Program has a great impact within the Family Health Strategy, as this program proposes to promote health considering the reality of life of the community in its various aspects, and in this reality, it finds the medicinal plants inserted in the family's health care even before seeking the health unit and the doctor. The Living Pharmacies program, in this context, is a health tool as it offers safe and scientifically validated medicinal plants with guidance on cultivation, preparation and use techniques.

Medicinal plants represent important savings for the Public Health System because they are cheaper and, if used correctly, also represent a lower risk of adverse events related to the medication. This happens because Live Pharmacies produce the herbal medicine using the active ingredient still in the plant and its extracts, unlike the pharmaceutical industry, which performs sophisticated procedures for the isolation of the active ingredient or imports it into other countries, which makes the procedure time-consuming and expensive.

In this way, Live Pharmacies can be used in public health services as a way to ensure safe medicines, with good acceptance by the community, as they already empirically know the benefits of the plant that gave rise to the medicine, and cheaper for managers, especially small municipalities, which suffer from the shortage of pharmaceutical services (LEÃO, 2015).

LIVING PHARMACIES: *CANNABIS SATIVA* L. NO SUS

The demand for patients in continuous treatment with *Cannabis* in Brazil is growing and these patients face many steps and bureaucratic challenges to get the medication, which has given visibility to the urgency of regulating the national production of this species, for the public health network. Thus, as the State is responsible for guaranteeing the right to health of the Brazilian population, the production and distribution of cannabis-based medicines through Live Pharmacies can be a viable alternative, promoting access in line with the fundamental principles of the SUS.

Initially, for a better understanding of the present proposal for the inclusion of *Cannabis sativa* L. in Live Pharmacies, it is important to know what they are and their models in order to adapt this proposal to an achievable reality.

LIVE PHARMACIES

The historical milestone in the development of Phytotherapy in Brazil was the creation of the Living Pharmacies, a social program based on the scientific use of medicinal plants and herbal medicines, idealized by Professor Francisco José de Abreu Matos in 1983, under the influence of the principles of the World Health Organization (WHO). At the time, this notable pharmacist and researcher from Ceará, knowing that more than 20 million people in the Northeast were outside the primary health care system, in addition to other regions of Brazil, who had as their only treatment option the medicinal plants available in the environment where they lived, asked:

I. What are the plants used in folk medicine?

II. How is it possible to select them by the healing activities assigned by the people? Which ones can be used without risk to health and life?

III. How can the plant selected according to the criteria of efficacy and safety reach the people and be used correctly, without encouraging self-diagnosis and self-medication?

It was seeking answers to these questions that Prof. Francisco José de Abreu Matos idealized the Living Pharmacies to bring medicinal plants and herbal medicines to communities with proven therapeutic efficacy and safety, defined as follows:

"*LIVING PHARMACIES are pharmaceutical units installed in governmental or non-governmental communities, where their users receive medication prepared with plants that have had confirmation of the activity attributed to them, harvested in the gardens themselves, which allow their users access to a list of truly medicinal plants and their products" (F. J. A. Matos).*

LIVING PHARMACY MODELS

The Farmácias Vivas aims to offer, on a non-profit basis, herbal pharmaceutical assistance to communities through the promotion of the correct use of plants of local or regional occurrence endowed with scientifically proven therapeutic activities.

Based on the types of activities developed, such as cultivation of medicinal plants, pre-processing, preparation of home remedies with medicinal plants and preparation of

herbal medicines, three models of Live Pharmacies are established, according to State Decree / Ceará No. 30016/2009 (Figure 1):

Figure 1 – Representation of the Living Pharmacy Models at the three levels of complexity.

Farmácia-Viva I

This model applies to the installation of medicinal plant gardens in Community Living Pharmacies units and/or SUS units maintained under the supervision of state/municipal public phytotherapy service professionals. The vegetable raw material, processed in accordance with Good Cultivation Practices (GCP), must come from official or accredited gardens and/or gardens. This model aims to carry out cultivation and guarantee the assisted community access to medicinal plants *in natura* and guidance on the preparation and correct use of home remedies, carried out by trained professionals.

Community health agents, rural agents or similar, duly trained and integrated into a Living Pharmacy unit, may participate in the orientation process regarding the correct use of medicinal plants.

Pharmacy-Viva II

It is intended for the production/dispensation of dried medicinal plants (plant drug), intended for the provision of SUS health units. The vegetable raw material, processed in accordance with Good Cultivation Practices (GCP), must come from official or accredited gardens and/or gardens.

The vegetable raw material will be subjected to primary operations, in specific areas, in accordance with Good Processing Practices (GMP).

Farmácia-viva II may also carry out the activities planned for Farmácia-Viva I, in compliance with its technical specifications.

Pharmacy-Viva III

It is intended for the preparation of herbal medicines for the provision of SUS units, in compliance with the specifications of the NUFITO Form. The plant drug for the preparation of these herbal medicines must come from official or accredited gardens and/or gardens, as long as it is processed in accordance with Good Processing Practices (GMP). . Herbal medicines are prepared in specific areas for pharmaceutical operations, in accordance with the Good Practices for the Preparation of Herbal Medicines (GMP), contained in the Regulation.

Model III may also carry out the activities foreseen for models I and II, in compliance with their technical specifications.

The Living Pharmacies, in their three levels of complexity, models I, II and III, must adapt their activities in the most convenient way to the health system in which they are inserted, respecting the limitations of financial, human and logistical resources, making the health of the system user prevail. In practice, there are two operating systems, described below:

These models of Living Pharmacies are adopted by several states in Brazil, although they are not described in RDC No. 18, of April 3, 2013, ANVISA, it is possible to distinguish between the lines models II and III, according to the activities described in this RDC, which deal with obtaining the drug of plant origin and preparing herbal medicines, respectively.

The Living Pharmacies aim to contribute to raising the level of health and quality of life of individuals and the community, integrating their activities with health actions, for the promotion, prevention and recovery of the individual and the community, through the correct and safe use of medicinal plants and herbal medicines. We can highlight the following guidelines:

- Articulate and coordinate Phytotherapy actions;
- Provide cooperation and technical advice to municipalities for the implementation of Live Pharmacies;
- Encourage the development of family farming with medicinal plants;
- Promote ecological educational actions for the conservation of medicinal plants;
- Promote standardization and regulation to promote the rational use of medicinal plants and herbal medicines;
- Ensure the insertion of medicinal plants and herbal medicines in primary health care;
- Establish and define attributions of health professionals and related professionals in the area of phytotherapy;

- Claim from the competent authorities a system of agreement of pharmaceutical inputs for the Municipal Live Pharmacy units;
- Promote educational actions with the community on the correct use of medicinal plants;
- Promote the development and training of health professionals and the like;
- Provide guidance on the correct use of medicinal plants and herbal medicines;
- Develop investigations and research as an instrument for evaluating the quality of herbal medicines;
- Develop pharmacovigilance of herbal medicines and clinical follow-up of patients using herbal medicines;
- Provide an internship field and training of specialized personnel;
- Increase new technologies for the advancements and consolidation of phytotherapy.

POLITICAL AND TECHNICAL GUIDELINES FOR THE VIABILITY OF LIVE PHARMACIES

The National Policy on Medicinal Plants and Herbal Medicines, instituted by Presidential Decree No. 5,813 of June 22, 2006, aims to guarantee the Brazilian population safe access and rational use of medicinal plants and herbal medicines.

The Ministry of Health, through Ordinance No. 886, of April 20, 2010, established the Living Pharmacy within the scope of the Unified Health System (SUS). This Ordinance considers Living Pharmacies to be those that carry out the stages of cultivation, collection, processing, storage of medicinal plants, preparation and dispensation of magistral and officinal products of medicinal plants and herbal medicines.

The Living Pharmacies was established by the Ministry of Health through Ordinance 886/2010, which was revoked by Consolidation Ordinance No. 5 of September 28, 2017:

The Living Pharmacy in the context of the National Policy of Pharmaceutical Assistance must carry out all stages, from the cultivation, collection, processing, storage of medicinal plants, manipulation and dispensation of magistral and officinal preparations of medicinal plants and herbal medicines. Emphasizing that the commercialization of medicinal plants and herbal medicines is prohibited.

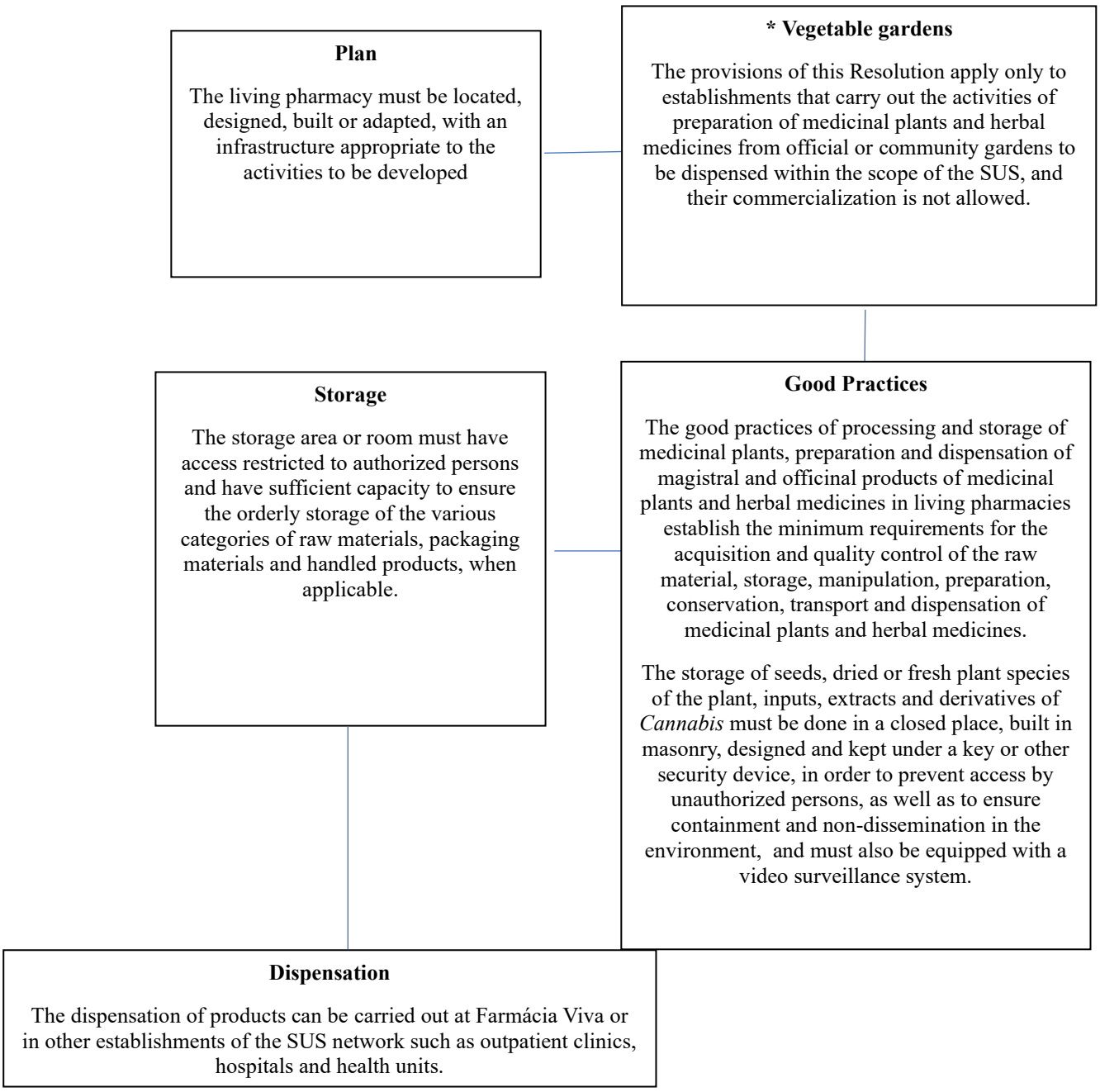
In this context, the National Health Surveillance Agency (ANVISA) approved Resolution – RDC No. 18, of April 3, 2013, which provides for good practices for processing and storage of medicinal plants, preparation and dispensation of magistral and officinal products of medicinal plants and herbal medicines in Living Pharmacies within the scope of the Unified Health System, as demonstrated in Scheme 1.

It is important to note that this ANVISA resolution compared to the proposal of Bill No. 399/2015, still on the agenda for approval by the Federal Chamber, which regulates the planting of marijuana, called *Cannabis sativa*, for medicinal purposes, in technical-scientific terms are convergent, but diverge mainly in the limitation of the planting of *Cannabis* which, in this should be equipped with a video surveillance system at all entry points, with access restriction and an alarm and security system, which does not currently occur with the medicinal plants of Farmácias Vivas.

Also, while RDC No. 18/2013 prohibits the sale of medicinal plants and herbal medicines in Farmácia Viva, the proposal of Bill No. 399/2015 allows the sale of medicines that contain extracts, substrates or parts of the plant, with proof of tests that validate the levels of the main cannabinoids present in their formula, including, minimally cannabidiol (CBD) and *delta-9-tetrahydrocannabinol (Δ9-THC*).

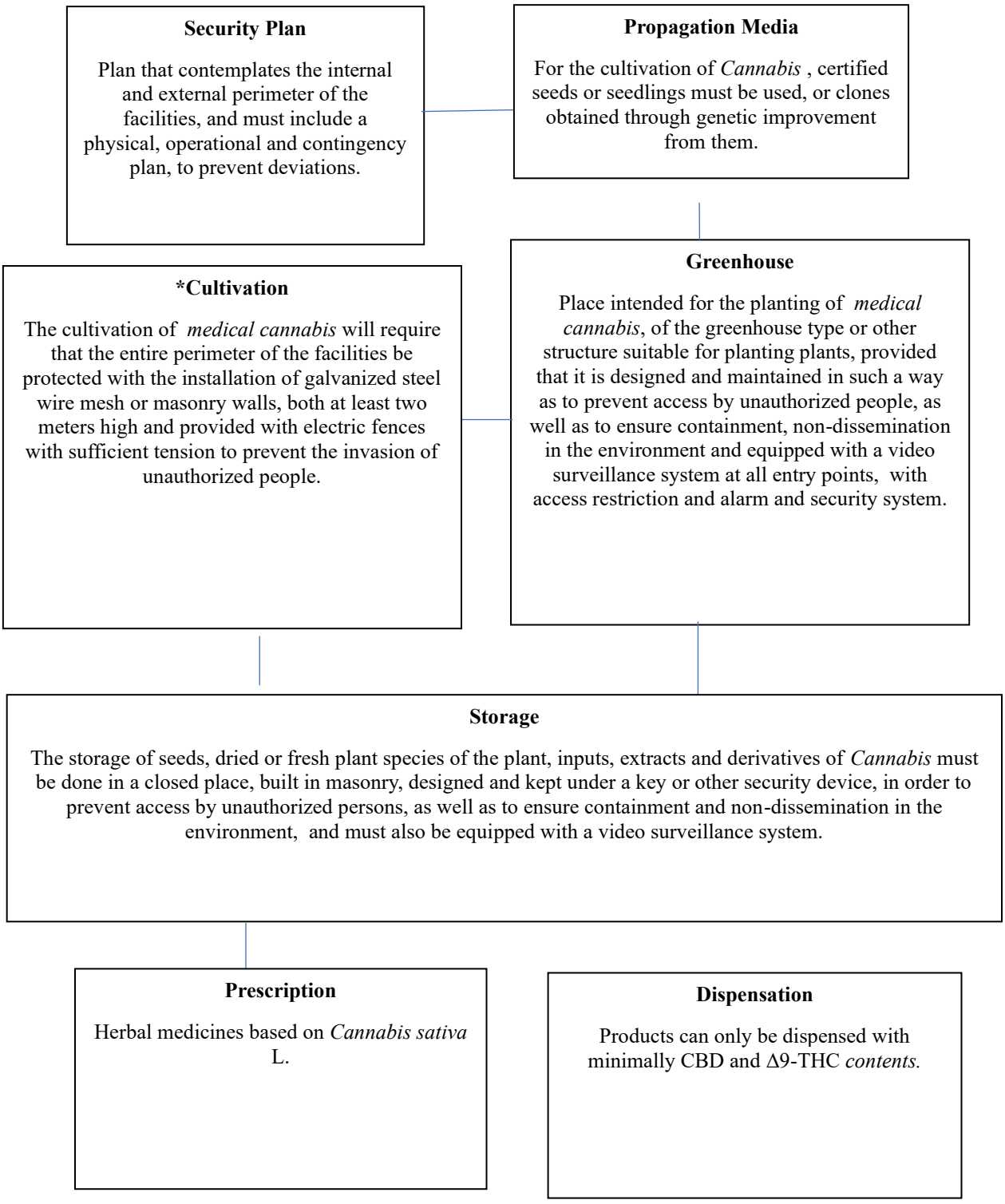
For a better understanding of the aforementioned convergences and differences, by way of comparison, the main recommendations of RDC No. 18/2013 are described in Scheme 1, which determine the minimum requirements required for the exercise of the activities of preparation of medicinal plants and herbal medicines in living pharmacies, while in Scheme 2 the main recommendations of the proposal of PL 399/2015 are described, understanding the security plan for the storage of *medical cannabis*.

Scheme 1 - Main recommendations of RDC 18/2013- ANVISA



(*) If necessary, raw materials of plant origin can be purchased from qualified suppliers.

Scheme 2 - Main recommendations of the Proposal of PL 399/2015



(*) The bill also establishes that the cultivation of *Cannabis* plants for medicinal purposes will be done exclusively by a legal entity, "previously authorized by the government".

PROPOSAL FOR THE INCLUSION OF *CANNABIS SATIVA L.* IN LIVING PHARMACIES: IMPLEMENTATION OF OFFICIAL GARDENS IN BRAZIL

Cannabis sativa L. is a truly medicinal plant, but in the current context it is very important to reflect that, according to the definition and models of Living Pharmacy

presented, the inclusion of this species in your gardens would limit the spaces of action with other medicinal plants and herbal medicines. Therefore, it is known that there would be a whole legal rigor around the cultivation and use of *medical cannabis*.

In this intent, it would be an important legal strategy to implement Official *Cannabis sativa Gardens* in Brazil with the support of the Ministry of Health. The implementation of these Official Gardens aims to establish the requirements for compliance with good practices for the cultivation and collection of *Cannabis sativa* L. This garden may be instituted through a bill to be implemented one in each region of the country, for example, or in each state, according to climatic conditions to be established for the quality of the species and cannabinoid content.

The Official Garden to be implemented, in addition to the support of the Ministry of Health, must have the adhesion of the State Health Secretariats, and may have the surveillance of actions through the State Secretariats of Public Security.

MAIN TECHNICAL REQUIREMENTS:

-The site of implementation of the Official Cannabis *sativa* L Garden and its adjacent areas must have its perimeter protected, in order to prevent access to unauthorized persons and ensure the necessary controls to mitigate the risks of dissemination and diversion, provided with a video surveillance system at all entry points, with access restriction, security alarm system, without prejudice to other security measures that may be adopted.

- For the cultivation of *Cannabis sativa* L *in* the Official Garden, certified seeds or seedlings must be used, in accordance with Law No. 10,711, of August 5, 2003, or clones obtained through genetic improvement, from them. For greater safety, cultivation should be carried out in a greenhouse. A security plan should be organised.

- In the Official Garden, there must be the presence of a technical responsible, who will be in charge of ensuring the application of good agricultural practice techniques, as well as being responsible for controlling the levels of Δ9 –THC in *Cannabis sativa* L.

-In the Official Garden, there should be a Pharmaceutical Laboratory for the production of extracts as raw material for *Cannabis sativa* L. for the Pharmaceutical Workshops of Farmácia Vivas for the preparation of herbal medicines.

FARMÁCIA VIVA AS A UNIT FOR THE PREPARATION OF HERBAL MEDICINES BASED ON *CANNABIS SATIVA* L.

In this system, Farmácia Viva would receive the extracts prepared from the Official Cannabis *sativa Garden* of the region or state and, according to pharmaceutical techniques, would develop the appropriate dosage forms in small batches, for greater quality control of operations.

The distribution of these herbal medicines would be done by the Pharmaceutical Supply Center of the Farmácia Viva unit or the Pharmaceutical Assistance Coordination, through a standardized form, to the Health Posts and Centers.

For the development of this work system, the following steps can be taken into account:

- ✓ It has the advantage of making the herbal medicine available with a greater territorial coverage, thus reaching a greater number of users of health services;
- ✓ The service user can find the herbal medicines at the nearest and most convenient Health Posts and Centers for him, without the need for Habeas Corpus or judicial process;
- ✓ In this system, greater effort is required from Farmácia Viva to provide training of human resources in service, on a regular basis, for professionals at health posts and centers, as a way to minimize failures in dispensing and/or storage;
- ✓ Guide for the proper storage of herbal medicines and pharmaceutical ingredients based on Good Storage Practices;
- ✓ Provide guidance on the distribution system of herbal medicines in the Health Centers, SUS, following the criteria for programming the preparation of these herbal medicines, according to the availability of pharmaceutical inputs, analysis of monthly movement;
- ✓ Promote the quality control of herbal medicines produced in the municipalities, through sampling, in Specialized Laboratories;
- ✓ Greater effort is required from Farmácia Viva to monitor the correct storage and stocks, to avoid deterioration and/or breakage, compromise of the schedule;
- ✓ Provide guidance on the distribution system of herbal medicines in the Health Centers, SUS, following the criteria for programming the preparation of these herbal medicines, according to the availability of pharmaceutical inputs, analysis of monthly movement;
- ✓ Promote the quality control of herbal medicines produced in the municipalities, through sampling in specialized laboratories;

- ✓ The products made by Farmácias Vivas can only be dispensed after proof of tests that validate the levels of the main cannabinoids present in their formula, among them, minimally CBD and Δ9-THC;
- ✓ Establish phytoeconomic indicators for monitoring and evaluation.

NOTE: Talk about associations and Living Pharmacies

https://agenciabrasil.ebc.com.br/politica/noticia/2021-06/comissao-da-camara-aprova-projeto-que-autoriza-plantio-de-cannabis

It is necessary to be aware that the insertion of *Cannabis sativa* in the SUS should come concomitantly with the acquisition of knowledge that guarantees a quality practice for the health care of patients. It is also urgent to implement Permanent Education in Health on the subject, which articulates management to guarantee spaces for education in service to health professionals.; professionals who are committed to a practice of popular health education, sharing knowledge and actions in the search for the collective good and users being co-responsible for the care of their health and that of the community, through social participation.

OFFICIAL LABORATORY FOR THE PRODUCTION OF HERBAL MEDICINES BASED ON *CANNABIS SATIVA* L. FOR THE SUS

In Brazil there is a current need to regulate marijuana (*Cannabis sativa* L.) for medicinal purposes and the production of herbal medicines, mainly motivated by the high costs of importation, bureaucracy and urgency for the treatment of pathologies by the administration of cannabinoids (epilepsy, sclerosis, anorexia, neuropathic pain, fibromyalgia, etc.).

The story of the first attempt to produce marijuana-based medicines in Brazil was through the Pharmaceutical Laboratory of the State of Pernambuco Governador Miguel Arraes (LAFEPE). This Laboratory was created in 1965 to produce quality medicines at low cost, being a mixed capital company, with administrative and financial autonomy, linked to the State Health Department. Classified as one of the three largest public laboratories in Brazil, it develops, produces and sells medicines and glasses, meeting public health policies.

It is important to note that LAFEPE stood out in the production of antiretroviral drugs and was the first institution in the country to prepare a formal request for the production of a drug derived from marijuana for the treatment of patients with AIDS, cancer and epilepsy, 20 years before the approval of the first drug authorized by the National Health Surveillance Agency (Anvisa). The request was denied.

What LAFEPE intended in this claim was to isolate cannabinoids (including THC), mentioning dronabinol. Currently, instead of isolating cannabinoids as phytopharmaceuticals, there are several attempts underway in which it is possible to prepare marijuana extracts enriched with cannabidiol, the cannabinoid, that is, herbal medicines, preferred in clinical medicine.

Thus, in the expectation of organizing Official Laboratories, it is appropriate to seek the LAFEPE model in the production of quality and low-cost medicines for the possible and necessary production of medicines based on *Cannabis sativa* L, integrated with the Official Gardens for the production of raw material of the aforementioned species, already described.

LOCAL PRODUCTIVE ARRANGEMENTS (APLs) WITH MEDICINAL PLANTS

Medicinal plants are part of a production chain in which they can originate industrialized or manipulated herbal medicines, from plant drugs or the plant *in natura*, and also participate in the production of foodstuffs, veterinary, phytosanitary and cosmetics. Active ingredients, the so-called phytopharmaceuticals, used by the pharmaceutical industry, can also be isolated from medicinal plants or their derivatives.

For the production of herbal medicines by the Living Pharmacy model III, it is necessary to produce raw materials, that is, medicinal plants. In this way, the production of herbal medicines can be compromised if the Medicinal Plants Garden of the municipality is not able to produce adequately and in sufficient quantity.

In view of this reality, the Local Productive Arrangements (LPAs) of medicinal plants and herbal medicines are an alternative to increase the production of this raw material and ensure the satisfactory production of herbal medicines through the participatory association of farmers who can produce medicinal plants in cooperatives with a view to the production of herbal medicines or for the pharmaceutical industry.

With this in mind, in 2006 the National Policy on Medicinal Plants and Herbal Medicines, brings as one of its guidelines the promotion of the inclusion of family farming in the chains and productive arrangements of medicinal plants, inputs and herbal medicines.

In this Policy, Local Productive Arrangements are conceptualized as territorial agglomerations of economic, political and social agents, focusing on a specific set of economic activities, which may present links and interdependence. Generally, they involve the participation and interaction of companies, which can range from producers of final goods and services to suppliers of inputs and equipment, consulting and service providers, traders, customers, among others – and their various forms of representation and

association. They may include several other public and private institutions focused on training and training human resources, such as technical schools and universities, research, development and engineering; policy, promotion and financing.

The National Policy on Medicinal Plants and Herbal Medicines was the basis for the construction of the National Program on Medicinal Plants and Herbal Medicines, which has the following principles: the need to expand therapeutic options and improve health care for SUS users through the use of phytotherapy; the sustainable use of the country's biodiversity; the appreciation and preservation of the knowledge of traditional communities and peoples; the strengthening of family farming; economic growth with job and income generation; technological and industrial development; social inclusion and reduction of social inequalities, in addition to encouraging popular participation and social control.

The APLs of medicinal plants and herbal medicines are potential spaces for the innovation of services and products, as a competitive strategy and market opportunity for the pharmaceutical industry of herbal medicines, encourage technological and economic development with job and income generation, strengthen family farming, generate the sustainable use of biodiversity and, above all, stimulate the production and use of medicinal plants and herbal medicines by SUS users. In this way, they respect the principles of the National Program of Medicinal Plants and Herbal Medicines and enable its effective implementation.

In addition to increasing the production of raw material, measures for the formation of LPAs aimed at the agricultural and commercial exploitation of medicinal plants and herbal medicines, can help reduce regional disparities in income concentration in Brazil, with emphasis on regions with fewer economic and social opportunities, as is the case of the Northeast, notably the backlands of Ceará.

The APLs bring to the region where they are inserted satisfactory results in terms of the generation of employment and income and improvement in the quality of life of the population, as it strengthens a local productive activity and the potential of each territory.

The Ministry of Health has the function of articulating and integrating social actors and enterprises in the area of cultivation, production, service, teaching and research, in medicinal plants and herbal medicines, in the public and private sectors, especially within the scope of the SUS. From this articulation, it will be possible that medicinal plants cultivated by family farming, in urban or rural areas, can be used as raw material for the production of herbal medicines. Users assisted in the Basic Family Health Units, of Primary Health Care, could then have access to services and products with quality, safety and efficacy throughout the country.

With this in mind, the Ministry of Health presented proposals to encourage the development of LPAs throughout the country. One of these initiatives was public notice No. 01, of May 24, 2013, which dealt with the public selection of projects for the local productive arrangement of medicinal plants and herbal medicines within the scope of the SUS. The main objective of this notice was to encourage the structuring, consolidation and strengthening of Local Productive Arrangements within the scope of the Unified Health System, according to the National Program of Medicinal Plants and Herbal Medicines and the National Program of Medicinal Plants and Herbal Medicines, with the purpose of strengthening pharmaceutical assistance and the production chain in medicinal plants and herbal medicines in the states and municipalities, assisting in actions to modify the socioeconomic and health situation of the local population.

In view of the above, it is clear that, for the elaboration of a Bill that inserts "family farming" for the cultivation of *Cannabis sativa* L. It would be of fundamental importance to make "real" and "achievable" reflections on the possible flexibility and monitoring of this activity to obtain the raw material, through the organization of Local Productive Arrangements of small producers.

The importance of including the Ministry of Agriculture, Livestock and Supply (MAPP) in the Bill to support the projects is highlighted, with the distribution of selected seed breeds and cultivation of the species, among others.

REFERENCES

1. Brasil. Portaria n° 971 de 3 de maio de 2006. Aprova a Política Nacional de Práticas Integrativas e Complementares (PNPIC) no Sistema Único de Saúde. Diário Oficial [da] República Federativa do Brasil, Poder Executivo, Brasília, DF, 2006a.

2. Brasil. Decreto n° 5813 de 22 de junho de 2006. Aprova a Política Nacional de Plantas Medicinais e Fitoterápicos e dá outras providências. Diário Oficial [da] República Federativa do Brasil, Poder Executivo, Brasília, DF, 2006b.

3. Brasil. Resolução da Diretoria Colegiada RDC nº 18 de 03 de abril de 2013. Dispõe sobre as boas práticas de processamento e armazenamento de plantas medicinais, preparação e dispensação de produtos magistrais e oficinais de plantas medicinais e fitoterápicos em farmácias vivas no âmbito do Sistema Único de Saúde (SUS). Diário Oficial [da] República Federativa do Brasil, Poder Executivo, DF, 5 abr. 2013a.

4. Brasil. Portaria Nº 2.761, de 19 de novembro de 2013. Política Nacional de Educação Popular em Saúde. Brasília, DF. 2013b. Disponível em: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt2761_19_11_2013.html. Acesso em 10/04/2022.

5. Bonfim, D. Y. G. Fitoterapia em Saúde Pública no Estado do Ceará: Levantamento Histórico das Farmácias Vivas. (2016). Dissertação. Rede Nordeste de Formação em Saúde da Família. Universidade Federal do Ceará, 2016, 121p. Disponível em: https://repositorio.ufc.br/bitstream/riufc/21904/1/2016_dis_dygbonfim.pdf.

6. Ceará. Decreto Nº 30.016, de 30 de dezembro de 2009. Regulamenta a Lei Nº12.951, de 07 de outubro de 1999, que dispõe sobre a política de implantação da fitoterapia em saúde pública no estado do Ceará. Disponível em: http://imagens.seplag.ce.gov.br/PDF/20100108/do20100108p01.pdf. Acesso em: 19/04/2022.

7. Ceará. Portaria No 275 de 20 de março de 2012. Promulga a Relação Estadual de plantas Medicinais (REPLAME) e dá outras providências. Diário Oficial do Estado. Caderno 2. Página 75. 2012. Disponível em: http://www.jusbrasil.com.br/diarios/35754014/doece-caderno-2-29-03-2012-pg-75. Acesso em: 19/04/2022.

8. Ceará. Comitê Estadual de Fitoterapia. A Fitoterapia no ciclo da assistência farmacêutica: Inserção das farmácias Vivas. Fortaleza: HBM Shopping das Cópias, 2015.

9. Matos, F. J. A. Farmácias Vivas: sistema de utilização de plantas medicinais projetado para pequenas comunidades. 4ª ed. rev. ampliada. Fortaleza: Editora UFC, 2002.

10. Castro Neto, A. G. et al. A história da primeira tentativa de produção de medicamentos à base de maconha: Entrevista com Antônio José Alves. Ciência & Saúde Coletiva, 25(6), 2020.

11. Pinheiro, B. S. et al. Importância da Incorporação da Cannabis sativa L. no SUS. Revista Científica Eletrônica de Ciências Aplicadas da FAIT, n. 1, maio, 2021.

THROMBOPHILIA AND PREGNANCY: MEANINGS ATTRIBUTED TO DRUG INTERVENTION WITH ENOXAPARIN SODIUM IN THE PREGNANCY-PUERPERAL PERIOD

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Flávia Caroline C. G. Mendonça[1], Kely Paviani Stevanato[2], Daniela Aparecida de Souza Nunes[3] and Rebeca Rosa de Souza[4]

ABSTRACT

Objective: to understand the feelings, perceptions and meanings attributed to the drug intervention with enoxaparin sodium in women with thrombophilia. Method: qualitative study, whose data were collected remotely between October 2021 and June 2022, through in-depth interviews with 13 women. The data were organized and analyzed in the MAXQDA plus 2020 Software and submitted to content analysis. Results: Two categories emerged that show that the diagnosis of thrombophilia and the use of enoxaparin sodium in the pregnancy-puerperal period represent a complex situation, permeated by feelings of fear, insecurity and uncertainty, which in addition to being linked to the complexity of the treatment, combine the complexity of having the medication released by the Unified Health System (SUS). However, the use of medication commonly means a proof of love, strength, courage and overcoming, being perceived as a unique moment worth living in pursuit of the dream of motherhood. Final considerations: drug treatment with enoxaparin sodium is meant as an act of love, strength and courage. It is perceived as the hope of life and as the overcoming of limits. Therefore, the need to disseminate information on thrombophilia and pregnancy among health professionals and managers is dazzled, favoring a greater understanding of this phenomenon, in order to ensure improvements in health care, as well as a safe and healthy pregnancy for women with thrombophilia.

Keywords: Thrombophilia. High-Risk Pregnancy. Enoxaparin. Nursing.

[1] Nurse. State University of Paraná, Paranavaí – Pr.
[2] Doctor in Health Sciences. State University of Paraná, Paranavaí – Pr.
[3] Master in Nursing. State University of Paraná, Paranavaí – Pr.
[4] Doctor in Nursing. State University of Paraná, Paranavaí – Pr.

INTRODUCTION

Thrombophilia is a set of hereditary or acquired pathologies, characterized by a compound of genetic conditions that predetermine the development of thrombosis in the circulatory system [1]. In this sense, the blood clotting process acts in a hyperactive way, intensifying the formation of clots inside the blood vessels, and consequently increasing the risk of developing thromboembolistic diseases [1-3].

Thromboembolic diseases and obstetric complications resulting from placental thromboembolism represent one of the main causes of obstetric and perinatal complications in Brazil and in the world [1-3]. Thus, it can be said that pregnancy is an independent factor for the development of thrombosis, since its risk is 5 to 6 times higher in pregnant women when compared to non-pregnant women, which is higher in the postpartum period [1].

Complications related to thromboembolism include fetal death, repeated abortions, premature birth, preeclampsia, HELLP Syndrome, Deep Vein Thrombosis (DVT), Cerebral Vascular Accident (CVA) and Pulmonary Embolism [4]. Due to such complications, pregnancy in women with thrombophilia is classified as high risk, requiring rigorous, continuous and longitudinal follow-up. In this context, thromboprophylaxis with low molecular weight heparin (LMWH) is the drug intervention of choice in most cases of gestational thrombophilia [5].

This corresponds to Enoxaparin sodium, an anticoagulant considered safe because it does not cross the placental barrier. However, although there is a vast literature on the association between thrombophilia and pregnancy, these are still controversial, especially in relation to the effect of LMWH use in the pregnancy-puerperal period [1, 3, 5, 6].

These studies seek to highlight the clinical and perinatal outcomes related to the use of enoxaparin sodium, and there are few studies in the literature that seek to understand the perceptions, feelings and meanings attributed by these women to the use of this drug. Since pregnancy is characterized by a complex phenomenon, with physical, psychological and social alterations [7].

At this juncture, being diagnosed with a rare, serious condition that requires rigorous care and treatment based on daily injectable solutions can significantly alter the gestational experience. In addition, enoxaparin sodium is a high-cost medication, which is not provided to all women diagnosed with thrombophilia, being offered by the Unified Health System (SUS) only for thrombophilias that fit the clinical protocols established by the system [8].

Therefore, taking into account that in Brazil the vast majority of women are assisted by a family health team, this study can contribute to scientific knowledge about the feelings, perceptions and meanings attributed by these women to this intervention, helping health

professionals and government officials in care planning, in order to ensure humanized care, integral and resolute.

In addition, knowledge about this phenomenon can contribute to the reduction of negative statistics in relation to complications that occur during the pregnancy-puerperal period, whether these are related to underlying pathology or to complications arising from the gestational process, such as psychosocial complications. In this scenario, this study aimed to understand the feelings, perceptions and meanings attributed to the drug intervention with enoxaparin sodium in women with thrombophilia.

METHODOLOGY

This is a descriptive exploratory qualitative study conducted with 13 women with thrombophilia who experienced the drug intervention with enoxaparin sodium during pregnancy. The participants were recruited from the private group "Thrombophilia and pregnancy Brazil" on *Facebook*.

The Thrombophilia and Pregnancy Brazil group was created on August 13, 2019 and consists of 4,875 members (05/07/2022), with a monthly number of approximately 300 monthly publications. The group aims to help women with thrombophilia to achieve the dream of motherhood by sharing the experiences lived by the participants. In addition, the group is explored as a space for support and mutual help, where, in addition to exchanging experiences, women routinely help each other in doubts related to the gestational process and drug treatment and in the donation of drugs used during pregnancy, especially enoxaparin sodium.

Data collection took place from October 2021 to June 2022. Initially, the participants were approached by the first author, through a public post in the group Thrombophilia and pregnancy Brazil. The post aimed to present the research project and invite women who would be interested in sharing their obstetric stories with thrombophilia and the use of enoxaparin sodium to participate in the research. The expression of interest of the interested parties took place through a response to the post and via direct.

At the time, the researchers contacted the possible participants, carrying out a prior and individual evaluation. In this contact, the presentation of the research team, the clarification about the proposal for an *online interview*, the objective of the research, as well as the risks and benefits offered by this study were established. In addition, in this first contact, the eligibility of the interested party was evaluated, that is, whether or not she had undergone drug treatment with enoxaparin sodium during pregnancy and puerperium. After

confirming the participant's interest, the remote interview was scheduled in advance on a day and time of her preference.

The following inclusion criteria were considered: being 18 years of age or older, having been diagnosed with hereditary or acquired thrombophilia, having undergone drug intervention with enoxaparin sodium during the pregnancy-puerperal period, having access to the internet network and equipment for video calls: cell phone, tablet, *notebook* or computer. Exclusion criteria were to have some comorbidity that could hinder communication between researchers and interviewees, such as deafness or muteness.

The interviews were previously scheduled according to the availability of the researchers and the participants and carried out through the communication application Facebook *Messenger* and the Google communication service "google *meet*" and Messenger. The choice for remote data collection occurred in view of the current COVID-19 pandemic scenario experienced by Brazil and the world, which limited contact between researchers and interviewees, compromising the development of face-to-face interviews and, consequently, the development of qualitative research.

On the other hand, the *online* scenario has been configured as a space conducive to the development of research from different perspectives, since the internet and social networks are increasingly inserted in people's daily lives and constitute a space where they routinely share their life stories and exchange information on various subjects, among which are issues related to pregnancy.

The interviews were audio recorded after authorization and used the OBS Studio application as support. They lasted an average of 60 minutes and took place in a single call. First, the participants signed *the* Informed Consent Form (ICF) online through Google forms, and then they were submitted to a semi-structured questionnaire of sociodemographic characterization: name; current age; municipality and state of residence; religion; marital status; race/color; level of education; profession and family income. Clinical characteristics: type of thrombophilia; associated diseases; age at first menstruation and age at the beginning of sexual activity. Obstetric and gynecological history: number of pregnancies; number of children born alive; number of abortions; use of enoxaparin during pregnancy and puerperium; quantity; trimester that started enoxoparin and use of other medications. Perinatal characteristics: type of delivery, gestational age at delivery; Complications; kilograms of the newborn, length and use of enoxoparin in the puerperium. Behavioral factors: smoking, alcoholism, and use of illicit substances during pregnancy.

The intensive interview was guided by the following guiding question: "tell me how it was for you to use Enoxaparin sodium during pregnancy and puerperium. To achieve the

proposed objective, support questions were used. The recruitment of the participants occurred gradually, over nine months and ended when there was theoretical saturation of the data, that is, when there was no new information in the interviews, thus concluding that the phenomenon was understood in its totality, and the objective proposed in this research was answered. It is noteworthy that the transcribed testimonies were not returned for approval by the respondents.

All interviews were transcribed in full and submitted to the study of the texts with a thorough and exhaustive reading of the information collected. The data were organized and analyzed in the MAXQDA plus 2020 software and submitted to thematic content analysis respecting the steps pre-established by the referential, which included: pre-analysis, exploration of the material and data treatment.

In the pre-analysis, the data set was transcribed, organized, read exhaustively, and separated, with the identification of common and most relevant aspects. In the material exploration stage, the classification and aggregation of the data was carried out based on a detailed reading process, with identification, by means of different colors, of the common and more specific terms and the selection of first-order codes - directly associated with the citations and using the participants' own words - called in vivo codes, which gave rise to the nuclei of meaning and the units of registration and which served as the basis for the subsequent categorization of the data. In the last phase of data processing, categorization was carried out, which consisted of grouping the elements, according to their similarities and by differentiation, with subsequent regrouping based on common characteristics, giving rise to thematic categories.

The research project was approved by the Permanent Committee for Ethics in Research with Human Beings of the signatory institution opinion No. 4.888.265 CAAE: 50136621.0.0000.9247. All participants, after reading and clarifying doubts, signed the Informed Consent Form online through Google *forms* and verbalized acceptance in a video call. To ensure anonymity in the presentation of the results, the extracts of the testimonies were coded with the letter P for participant followed by an Arabic numeral which refers to the order of the interviews (e.g., P1).

RESULTS

A total of 13 women participated in this study. Their ages ranged from 28 to 42 years, of which 11 were married and two were single, ten Catholic, three Evangelical, nine considered themselves white and four brown. Regarding the level of education, seven have higher education, four high school and two postgraduate degrees. Family income ranged

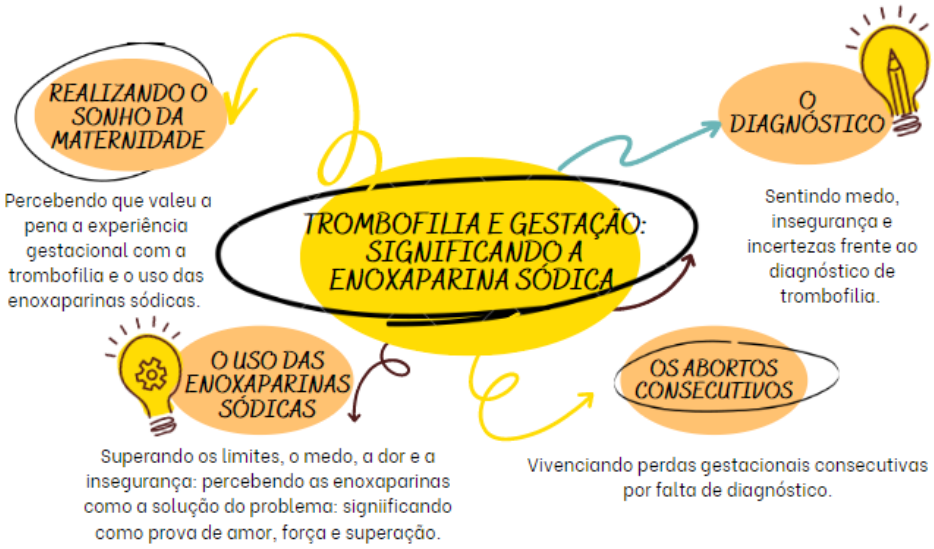
from one to six minimum wages. Women from the states of Paraná, São Paulo, Mato Grosso, Mato Grosso do Sul, Recife, Santa Catarina and Rio Grande do Sul participated.

Regarding clinical and obstetric conditions, the age at menarche ranged from nine to 13 years of age, the onset of sexual activity between 15 and 24 years. The number of pregnancies ranged from two to six pregnancies, totaling 46. Of these, 27 resulted in miscarriages, ranging from one to five miscarriages per woman, of which 20 occurred in the first trimester of pregnancy. The number of live births was 19, with a total of 14 cesarean deliveries and five normal deliveries. Nine resulted in preterm births between 32 and 36 weeks, eight at term and two post-term with more than 42 weeks.

Regarding thrombophilia, seven had a diagnosis of hereditary thrombophilia: protein S, protein C, antithrombin III, Leiden Factor V, heterozygous MTHFR C677T and A1298C deficiency, and six had acquired deficiency: antiphospholipid syndrome (APS). Regarding the use of enoxaparin sodium, the total number of applications ranged from 275 to 412. Of the 13 participants, eight reported having started treatment after the positive test and five in the attempts. Of these, seven used ASA and other medications along with enoxaparin sodium. All of them maintained the treatment for 40 to 45 days postpartum, according to the guidance received.

From the analysis of the data, two categories emerged, which will be described below.

Image 1 – Diagram: thrombophilia and pregnancy: meanings attributed to drug intervention with enoxaparin sodium in the pregnancy-puerperal period.



Source: Authors (2022)

FROM THE DIAGNOSIS OF THROMBOPHILIA TO THE USE OF ENOXAPARINS SODIUM: FACING THE CHALLENGES OF THE CLINICAL CONDITION IN SEARCH OF THE DREAM OF MOTHERHOOD

Being diagnosed with a rare condition that was previously unknown and that reflects on serious risk factors for mother and child represents a complex situation, causing the woman feelings of fear, insecurity and uncertainty.

> [...] I had never heard of this before, the first thing I thought when the doctor said was that I have thrombosis and what does this have to do with pregnancy? When he explained it to me I almost fell off my legs, it was a fright, a very big feeling of fear and insecurity [...] (P1).
> [...] I had already seen it on television on the internet, of women who had to take injections in the belly every day to have the child, but I never thought I would go through this, I almost didn't believe it, I refused to believe it, I was always very afraid of needles and knowing that I had to use that all the pregnancy, It was desperate, I was very afraid and suffered a lot from all this [...] (P3).

Nevertheless, the diagnosis of thrombophilia is most often established after the woman experiences one or more pregnancy losses, which causes suffering, pain, feelings of incapacity, guilt and sometimes fear of not being able to conceive again.

> [...] Hearing that you have a disease like this makes you feel very guilty, because I lost three children and then out of nowhere you discover that the fault is yours, that you could have avoided it if you had been treated, investigated before [...] (P8).

> [...] I felt very incapable, guilty, I don't know, these are very bad feelings, because you never imagine that something like this can happen to you [...] it was my dream to be a mother, it always was and then you can't hold your child in your womb and no one finds out why, no doctor, everyone said the same thing, it's normal, This happens and you are suffering, crying, feeling like the worst woman in the world [...] (P9).

> [..] I had a fetal death at 35 weeks, which I was very shaken because it was my first pregnancy I was immature and didn't understand much, but I was a very planned, loved, expected and desired child, I suffered from anxiety, I blamed myself a lot for what happened and I thought how much my baby suffered, I thought I would never be a mother again. (P12).
> [...] we were sad about the loss because we were waiting for this baby a lot, and I was also worried, afraid because I was already at the age limit to get pregnant, I was afraid of not being able to get it anymore (P14).

According to the protocol established by the Ministry of Health for the investigation of thrombophilia by the Unified Health System (SUS) should only occur from the third consecutive pregnancy loss, such a guideline is perceived by women diagnosed as an inhumane conduct, not considering the woman's feelings or even the impacts that these losses have on physical and mental health.

> [...] I've heard a story of a person who lost three, four and only after they found out, I say people can't, my God, how is that sir? Expect to lose so much, because the first

> is normal beauty, but the second is not, right? Not losing the second one, right? The third, fourth child much less [...] (P3).
> [...] I sought a diagnosis on my own because for the doctors I needed to abort three times for them to investigate something, right? Absurd, where is our mental health? Doesn't it count? No matter our suffering [...] (P1).
> [...] I think it's absurd for the SUS to only investigate thrombophilia after the third pregnancy loss, where has it been seen, where is the humanization they talk about so much? And doesn't a woman's mental health count? Is it worthless? This, in my perception, is inhumane, it is absurd [...] (P14).

From the diagnosis, the daily life of women with thrombophilia in the gestational process is permeated by ups and downs, which run through feelings of fear and uncertainty to hope. The use of enoxaparin sodium requires, in addition to strength and courage, overcoming the limitations and fears related to the needle and the pain of administration.

> [...] It was a pregnancy full of ups and downs, a lot of anxiety, moments of despair and anguish, with each ultrasound it was nervous, anguish. Every day they had the injections and of course this brought even more anxiety, fear [...] it was a painful process, more hopeful, because I knew I was getting the appropriate treatment (P12).

> [...] I was always terrified of needles, how was I going to do that every single day? It's really facing your fears in search of your dream [...], it hurts, bleeds, hurts, it's very sad, but we do it because we know it's for the greater good [..] (P3).

Being diagnosed with thrombophilia and submitted to drug intervention with enoxaparin sodium makes it necessary to request the release of medications from the SUS, in addition to the clinical and personal conditions of the women, since they have a high cost. In this context, the participants report great challenges, since the release of medication is permeated by a complex process that requires time and patience, and it is necessary to resort to other forms of funding to maintain the treatment.

> [...] the treatment of thrombophilia was not easy for me because I needed to take 60mg of Clexane a day and the SUS did not provide it, so I had to buy it, and to compensate I also bought insulin syringes and fractionated [...] you even need to learn how to handle these things [...] (P2).

> The hardest thing is not getting it through SUS, SUS does not treat hereditary thrombophilia with the dosage that gave my changes, so I had to buy it, it was around 1,500.00 a month of injections [...] (P9).

In this category, it was possible to observe that in the vast majority of cases the diagnosis of thrombophilia is only established after the woman experiences pregnancy loss, and is not previously investigated before the gestational process. Nevertheless, this causes feelings of fear, insecurity and uncertainty in women, since it refers to a relatively rare, unknown condition that requires complex treatment.

In addition, because it is a high-cost medication, these women travel a complex path, permeated by obstacles that do justice to the difficulty of releasing the medication by the SUS, the release of the medication in milligrams and necessary doses and the interruption of supply without prior notice, which predisposes these women to lack of security to continue with the pregnancy.

THE STINGS OF LOVE: MEANING SODIUM ENOXAPARINS AS PROOF OF LOVE, STRENGTH, PERSISTENCE AND OVERCOMING

Using enoxaparins sodium daily is perceived as a proof of love, strength, persistence and overcoming, it is facing the fears and challenges of treatment in pursuit of the dream of motherhood.

> [...] The pricks of love symbolize love itself, the strength and courage of a mother in search of her dream, they are an act of love, piercing yourself every day, seeing your body bleed with each puncture, seeing the huge bruises that formed on your belly is an act of love [...] for me they are life, hope, I believe that if it wasn't for God and the injections I would never get it. I would do it all over again, I would take double if necessary [...] (P9).
> [...] their meaning for me is proof of love, it is really facing everything to have your child because it is very difficult, it is facing your fears, your misgivings, it is overcoming your limits in search of your dream, it is discovering that you are stronger than you imagine yourself (P10).

Enoxaparin represents for women with thrombophilia the solution to problems, being placed in them all the hopes that permeate the gestational process, it is believing that without it it is not possible to get pregnant, it is waiting for the medication schedule daily, it is believing that everything will be fine.

> [...] Medication is all we have, it's our hope that everything will be fine and that we'll be able to reach the end of pregnancy [...] it's feeling a huge fear of losing, and feeling a huge fear of being without the injection, those who have already suffered a loss understand how important it is, so the injection is all we have and thank God it exists, She ensures that our blood reaches the baby and that his heart continues to beat until the end within us [...] (P3).
>
> [...] we put all our hope in that injection, it was the sacred time, no matter where I was, the clock woke up, I did it, without fail (P9).
>
> [...] I took around 200 injections during pregnancy, they are my love bites that without a doubt was the greatest collaborator in the miracle of having my daughter today [...] (P12).

In addition to the pain and discomfort perceived in the administration of enoxaparins, women experience the formation of hematomas which are related to the transection of blood vessels and repeated traumas in the application region. However, these bruises are

also perceived and signified as a proof of love and overcoming, making women a source of pride, which is immortalized in photos and memories.

> [...] For me those bruises were proof of love, it was proof that I overcame my limits, it was proof that I faced everything to have my son in my arms [...] (P2).
> [...] When I did the pregnancy photo shoot I told my photographer that I didn't want any spot to be removed from my belly because it's a sign, a sign of my strength and my love, so I wanted them to appear so I could always remember that I had to go through this [...] (P3).
> [...] The syringes used during pregnancy are kept as a reminder of a moment of struggle and overcoming, they are proof that through love everything is overcome everything is overcome [...] (P9).
> [...] I never felt ashamed of my bruises, I felt that those marks from the bites were my trophy of courage, because that medication would help me overcome thrombophilia, placental insufficiency, preeclampsia and low percentile, in my photos of the book of pregnant women I made a point of not using a photo shop and leaving the marks there for me to see and remember all the way to have my lap full with my baby. (P12).

After experiencing a high-risk pregnancy, based on a complex clinical treatment, women with thrombophilia mean this phenomenon as a moment of overcoming limits, recognizing strength, persistence and proof of love, making up the feeling of achievement and compensation, since they report that the whole struggle was worth it and that they would do it all again if necessary.

> [...] For me, having managed to reach the end is a proof of love, of courage, I faced everything for the dream of having a child, and I did it [...] it was worth it, for sure, I would do it all again [...] (P3).
>
> [...] The feeling that remains is overcoming and victory, when we hold our son in our arms we realize that it was all worth it, I would do it again a thousand times if necessary [...] (P9).
>
> [...] It's a mix of feelings, emotion, crying, laughter, victory, overcoming, strength and fear too, for many days I couldn't sleep, I was on top of him all the time, I didn't want to move away, after the suffering we go through even after being born we are still afraid, but having gone through everything I went through what I went through what I can say is that it was worth it, very, very]even [...] (P11).
> [...] It is worth going through everything, everything is worth it when it comes to a child [...] (P13).

Reports in this category showed that women with thrombophilia perceive enoxaparin sodium as an essential medication, placing all their trust and hope in it in relation to the success of the pregnancy. This is meant as a proof of love, strength, courage and overcoming, being seen as a unique moment worth facing in pursuit of the dream of motherhood.

DISCUSSION

Characterized as a high-risk condition during pregnancy and puerperium, thrombophilia is a clinical condition caused by genetic and acquired factors that reduces uteroplacental blood flow during pregnancy, leading to substantial risks to the mother-child binomial ([2-3].

Receiving the diagnosis of a condition hitherto unknown, relatively rare and complex, causes women to feel anguish, despair and insecurity about the future. Such feelings are also perceived when it comes to diagnoses of autoimmune, rare and complex diseases [9] especially when they compromise the safety and healthy termination of the pregnancy [9].

The gestational process represents for the vast majority of women a stage of life that needs to be experienced, in this conjuncture pregnancy is seen as a dream that must be conceived as safely as possible [10]. Therefore, being diagnosed with a rare condition and with gestational impacts undoes positive thoughts and feelings about pregnancy.

As evidenced in this study, these diagnoses are complex and cause women to feel fear, insecurity and uncertainty about the future. In agreement with these findings, a study published in 2019 that aimed to describe the perception of pregnant women and family members about the condition of vulnerability of a high-risk pregnancy showed that being diagnosed with conditions of risk during pregnancy causes these women feelings of worry, anxiety, fear and stress in the face of the condition of vulnerability [10]. In the same direction, the feelings and perceptions of women diagnosed with Systemic Lupus Erythematosus [9] and Gestational Diabetes [11] are moving in the same direction. Systemic Arterial Hypertension, heart disease and depression [10].

In the case of thrombophilia, these feelings, perceptions and meanings are also related to the diagnosis process, which in most cases is only established after the woman experiences one or more consecutive abortions, which is perceived as an inhumane condition, which does not value feelings, nor the physical and mental health of the woman who experiences the condition.

This statement is confirmed in the clinical protocol and therapeutic guidelines for the prevention of venous thromboembolism in pregnant women with thrombophilia, within the scope of the Unified Health System (SUS) of the Ministry of Health (MS), which provides that laboratory investigation (screening) of thrombophilias is not indicated for all pregnant women. This is indicated in cases of pregnant women with a personal history of deep venous thromboenbolism, with or without recurrent risk factor and without previous thrombophilia testing, and pregnant women with a family history of high-risk hereditary thrombophilia in first-degree relatives [8].

In this scenario, it is perceived that the humanization of health care, as well as the guarantee of safety, quality, comprehensiveness and problem-solving capacity of care, does not happen as proposed by the principles and guidelines of the SUS, as well as does not follow the precepts established by the National Policy for Comprehensive Attention to Women's Health [12-13].

Fetal loss in patients with thrombophilia could be explained by the excessive formation of intraplacental venous thrombi and placental infarctions, leading secondarily to placental insufficiency. However, other pathophysiological mechanisms must be involved, since it is possible to have adverse gestational outcomes even in the absence of placental thrombosis [14].

In addition, it is perceived that the mental health of women who experience repeated miscarriages is highly compromised [15]. According to the findings of this study, it is perceived that the experience of abortion is perceived, experienced and experienced by the woman as a deep, continuous and endless mourning, regardless of the period in which it occurred.

In agreement, previous research has shown that abortion can modify the way women perceive and signify pregnancy, causing feelings of fear, anguish, loneliness, guilt, depression and revolt [15]. In addition, women in situations of abortion faced, in addition to psychological pain, fear and sadness, physical pain, sometimes accompanied by obstetric violence during hospital care, and the lack of humanization of people with the grief experienced by the woman [16]. In this context, it is perceived that the abortion process impacts the physical and mental health of women, as well as is related to the way they are perceived and cared for by health professionals, thus making their perception of the gestational process [15].

After experiencing the abortion process and receiving the diagnosis of thrombophilia, the vast majority of women experience a new pregnancy and in this process they are required to undergo high-risk follow-up, which requires greater attention to maternal-fetal health throughout the pregnancy-puerperal cycle in an intensive and continuous way [10]. This process was also perceived as a complicating factor, since it requires specific care and attention from the pregnant woman, causing feelings of fear and insecurity in relation to pregnancy.

Nevertheless, these women are faced with the essential need to use low molecular weight heparin (LMWH) prophylactically throughout the pregnancy-puerperal cycle, subcutaneously, accompanied or not by other medications. Making even more feelings of fear and uncertainty related to the risk of aggravations and complications.

The scientific literature predicts that in cases of thrombophilia, which require the daily use of LMWH, pregnancy is configured as a high-risk condition, which is related to the high risk of blood hypercoagulation [17]. It is known that pregnancy itself is configured as a process of hypercoagulation, where the risks of thromboembolism increase by up to ten times, which is more significant in the puerperal period. In this sense, in thrombophilia diagnoses, the use of anticoagulant or antiplatelet is indispensable [3].

Due to prophylactic treatment, many pregnancies go through an arduous, complex process permeated by ambiguous feelings that reflect fear and hope [3]. In this study, the results showed that the use of LMWH or enoxaparin sodium is perceived and signified as an overcoming of limits, a proof of love, struggle and faith. By using the medications, women place their hopes, strength and also surrender their limitations, they realize that the treatment is difficult, painful and suffering, but they mean it as a unique moment that brings positive expectations in relation to the realization of the dream of motherhood.

Similar perceptions and feelings are observed in different populations. A study carried out with women diagnosed with gestational diabetes who used insulin therapy during the pregnancy-puerperal cycle found that they were terrified, feared, insecure, and uncertain about pregnancy [18]. In this sense, it is possible to perceive that treating clinical conditions of risk during pregnancy and that makes the need for daily invasive treatments is a difficult process that impacts the physical and mental health of the woman who experiences it.

Literature focused on the use of LMWH in the treatment of thrombophilia has identified that it is considered a beneficial prophylaxis, especially when it comes to hereditary thrombophilias [1-3]. However, in terms of humanization and quality of pregnancy, the premises and difficulties perceived by women in the face of treatment cannot be omitted.

In addition to LMWH, the associated use of other medications is necessary in some conditions, women with antiphospholipid syndrome, for example, should use antithrombotic prophylaxis both during pregnancy and in the puerperium, combined with low doses of acetylsalicylic acid (75 to 100mg/day) [19]. In this sense, it is perceived that health care is even more peculiar.

In this scenario, it is possible to perceive that the pregnancy experienced with thrombophilia and the need for the routine use of LMWH, makes up a complex process that requires specific care and attention to health in order to ensure a healthy, quality pregnancy with good gestational prognosis.

A possible limitation of the study refers to the fact that the informants were located from a virtual platform and, therefore, their results may be subject to contextual influences of this means of communication. Another limitation is related to the fact that the interviews were conducted remotely, causing a risk of selection bias, since participation became restricted to women with access to the Internet network. In addition, participants were selected based on their willingness to share their experiences with the study phenomenon. Therefore, women with lower communication skills were not considered as potential participants.

There is a need to disseminate information on thrombophilia and pregnancy among health professionals and managers, in order to help them understand this phenomenon during pregnancy and the puerperium, with a view to improving health care during the gestational process. However, because it is a relatively rare and complex condition, the dissemination of information can contribute to previous diagnoses, safe treatments, planned pregnancies, as well as to the reduction of complications arising from this process.

FINAL CONSIDERATIONS

Experiencing a high-risk pregnancy based on a relatively rare condition and with complex treatment is a difficult experience, permeated by ambiguous feelings that range from fear and insecurity to hope, joy and overcoming. Because it is a little-known condition, the time to establish the diagnosis can be too long and permeated by bad experiences that range from miscarriage to late fetal loss, leading the woman to live a traumatic experience, permeated by pain, suffering and hopelessness. From the diagnosis and a new pregnancy, women with thrombophilia experience difficult routines, permeated by a complex treatment that routinely requires the application of injectables that cause pain, bleeding and bruising. In addition, they experience a period of uncertainty, ranging from the need to guarantee medication to the need for rigorous and continuous monitoring.

However, pregnancy with thrombophilia is perceived as an overcoming. Drug treatment with enoxaparin sodium is meant as an act of love, strength and courage. It is perceived as the hope of life, as the overcoming of limits. It is discovering that you are stronger than you believe, it is facing the world in search of the dream of motherhood. Thus, it is concluded with emphasis on the need for information on thrombophilia and pregnancy among health professionals and managers, favoring a greater understanding of this phenomenon, in order to ensure improvements in health care, as well as a safe and healthy pregnancy for women with thrombophilia.

REFERENCES

1. Andrade, J. R., Camargos, M. V., Reis, M. F. de R., Maciel, R. A. B., Melo, T. T., Batalha, S. H., Matos, V. M., Salgado, H. C., Rangel, J. M. de C., & Zimmermmann, J. B. (2022). A história obstétrica de gestantes com trombofilias hereditárias. *Clin Biomed Res* [Internet]. [citado 13 de agosto de 2022]; 39(2). Disponível em: https://seer.ufrgs.br/index.php/hcpa/article/view/86858

2. Calu, C. L., Silva, F. A., Medeiros, R. L. S. F. M., & Freitas. (2018). Trombofilia em Gestantes: Uma Revisão de Literatura. *Revista Interdisciplinar em Saúde*, 20, 671–685. [citado em 13 de Outubro de 2022]. Disponível em: https://www.interdisciplinaremsaude.com.br/Volume_20/Trabalho_04.pdf

3. Clavijo, M. M., Mahuad, C. V., Reparaz, M. L. A. V., Aizpurua, M. F., Ventura, A., & Casali, C. E. (2019). Risk factors and role of low molecular weight heparin in obstetric complications among women with inherited thrombophilia – a cohort study. *Hematology, Transfusion and Cell Therapy*, 41(4), 303–309. https://doi.org/10.1016/j.htct.2019.03.003

4. Carvalho, S. S., Oliveira, B. R., & Oliveira, G. M. (2018). Assistência de Enfermagem no tratamento da trombose venosa profunda em gestantes: revisão de literatura. *Revista UNIANDRADE*, 20(2), 99–106. DOI: http://dx.doi.org/10.5935/1519-5694.20180012/revuniandrade.v20n2p-99-106

5. Rodger, M. A., Gris, J. C., Vries, J. I. P., Martinelli, I., Rey, É., Schleussner, E., et al. (2016). Low-molecular-weight heparin and recurrent placenta-mediated pregnancy complications: a meta-analysis of individual patient data from randomised controlled trials. *The Lancet*, 388(10060), 2629–2641. Doi: 10.1016/S0140-6736(16)31139-4

6. Skeith, L., Carrier, M., Kaaja, R., Martinell, I., Petroff, D., Schleußner, E., et al. (2016). A meta-analysis of low-molecular-weight heparin to prevent pregnancy loss in women with inherited thrombophilia. *Evidence-Based Focused Review*, 127(13), 1650–1655. Doi: 10.1182/sangue-2015-12-626739

7. Errico, L. S. P., Bicalho, P. G., Oliveira, T. C. F. L., & Martins, E. F. (2018). The work of nurses in high-risk prenatal care from the perspective of basic human needs. *Rev Bras Enferm*, 71(3), 1257–1264. Doi: https://doi.org/10.1590/0034-7167-2017-0328

8. Brasil. Ministério da Saúde. (2019). Comissão Nacional de Incorporação de Tecnologias no SUS (Conitec). Relatório de Recomendação n.o 502 - Protocolo Clínico e Diretrizes Terapêuticas da Prevenção do Tromboembolismo Venoso em Gestantes com Trombofilia. Brasília: Ministério da Saúde.

9. Souza, R. R., Barreto, M. S., Teston, E. F., Reis, P., Cecilio, H. P. M., & Marcon, S. S. (2021). Dualidade da convivência com o lúpus eritematoso sistêmico: oscilando entre “dias bons” e “dias ruins”. *Texto Contexto Enferm*, 30. Disponível em: https://doi.org/10.1590/1980-265X-TCE-2020-0210

10. Vieira, V. C. L., Barreto, M. S., Marquete, V. F., Souza, R. R., Fischer, M. M. J. B., & Marcon, S. S. (2019). Vulnerabilidade da gravidez de alto risco na percepção de gestantes e familiares. *Rev Rene*, 20, e40207. Doi: 10.15253/2175-6783.20192040207

11. Nicolosi, B. F., Lima, S. A. M., Rodrigues, M. R. K., Juliani, C. M. C. M., Spiri, W. C., & Calderon, I. M. P., et al. (2019). Prenatal care satisfaction: perception of caregivers with diabetes mellitus. *Rev Bras Enferm*, 72(Suppl 3), 305–311. Doi: http://dx.doi.org/10.1590/0034-7167-2018-0978

12. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. (2004). *Política nacional de atenção integral à saúde da mulher: princípios e diretrizes*. [citado em 13 de Agosto de 2022].

13. Jorge, H. M. F., Hipólito, M. C. V., & Masson, V. A., Silva, R. M. (2015). Assistência pré-natal e políticas públicas de saúde da mulher: revisão integrativa. *Revista Brasileira em Promoção da Saúde*, 28(1), 140–148. Doi: 10.5020/18061230.2015.p140. Disponível em: https://periodicos.unifor.br/RBPS/article/view/2864

14. Barros, L. I. P. V. L., Igai, A. M. K., Andres, M. P., Francisco, R. P. V., & Zugaib, M. (2014). Resultados Gestacionais e Trombofilia em Mulheres com História de óbito fetal de repetição. *Revista Brasileira de Ginecologia e Obstetrícia*, 36(02). Doi: https://doi.org/10.1590/S0100-72032014000200002

15. Silva, L., Sales, N., Santos, R., & Albuquerque, N. (2020). Percepção das mulheres em situação de abortamento frente ao cuidado de Enfermagem. *Revista Ciência Plural*, 6(1), 44-55. Doi: https://doi.org/10.21680/2446-7286.2020v6n1ID18627

16. Carvalho, C. S., Santos, F. S., Siqueira, L. S., Santos, L. F. S., Neto, M. S., & Pascoal, L. M. (2021). Vivências e percepções de mulheres em situação de abortamento espontâneo em maternidade pública. *Revista Recien*, 11(36), 490–497. DOI: 10.24276/rrecien2021.11.36.490-497

17. Oliveira, A. L. M. L., & Marques, M. A. (2016). Profilaxia de tromboembolismo venoso na gestação. *Jornal Vascular Brasileiro*, 15(4), 293–301. DOI: https://doi.org/10.1590/1677-5449.006616

18. Machado, R. C. M., Baião, M. R., Saunders, C., Santos, K., & Santos, M. M. A. S. (2021). A gestante e o processo de viver com diabetes mellitus. *Cad Saúde Colet*, 29(4), 595–603. Doi: https://doi.org/10.1590/1414-462X202129040329

19. Nascimento, C. M., Machado, A. M., Guerra, J. C., Zlotnik, E., Campêlo, D. H., Kauffman, P., et al. (2019). Consenso sobre a investigação de trombofilia em mulheres e manejo clínico. *Einstein*, 17(3), eAE4510. Doi: http://dx.doi.org/10.31744/einstein_journal/2019AE4510

ALZHEIMER'S DISEASE: PERSPECTIVE OF FAMILY CAREGIVERS IN THE FACE OF HOME CARE EXPERIENCED DURING THE COVID-19 PANDEMIC

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Geovana da Silva Lima[1], Daniela Aparecida de Souza Nunes[2], Kely Paviani Stevanato[3] and Rebeca Rosa de Souza[4]

ABSTRACT

Objective: to understand how family caregivers of the elderly with Alzheimer's disease experienced home care during the COVID-19 pandemic. Methodology Exploratory, descriptive qualitative research carried out with family caregivers of elderly people diagnosed with Alzheimer's disease in a municipality in the Northwest region of Paraná, Brazil. The interviews were conducted through home visits mediated by the Community Health Agents, the participant was invited to answer the demographic characterization questionnaire and with their authorization the face-to-face interview was recorded. Subsequently, they were transcribed and organized in the MAXQDA Plus 2020 software and analyzed using Bardin's methodological framework. Results: 12 family caregivers of elderly people with Alzheimer's disease participated in this study, the data showed that the process of caring, whether in normal times or in pandemic periods, generates physical and emotional overload, especially when this is the only responsible caregiver. Burden resulting from the change in routine, lack of freedom and social life, which can influence the caregiver's quality of life. Conclusion: the need to implement a professional support network and disseminate information on home care for elderly people with Alzheimer's disease and/or other dementias is dazzled. Offering professional, personal and emotional support contributes not only to the quality of care received by the elderly, but also to the reduction of risks of physical and mental illness by the family caregiver.

Keywords: Alzheimer's disease. Carer. Aging. Pandemic.

[1] Nurse. State University of Paraná, Paranavaí – Pr.
[2] Master in Nursing. State University of Paraná, Paranavaí – Pr.
[3] Doctor in Health Sciences. State University of Paraná, Paranavaí – Pr.
[4] Doctor in Nursing. State University of Paraná, Paranavaí – Pr.

INTRODUCTION

Population aging is a natural, gradual and inevitable process. According to data from the 2010 Demographic Census of the Brazilian Institute of Geography and Statistics – IBGE, by the year 2025 Brazil will be the sixth country in the world with the highest rate of elderly people. In this scenario, increased longevity involves a series of physical, cognitive, and emotional changes that can contribute to the emergence of dementia and neurodegenerative diseases, such as Alzheimer's Disease (AD).[1]

Alzheimer's is a progressive and incurable neurodegenerative disease that manifests itself through the deterioration of brain functions such as cognitive function and short-term memory.[2] In addition, it causes a variety of neuropsychiatric symptoms, behavioral changes, and impairment of motor skills that worsen over time.[2, 3]

According to data from the World AD Report, from the Alzheimer's Disease International Federation (ADI), about 47 million people live with dementia worldwide. This number is predicted to increase to over 131.5 million by the year 2050. In addition, the estimated number of people with AD reaches 35.6 million worldwide, and this number continues to increase significantly.[1]

In this scenario, when the elderly person is affected by AD, he or she presents significant difficulties and limitations in the performance of his or her daily activities, requiring continuous monitoring and supervision by a caregiver, who may or may not be a family member.[1] Thus, daily care becomes complex, since it provides a significant work overload, permeated by feelings of uncertainty, hopelessness and responsibility on the part of the caregiver, and may also negatively compromise their physical and mental health.[2]

Nevertheless, in addition to experiencing enigmatic care, caregivers of people with AD, as well as affected users, experienced an important and significant global pandemic triggered by COVID-19.[4], which made the care process even more complex. In addition, the pandemic favored an increase in the work overload of the family caregiver of the elderly with AD, given the restrictions on social contact established. In this sense, it can be inferred that the family caregiver suffered from the limitations imposed by the disease.

In view of these peculiarities, it was believed that it is necessary to understand how family caregivers of the elderly with AD experienced home care in times of the COVID-19 pandemic. Thus, this study aimed to understand how family caregivers of elderly people with Alzheimer's disease experienced home care during the COVID-19 pandemic.

MATERIALS AND METHODS

This is an exploratory, descriptive qualitative research carried out with family caregivers of elderly people diagnosed with AD in a municipality in the Northwest region of Paraná, Brazil. It has an estimated population of 91,950 inhabitants (IBGE 2022), fully covered by 24 Family Health Strategy (ESF) teams, distributed in 16 Basic Health Units (UBS). The data were collected between the months of March and July 2022.

The inclusion criterion were: being the main family caregiver of the elderly person with AD in the last three months and being 18 years of age or older. The exclusion criterion was established: having some comorbidity that would hinder communication between researcher and interviewee. For the selection of participants, the researchers requested authorization from the Municipal Health Department of the study municipality and, later, they will connect the community health agents (CHA) so that, with their help, possible participants could be identified.

The initial contact with the participants took place through a home visit with the CHA responsible for the coverage area. At the time, the family caregiver was invited to participate in the study, and the Free and Informed Consent Form (ICF) was read, explaining the objective of the research, its methodological aspect, risks and benefits. In cases of acceptance, the participant can choose to participate at that time or schedule the interview on a day and time of their preference. It is noteworthy that all of them agreed to participate at the time of the home visit.

It is noteworthy that during the initial contact with the participant, as well as during the course of the interview, researchers and participants made use of Personal Protective Equipment (PPE), especially the use of masks, 70% alcohol gel and the distance of 1.5 meters between the parties, according to the recommendations of the Ministry of Health and the World Health Organization to contain the spread of COVID-19. In addition, all the material used for the development of the interview, namely: pen and MP3 audio device, were sanitized before and after use.

At the time of the interview, the participants read the ICF and, after their consent, they were invited to sign the informed consent form in two copies of the same content. Subsequently, the participant was invited to answer a questionnaire for sociodemographic characterization: gender, age, marital status, religion, family income, employment status, and clinical characteristics: comorbidities, use of continuous medications, alcoholism, smoking, physical activities, and body mass index (BMI).

For the descriptive stage of the interview, the participant was asked for authorization for the audio recording of the interview, explaining that it would be used later for the

transcription of the interview and data analysis. The face-to-face interview was guided by the following question: tell me what it was like for you to take care of your family member with AD during the COVID-19 pandemic. Support questions were used, such as: what were the weaknesses and potentialities that you found in daily care? Has the COVID-19 pandemic impacted your daily care for your family member with AD? If so, how? Tell me more about it. The interviews will take place until the moment that no new information has emerged in the process of data collection and analysis, thus reaching theoretical saturation.

The interviews were transcribed in full after their completion, organized and analyzed in the MAXQDA Plus 2020 software. For data analysis, the methodological framework of the content analysis proposed by Bardin was used. The analysis process followed the pre-analysis, with transcription, organization, studies of the texts, floating reading, data separation with initial identification of relevant aspects.

Subsequently, the data were submitted to an exploration stage where the classification and aggregation of the data was developed, with identification, through colors, of the common and more specific terms, giving rise to the previous categories. Finally, in the treatment of the data, the categories were deepened through the articulation of the findings, constantly considering the objective of the investigation. Thus, the following central category was identified: *Home care for the elderly with Alzheimer's disease: the impact of the COVID-19 pandemic on the execution of care*, complemented by the categories: *Caring for the elderly with Alzheimer's: perception and perspectives of care before the pandemic* and *The pandemic period: potentialities and challenges in the daily care of the elderly with Alzheimer's.*

The study was approved by the Permanent Committee for Ethics in Research with Human Beings CAAE: 52244321.7.0000.9247, approval protocol: 5.029.324. To ensure anonymity, the strata of the participants' reports are identified by the letter P for participant followed by an Arabic numeral which refers to the order in which the interviews were conducted (e.g., P1).

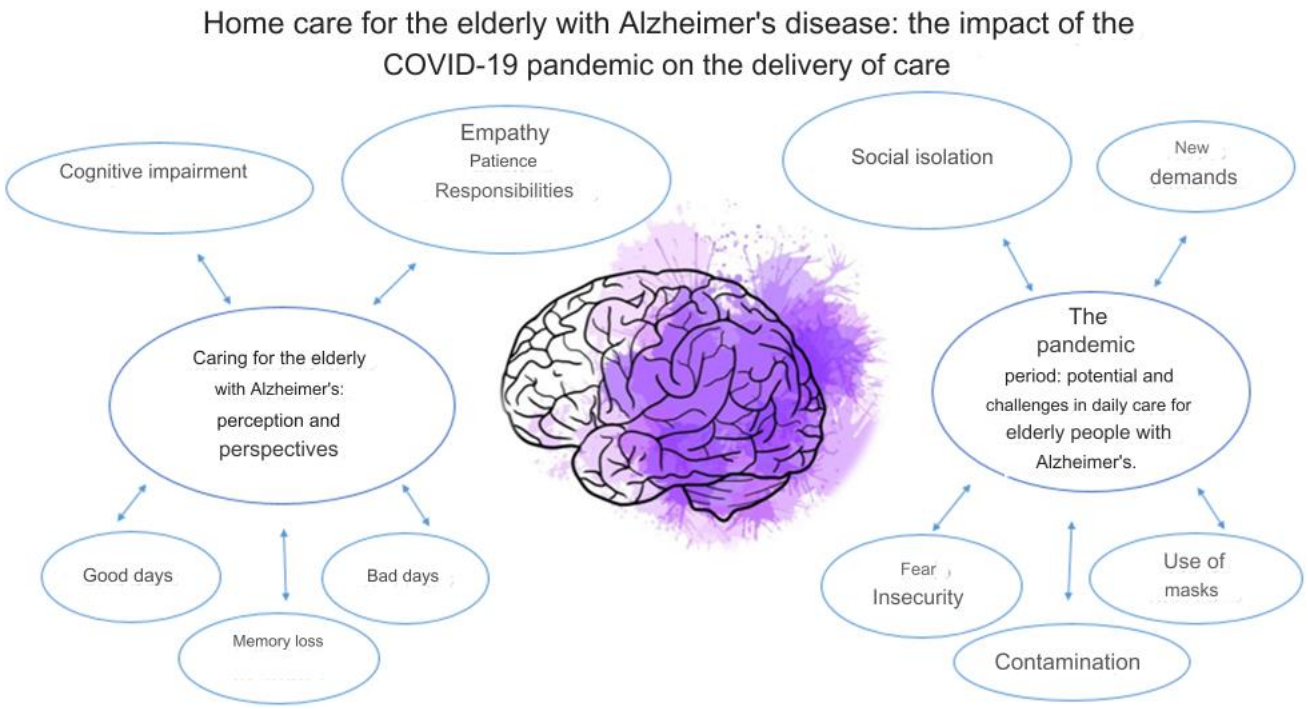
RESULTS

12 family caregivers of elderly people with AD participated in this study. Of these, four were male, aged between 39 and 70 years, ten were married, and two were single, seven Catholic, nine considered themselves white, two brown and one black, nine reported having attended high school and three higher education. Two had Diabetes Mellitus, two had Systemic Arterial Hypertension and two had heart disease, one reported routine tobacco use and one had alcoholism. Regarding the care time of the elderly with AD, there

is a variance from four months to five years. As for the family bond, two were spouses, eight sons, a daughter-in-law and a granddaughter.

The thematic categories evidenced during the data analysis process are presented below:

Figure I: Illustrative diagram of the central category and its subcategories.



The Author (2023)

CARING FOR THE ELDERLY WITH ALZHEIMER'S: PERCEPTION AND PERSPECTIVES

The daily care of the elderly with Alzheimer's disease was perceived by the family caregivers as a challenging task that is characterized according to the daily experience, with this experience being a great oscillation between good and bad days.

> [...] There are very bad days that he doesn't know where he is, he doesn't recognize his own house, he doesn't recognize his grandchildren, the people on the street, he doesn't remember that he's already eaten, sometimes he has lunch three times, sometimes he says he's already eaten and doesn't eat again and there are days when it's great it doesn't even seem like there's anything, very good days, So it's very relative, each day is a day, they have a very large oscillation from one day to the next [...] (P2).

In daily care, caregivers experienced some weaknesses, such as the risk of letting the elderly go out alone and get lost, a classic sign of Alzheimer's disease. And in this scenario, family caregivers will seek to take their loved ones for a walk, which has also sometimes been perceived as a challenging task.

> [...] The difficulties were and are to be able to keep him indoors, not to let him go out alone, I always take him for a walk practically every day, but letting him go alone is not possible, and sometimes he arrives in places he already wants to come back, come back than go, it is complicated [...] (P2).

However, the lack of memory caused by the disease also leads to impairment of basic human needs such as hygiene, comfort and food.

> [...] We always try to help as much as possible, because she forgets, her memory is slow, she doesn't remember things, so I help her in the bath, for example, sometimes she forgets that she has already taken a shower, sometimes she takes it alone, sometimes she needs help, there is the issue of taking care of her not to fall into the bathroom and so we go on living [...] (P1).
> [...] taking care of those who have Alzheimer's is not an easy task, they forget things, moments, here I have to take care of them all the time, for lunch I have to call about 10 times because sometimes they think they have already eaten, they forget that they have to take a shower, they forget basic care and essences of a day to day, so we take care of everything [...] (P6).

In addition to the limitations and weaknesses found in daily care, being of the opposite sex is perceived by the family caregiver as an additional limitation, since personal care such as hygiene and comfort is perceived as a complicating factor for both those involved in care. Nevertheless, the lack of knowledge about the disease and the lack of experience with care reflect as significant limitations in daily care.

> [...] It's difficult, due to inexperience, lack of knowledge of the disease, being of the opposite sex and not being able to help with hygiene care, even being a mother is very difficult, it's complicated for both parties, for respect and also for those who are ashamed, right? Because at 90 years old, it is not common for sons to take care of their mother [...] (P4).
> [...] Sometimes I feel a little lost, I don't know how to deal with this disease, how to help her, I don't have knowledge about this disease, so I seek help from doctors to know what to do [...] all of this is new to me, new to her, and we are facing this new phase together, we are going through this together, But it is difficult to take care of an unknown disease like this [...] (P8).

Caring for a family member with AD reflects on a job that requires, in addition to empathy, patience and responsibility, time and dedication, in this sense caregivers feel a lack of support and help from the family in this process, with care being the responsibility of only one person, which leads to overload and sometimes dissatisfaction with other family members.

> [...] The problem is that I am the closest, I am the one who takes care of the mother on a daily basis and sometimes I feel the lack of support from my sisters who live in other cities. They do not participate in care on a daily basis and when they come to visit or call they criticize what is being done, but they are not willing to help in any way, they ignore the problem [...] it would be easier if there was more support from the family [...] (P4).

In addition to the weaknesses and limitations perceived and experienced by family caregivers, they face difficulties in hiring health professionals for home care, realizing that they are not always prepared to develop such activities, which require patience, technical knowledge and empathy for the other.

> [...] caregivers are also complicated, people don't take care of them as they should, they don't have much to do with the other's father, they think that everything they do is already too much, most of these caregivers lack professional preparation, preparation and respect for the elderly [...] it's no longer a job, it's no longer an old man, it's someone's father, he is important to someone, so with caregivers it is also difficult to find someone who really cares and who we can trust to have empathy [...] (P2).

Care in daily life also refers to following the guidelines of health professionals to the letter, realizing that they know what they are guiding and that it is best to follow the guidelines.

> [...] I try to follow the guidelines of doctors and health professionals, we comply because they are in the area, they know what they are advising [...] so I take care of her this way, I give her medications at the times that the doctor ordered, and I take care of the other things that are also important: food, hygiene, exercise, walking, these things [...] (P1).

Notwithstanding the fact that experiencing home care for the elderly with AD reflects on the family caregiver, a feeling of sadness and pity, especially when the sick individual begins to be unaware of the family and the people in their daily life

> [...] It's sad to see my father not remembering people, grandchildren, friends, it's very sad, we would like to be able to help, you know? But what to do, right? [...] (P2).
> [...] It's very sad to see her forget, not recognizing the people (people she liked the most), it's very sad, it hurts her, she doesn't know who she is and who anymore, she doesn't recognize the people around her [...] (P3).

The classic symptoms of the disease such as losing one's recent memory, and repeating the same thing several times are also perceived as a complicating factor, which over time becomes tiring in the eyes of caregivers.

> [...] They forget very quickly about recent things, right? They only talk about things from the past and about people who have passed away, they talk all the time, we explain that this has passed, and it doesn't take ten minutes to talk again, sometimes it gets tired, stresses, always hearing the same thing, and knowing that what he is saying makes no sense, it's sad we feel bad for him and for us too, It's hard to see a father in this situation, but to be honest this is quite tiring [...] (P8).
> [...] She tells many things from the past and sometimes it becomes tiring to hear the same thing over and over again, as well as to help look for what, in her head, is missing [...] (P5).

THE PANDEMIC PERIOD: POTENTIALITIES AND CHALLENGES IN THE DAILY CARE OF THE ELDERLY WITH ALZHEIMER'S

The COVID-19 pandemic is perceived by caregivers as a period that significantly compromised daily care. The fear of contamination in the face of the life habits and behaviors of the elderly favored a negative perception of childbirth by caregivers at this moment.

> [...] the pandemic impacted everyone's lives, including the Alzheimer's patient, as the lack of awareness made it (even more) difficult to understand the problem, and our care was redoubled so as not to transmit (if positive) COVID-19 [...] it was difficult to make her understand the importance of wearing a mask, the prohibition of hugs, she didn't understand, this care with hygiene and distancing was difficult [...] (P5).
> [...] I work in the health area, so the fear of contamination was even greater, I got home and removed all my clothes before entering, I lived with a mask. I did everything, it was terrible, desperate [...] (P12).

Health demands, such as going to medical appointments, were also seen as a complicating factor during the pandemic.

> [...] taking her to the doctor to control the disease was another problem, many times the appointments had to be postponed, there was a lot of fear of leaving the house with her, and getting contaminated, so we were trying to take her home, without going out, without going to the doctor, just in extreme need [...] (P3).
> Moving with her to take her to the doctor was very complicated, I took her, but I couldn't keep up, I was outside the clinic and she was there alone. It was very difficult to live this, even more so being an elderly woman and having to go to see it alone, I had no way to understand, but I had to accept [...] (P11).

In the face of the pandemic, family caregivers realized that in addition to the demands and care that AD requires, they needed to worry about and protect the elderly from another disease, which brought risks and a lot of fear to people.

> [...] the pandemic brought even more limitations, in addition to Alzheimer's we had to take care of and protect ourselves from another disease, in addition to the ones he already has, we had to protect him, protect him from another evil [...] (P9).
> It was even more difficult because I couldn't catch it, it was just to catch it and die, so it was another difficult task [...] leaving the house was difficult, going to the doctor was a nightmare, not being able to let him leave the house and he didn't understand anything, you know, I thought it was our evil [...] (P10).
> [...] Covid has always hindered us, staying at home to be more careful with it, it was a little different, we need to redouble care, protect ourselves from the disease, it was complicated, a mission for more than we have gained [...] (P7).

Even more complicated was when the elderly, even with all the care of caregivers, still contracted the COVID-19 virus, a situation that brought even more concern to caregivers.

> [...] in June 2022 she contracted the COVID disease precisely because of the inappropriate use of the mask and other care, it was very difficult, because her husband also contracted it, and we to take care of it? It was a challenge, an anguish mixed with fear and concern about what could happen, even more so because she was elderly, but with outpatient treatment and home care, she was well [...] (P3).

It is possible to see that regardless of the period of care, whether in a pandemic or not, caring for the family member with AD is a difficult task that also impacts the way the caregiver perceives, behaves and means this care.

> [...] Alzheimer's causes a lot of sadness and suffering for family, friends and everyone who lives with the person with it, care is very difficult and hurts a lot those who care for it, the psychological knows? [...] I think that every day she is becoming more distant, she can't interact with people even with family members and this is very sad, very difficult [...] mood swings, lack of organization, manias, fear of being alone, all this influences daily life [...] (P9).
> [...] taking care of a person with Alzheimer's is much more than caring, you know? It's love, it's affection, it's having patience, that's what I feel for my mother and that's why I take care of her, there are days when things are easier, there are days that are very difficult and so we live one day after another [...] (P6).
> [...] I try to take care of her with affection, with love, to be patient, I try to do my best to make her feel good, and today we try to be better than yesterday and so we go on, there are good days, others bad, but it will pass [...] (P7).
> [...] Care has always been difficult, the person with Alzheimer's disease isolates himself, it is a complicated phase, which both the person and the people who care need to adapt. In the pandemic it was more difficult for sure, but before it was already complicated and now it continues to be [...] (P12).

Faith and hope that better days would come was essential to maintain strength and courage during the pandemic.

> [...] it is necessary to have faith in God and believe that the bad times will pass, as in the pandemic, it was difficult, very difficult but it has passed [...] (P4).
> [...] I was very afraid, but I also had a lot of faith, that all that would pass and that better days would come, my faith strengthened me, and made me face the barriers [...] (P10).

Finally, this research showed that the participation of the health team in the care process of an elderly person with AD was essential, both in person and through telehealth.

> The staff at the health center helped a lot in caring for the mother, this was essential, they always visited her and did all the care, the guidance, we felt safer [...] (P1).
>
> We were very well assisted during the pandemic by the staff at the health center, the team never left us helpless, they were always here [...] it was a very great and very important support for us [...] (P10).
>
> .
> Technology has made care much easier, both during the pandemic and now, WhatsApp, contact with health professionals, today I have contact with the Community Health Agent by cell phone, she makes visits, schedules appointments, the best me casa comes to serve her, whenever I need something technology helps me, this is also important [...] (P 11).

DISCUSSION

The results showed that caring for an individual with AD is always the responsibility of a family member, especially the children who become responsible for the daily care as well as for the other demands of the elderly, in this study more than half of the participants were children, which corroborates studies that also investigated the care in AD.[3]

Being affected by a neurodegenerative disease such as AD is a complex condition that leads the individual to gradually compromise their physical and cognitive functions, being at first a great oscillation of symptoms and behaviors, which leads to the perception that some days are good, others bad.[5]

By taking into account the particularities of the AD disease, especially the progressive loss of memory, family caregivers play a fundamental role, since they develop all the care pertinent to the daily life of the elderly.[6] The loss of memory, as well as the change in the behavior of the elderly, causes them to progressively lose the care of basic human needs such as food, hygiene and comfort, and the family caregiver is responsible for providing this care.[3]

In this study, it was possible to understand that such peculiarities occur routinely in the different families investigated, the Brazilian literature on daily care of elderly people with AD also evidenced these results1-3, thus allowing the generalization of these findings in the investigated theme. For these researchers, family care tends to assume responsibility for this care, which progressively extends according to the evolution of the disease, making the elderly increasingly dependent on help for the development of activities of daily living (ADL).[1-3] From this perspective, in addition to memory loss, symptoms include mental or spatial confusion, loss of decision-making, changes in behavior, mood and personality, and progressive loss of ADLs such as work and social activities.[7]

The lack of knowledge about the disease as well as the lack of training and preparation for daily care was also understood as a challenge by the participants, similar results were also evidenced in a study published in 2018 which showed that there is still a need to train and prepare the population for this care, with nursing being the link and responsibility for this work "the work performed by nursing must have as its ensuring the physical and mental health of the caregiver, using mechanisms that aim to promote health, especially in cases of dementia, improving the quality of life of all those involved in the care of the patient and the elderly themselves".[1]

Caring for an elderly person with Alzheimer's was elucidated in this study as a task that generates physical and emotional overload for the family caregiver, especially when this is the only responsible caregiver. This burden is due to a change in routine and habits,

as well as the lack of freedom and social life after the disease, requiring an abdication of the previous life, such peculiarities can favor a negative perception of care and negatively influence the physical and psychological health of both the care and the individual being cared for.[3]

The COVID-19 pandemic, experienced by Brazil and the world since 2020, has brought even more concern and limitations in the daily care of the elderly with AD, since the elderly public has become the most vulnerable risk group to contamination and complications from the coronavirus8-9, from this perspective, the world has witnessed the significant loss of elderly people during the pandemic, most of the time with associated degenerative comorbidities, as well as AD, which was a double blow for family members and/or caregivers of these elderly people10.

From the perspective of daily care, this study allowed us to identify that the pandemic brought fear, limitations and made daily care even more difficult, especially with regard to routine care, such as the use of masks, a fact pointed out by the participant care as something complex, since the elderly did not understand, did not accept and did not remember the need and importance of using this equipment to protect against the disease. In this sense, the use of masks by the elderly during the pandemic was also pointed out by other studies as a complex equipment and sometimes with a greater potential for contamination due to inappropriate use and non-use of the equipment.[8-11]

The mandatory use of masks has become a complex task for the entire population, however, for the elderly diagnosed with AD and other dementias, this process has become even more difficult, since in addition to the special need for care and/or supervision of activities of daily living, they began to experience the need for specific care against COVID-1910-11. Despite the loss of recent memory, the lack of motor skills, as well as the difficulty in understanding, made the elderly more vulnerable and susceptible to contamination12-13.

Another limitation identified in this study is due to social distancing and the need for home isolation, family care reported that the elderly could not understand why they could not leave the house or even receive visits from loved ones, this need for care was sometimes seen as a limitation imposed by the caregiver, and it was not possible to explain to the elderly the emerging need for this practice.[8-14] From this perspective, protecting the elderly from COVID-19 was another attribution linked to family caregivers in daily care.

As potentialities experienced in this period, faith in God, hope for better days and the support of health professionals became essential, strengthening the care process of the elderly with AD. Previous studies that investigated AD during the pandemic period observed that the physical and mental state of family caregivers of elderly people with AD was fragile,

however, in some cases there was also the support of the health team, through the dissemination of information and assistance in daily care15-16, favoring the provision of care with more quality and effectiveness.

Likewise, the literature notes the emerging need to expand health care aimed at family caregivers of elderly people with AD and/or other dementias, since the lack of information and knowledge favors the occurrence of complications and consequently complexity of care16.

In this sense, this study also shows that there is an emerging need for updates in the context of care for elderly people with AD, updates aimed at the caregiver, which favors the execution of home care aimed not only at the elderly but also at the hospital.

In agreement, Alzheimer Disease International (2019) draws attention to the need to implement psychosocial support networks and support for this public, in order to minimize the occurrence of mental illness in family caregivers, as well as to favor quality care for the elderly. The implementation of support networks can also favor a significant reduction in caregiver stress and burden, which can also be implemented virtually, since we live in a computerized environment, where technology and access to information are found in the palm of our hands[11,16-17].

A study published in 2022 that aimed to report the experience of the extension action of telephone calls to family caregivers during the period of social isolation due to the pandemic caused by COVID-19, showed that the use of telephone calls during the pandemic period allowed the identification of the strengths and weaknesses existing in the daily care of family caregivers, realizing that the physical and emotional overload of this audience had a significant increase during the pandemic. Nevertheless, this study concluded that caregivers need support and attention in the execution of home care actions, in order to ensure quality care with problem-solving capacity, whether in normal times or in pandemic periods, such as the one experienced by COVID-19[18].

In view of this, the work of nursing stands out, a profession seen as the link between the population and the health services, as well as the one that care is the essential part of the profession. In this sense, nursing inserts a look at care that goes beyond knowledge and care techniques, favoring health promotion and disease prevention through work that values the uniqueness of human beings and their families[19]. Thus, nursing can be seen as the model professional category for the implementation of the support network for family caregivers of elderly people with AD and/or other dementias.

In view of the demands arising from the pandemic, as well as the gradual and irreversible course of AD, family caregivers of these elderly people suffer stress and

significant work overload on a daily basis, which can lead this public to physical and mental illness[14-15]. As AD evolves, the responsibilities of caregivers increase, which can further favor the risk of illness. In this sense, it is noteworthy that such risks were more significant during the pandemic, especially due to the complexity of the period experienced.

From the findings of this study, it was possible to perceive that with the increase in the population's life expectancy, AD is increasingly emerging, and in this sense it requires more and more attention, preparation and training for care, both at home and at other health care points. Home care, whether developed in pandemic periods or not, reflects on a complex activity that requires, in addition to training, empathy, responsibility, and patience on the part of those who care.

The low number of participants can be considered a limitation of this study, and it is not possible to generalize the findings, however, they can be considered valid, since it allows to demystify the care of the elderly with AD in the home environment, as well as to understand how family caregivers perceive, behave and signify this care in their daily lives. Understanding this phenomenon in the pandemic period also contributes to understanding the fragility of the elderly with AD in the face of a new threat, the peculiarities of care, as well as the limitations and fragilities exposed by caregivers.

FINAL CONSIDERATIONS

The results showed that caring for the elderly with Alzheimer's, whether in pandemic periods or not, reflects on a challenging task that requires physical, technical, and emotional skills from the caregiver that favor daily care. The lack of knowledge about the disease, the overload of care, as well as being of the opposite sex, are perceived as weaknesses in daily life, however, they are characterized as a situation that, even though it is difficult, is gratifying, since in addition to care, the family bond, love, affection and respect for the elderly are involved in this process.

The pandemic period brought limitations, fears, insecurities and new responsibilities, especially in the face of the risk of contamination of the elderly. This was meant as a complex period that in some cases was minimized by professional support, elucidating the importance of creating bonds and support between family and health team.

In this sense, understanding the experiences and perspectives of family caregivers about the daily care of the elderly with AD allows us to demystify care, as well as to broaden the view of health professionals and the community in general about the peculiarities of this process and the importance of care. Thus allowing the elucidation of gaps that need attention, care and professional education that envisions quality care.

Therefore, the need to disseminate information about the daily home care of elderly people with Alzheimer's is dazzled, in order to contribute to the evolution of knowledge, as well as to the organization and reorganization of educational practices and care in the field of health. Taking care of those who care, as well as offering professional, personal and emotional support, contributes not only to the caregiver but also to the quality of care offered to the elderly.

REFERENCES

1. Silva, M. I. S., Alves, A. N. O., Salgueiro, C. D. B. L., & Barbosa, V. F. B. (2018). Doença de Alzheimer: repercussões biopsicossociais na vida do cuidador familiar. *Revista de Enfermagem UFPE on line*, 12(7), 1931–1939.

2. Rodrigues, T. de Q., Castro, A. da S. de, Conceição, T. F. da, Leite, J. G. A. M., Ferreira, V. H. S., & Faustino, A. M. F. (2020). Impacto da Doença de Alzheimer na qualidade de vida de pessoas idosas: revisão de literatura. *Revista Eletrônica Acervo Saúde*, 12(4), e2833. Recuperado de https://acervomais.com.br/index.php/saude/article/view/2833

3. Mattos, E. B. T., & Kovács, M. J. (2020). Doença de Alzheimer: a experiência única de cuidadores familiares. *Psicologia USP*, 31(1986), 1–11.

4. Costa, R., Lino, M. M., Souza, A. I. J., Lorenzine, E., Fernandes, G. C. M., Brehmer, L. C. F., Vargas, M. A. O., Locks, M. O. H., & Gonçalves, N. (2020). Ensino de enfermagem em tempos de COVID-19: como se reinventar nesse contexto? *Texto Contexto Enfermagem*, 29(e20200202), 2–4.

5. Sales, J. N. F., Miranda, R. N. C., Silva, M. A. S., Batista, E. S., Silva, J. R., et al. (2019). A enfermagem no cuidado com o idoso portador de Alzheimer. *Revista Eletrônica Acervo Saúde*, 18, e235.

6. Anjos, Z. S., Lohmann, P. M., Medeiros, C. R. G., & Brietzke, A. P. (2022). O cuidado de enfermagem na doença de Alzheimer: uma revisão integrativa. *Research, Society and Development*, 11(7), e37911728874. https://doi.org/10.33448/rsd-v11i7.28874

7. Alzheimer's Association. (2018). Alzheimer's Disease Facts and Figures. *Alzheimer's & Dementia*, 14(3), 367–429.

8. Junior, J. C. P. R., Melo, G. O., Cardoso, V. N. S., Franca, G. S., Silva, G. O., & Gentil, V. N. (2021). O impacto do coronavírus na doença de Alzheimer: uma revisão narrativa. *Revista Eletrônica Acervo Saúde*, 13(8). https://doi.org/10.25248/REAS.e8470.2021

9. Kontoagelos, K., Economou, M., & Papageorgiou, C. (2020). Mental health effects of COVID-19 pandemia: A review of clinical and psychological traits. *Psychiatry Investigation*, 17(6), 491–505.

10. Bianchetti, A., Rozzini, R., Guerini, F., Boffelli, S., Ranieri, P., Minelli, G., Bianchetti, L., & Trabucchi, M. (2020). Clinical presentation of COVID-19 in dementia patients. *The Journal of Nutrition, Health & Aging*, 24(6), 560–562. https://doi.org/10.1007/s12603-020-1389-1

11. Mattos, E. B. T., Francisco, I. C., Pereira, G. C., & Novelli, M. M. P. C. (2021). Grupo virtual de apoio aos cuidadores familiares de idosos com demência no contexto da COVID-19. *Cadernos Brasileiros de Terapia Ocupacional*, 29, e2882. https://doi.org/10.1590/2526-8910.ctoRE220

12. Huali, W., Li, T., Barbarino, P., Gauthier, S., Brodaty, H., Molinuevo, J. L., Xie, H., Sun, Y., Yu, E., Tang, Y., Weidner, W., & Yu, X. (2020). Dementia care during COVID-19. *The Lancet*, 395(10231), 1190–1191. https://doi.org/10.1016/S0140-6736(20)30755-8

13. Schapira, M., Cohen, G., Guajardo, M. E., Martinez, D., Schapira, M., Seinhart, B. D., & Soderlund, M. E. (2020). Reflexiones sobre vivir con demencia en épocas del COVID-2019. *Archives of Gerontology and Geriatrics*, 34(1), 19-20.

14. Mattos, E. B. T., & Kovács, M. J. (2020). Doença de Alzheimer: a experiência única de cuidadores familiares. *Psicologia USP*, 31, e180023. https://doi.org/10.1590/0103-6564e180023

15. Holmes, E. A., O'Connor, R. C., Perry, V. H., Tracey, I., Wessely, S., Arseneault, L., Ballard, C., Christensen, H., Cohen Silver, R., Everall, I., Ford, T., John, A., Kabir, T., King, K., Madan, I., Michie, S., Przybylski, A. K., Shafran, R., Sweeney, A., Worthman, C. M., & Bullmore, E. (2020). Multidisciplinary research priorities for the COVID-19 pandemic: A call for action for mental health.

16. Chan, E., Gobat, N., Kim, J. H., Newnham, E. A., Huang, Z., Hung, H., Dubois, C., Hung, K., Wong, E., & Wong, S. (2020). Informal home care providers: The forgotten health-care workers during the COVID-19 pandemic. *The Lancet*, 395(10242), 1957-1959. https://doi.org/10.1016/S0140-6736(20)31254-X

17. Alzheimer's Disease International – ADI. (2019). *World Alzheimer Report: Attitudes to dementia*. London: Alzheimer's Disease International.

18. Oliveira, S. G., Oliveira, R. G., Fonseca, M. R., Mello, F. E., & Almeida, C. (2022). Diálogo com os cuidadores familiares a partir de ligação telefônica na pandemia. *Extensio: Revista Eletrônica de Extensão*, 19(41), 91-104. https://doi.org/10.5007/1807-0221.2022.e82278

19. Batello, G. V. V. A. T., Guimarães, M. A. S., Pereira, I. A. C., Bandeira, M., & Nunes, D. P. (2020). Cuidadores de idosos em situação de pandemia: Reflexões sobre o cuidar e ser cuidado. In R. F. Santana (Org.), *Enfermagem gerontológica no cuidado do idoso em tempos da COVID-19* (2ª ed., pp. 20-24). Brasília, DF: Editora ABEn. https://doi.org/10.51234/aben.20.e02.c03

THE IMPORTANCE OF VITAMIN A DURING EARLY LIFE AND THE IMPACT ON INFANT MORTALITY

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Andressa Soares[1], Adryana Cordeiro[2] and Andrea Ramalho[3]

ABSTRACT

The Under-Five Mortality Rate (MMR5) measures the number of deaths per thousand live births in this age group, reflecting aspects such as malnutrition and quality of maternal and child health care. Despite global efforts, the 5MWR is still high in developing countries, and about 48.1 million deaths are projected in this population by 2030. In Brazil, the 5MMR presents a worrying situation due to its slower reduction in recent years, with a high occurrence of deaths from preventable diseases. Vitamin A (VA) is essential for the immune system, cell development, and maintenance of the body. Vitamin A deficiency (VAD) mainly affects pregnant women, newborns and children under five years of age, and can cause blindness, infections and congenital malformations. Globally, millions of children and pregnant women suffer from VAD, which negatively impacts child growth and survival. In Brazil, the prevalence of VAD is significant, with 10 to 20% of children at risk, and it is a moderate to severe public health issue. Measures are carried out at the government level, such as the promotion of breastfeeding, supplementation and food enrichment. However, few studies report the impact of the consumption of fortified foods in the country, there are controversies regarding the effectiveness of supplementation in the long term, especially after childbirth, and breastfeeding remains insufficient, factors that contribute to the permanence of VAD. It is essential to improve the maternal and child care system in Brazil to reduce infant morbidity and mortality, especially in the most vulnerable populations. The adequacy of the VA, both for the mother and the baby, is essential to ensure health during the first years of life.

Keywords: Vitamin A deficiency. Infant mortality. Child health.

[1] Nutritionist/UFRJ
Master in Human Nutrition/UFRJ.
Scientific Researcher at NPqM/UFRJ
[2] Nutritionist/UNIRIO
PhD in Sciences/UFRJ
Scientific Researcher at NPqM/UFRJ
Professor at the International Ibero-American University
[3] Nutritionist/UFPE
PhD in Public Health/FIOCRUZ
Full Professor and Scientist/UFRJ
Coordinator of NPqM/UFRJ

INTRODUCTION

Infant mortality, especially in children under five, is an important public health indicator. The mortality rate in this age group (5MMR), which includes neonatal and post-neonatal deaths, reveals the level of care and health of a population, in addition to serving as a basis for the development of prevention policies (UN, 2024a). Although global infant mortality rates are decreasing, the pace of this reduction is still insufficient in many countries, especially developing countries such as Brazil, which has experienced a slower decline in infant mortality since 2009 (UN, 2024b; WHO, 2023).

Among the main causes of death of children in Brazil are perinatal conditions, congenital malformations, and infectious diseases, highlighting the importance of targeted interventions (MOURA et al., 2022). In this context, proper nutrition in the first years of life plays a key role. The period of the first 2,200 days of life is recognized as fundamental for the child's future health (ALMEIDA et al., 2022).

Vitamin A (VA) emerges as one of the essential nutrients in this process, with a direct impact from conception to the first years of the child's life. Its functions include promoting healthy growth and preventing infectious diseases (MEZZANO et al., 2022). However, vitamin A deficiency (VAD) is a public health problem, with serious consequences for both pregnant women and children, and is a risk factor for infant mortality (WHO, 2011a).

Given the importance of vitamin A in child development and in reducing the risks associated with mortality, this book seeks to explore the mechanisms of vitamin A transmission throughout child development, as well as to discuss the implications of vitamin A deficiency for maternal and child health. Understanding this relationship is essential for the evaluation of supplementation policies and the implementation of preventive care measures aimed at reducing infant mortality.

MORTALITY IN CHILDREN UNDER FIVE YEARS OF AGE

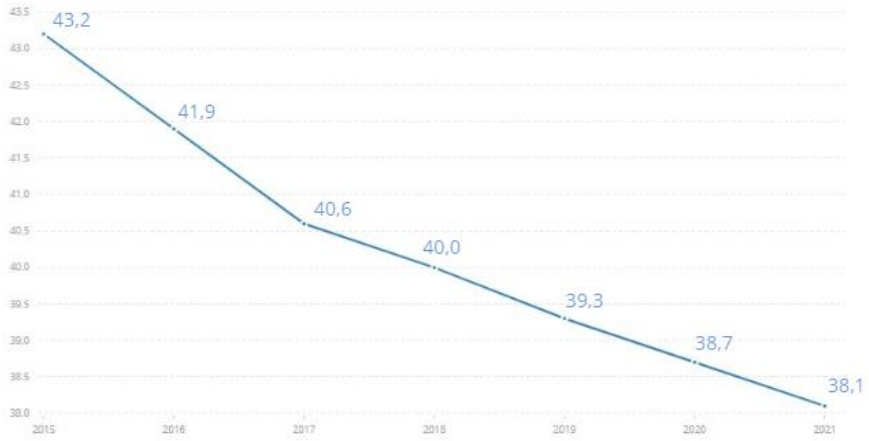
The 5MMR is defined as the number of deaths of children under five years of age, per thousand live births, in a population in the year considered. It expresses, in general, environmental aspects that condition child malnutrition, such as poverty, food insecurity, malnutrition during pregnancy, breastfeeding, complementary feeding, infectious diseases, water, hygiene and sanitation, as well as the infections associated with it, in addition to access and quality of resources available for maternal and child health care, determinants of mortality in this age group (WHO, 2024; DHAGE, 2024). This rate is a key indicator in assessing the health situation of a population, and is essential for the development of

preventive strategies aimed at reducing the risk of death in this age group (DHAGE, 2024; FRANÇA et al., 2017; BUGELLI et al, 2021)

It is possible to observe the importance of the 5RM through the global effort to reduce this index. In 2015, the United Nations (UN) General Assembly established the Sustainable Development Goals (SDGs), which include an infant mortality target, in which all countries must eradicate deaths in children under five years of age, in addition to achieving a 5MWR of 25 or fewer deaths per 1,000 live births by 2030. (DHAGE, 2024; UN, 2024a; SHARROW et al, 2022)

With these deployments, the worldwide RMT5 has been shrinking in recent years, however, there is still a long way to go. In 2015, when the SDGs were implemented, the rate was 43.2 per 1000 live births. In 2017, this rate was 40.6, indicating 5.7 million deaths per year. In 2021, this figure appears to have reduced to 38.1 (approximately five million deaths per year), but progress has been slow in recent years, particularly in developing countries *(Chart 1)* (UN 2024b; WHO, 2023). In 2022, 4.9 million deaths of children under five years of age were recorded, of which 2.3 million occurred during the first month of life and 2.6 million between 1 and 59 months of age (UNICEF., 2024). If current trends continue, 48.1 million under-five deaths are projected to occur between 2020 and 2030, almost half of them projected to occur during the neonatal period (UN, 2024b; WHO, 2023; SHARROW et al, 2022).

Graph 1 - World mortality rate, children under five years of age per 1,000 live births

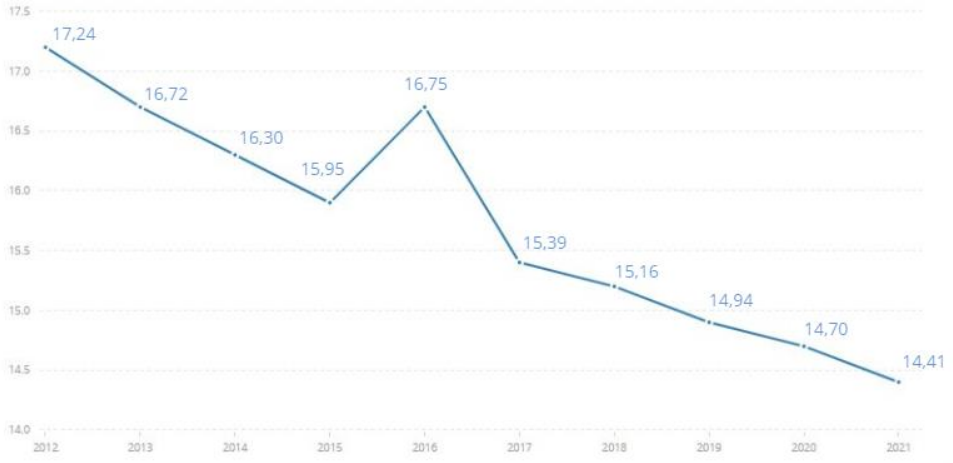


Source: Adapted from WHO, 2023 and ONE, 2024b

Despite being one of the countries that met the SDG target, the mortality of children under five years of age in Brazil foreshadows a worrying situation. The 5RM in Brazil shows a decreasing pattern (UN, 2024b; WHO, 2023; FRANÇA et al, 2017), however, since 2009, Brazil has been experiencing a slower decline in infant mortality, which has remained at high levels and has significant regional disparities. In 2016, the country recorded an

increase in the mortality of children under five years of age, which interrupted a 25-year period of downward trend (Graph 2) (UN, 2024b; WHO, 2023; BUGELLI et al, 2021).

Graph 2: Mortality rate in Brazil, children under five years of age per 1,000 live births



SOURCE: Adapted from WHO, 2023 and UN., 2024b

Deaths from communicable diseases, maternal, neonatal and nutritional disorders are the main causes of death in children under five years of age in Brazil, and in general can be considered preventable. On the other hand, congenital anomalies, with relatively stable rates in Brazil, occupy the first place among the causes of death, especially in states with lower mortality rates, approaching the profile found in high-income countries (SECRETARIA DE VIGILÂNCIA EM SAÚDE E AMBIENTE, 2022; FRANÇA et al, 2017).

METABOLIC ASPECTS OF VITAMIN A

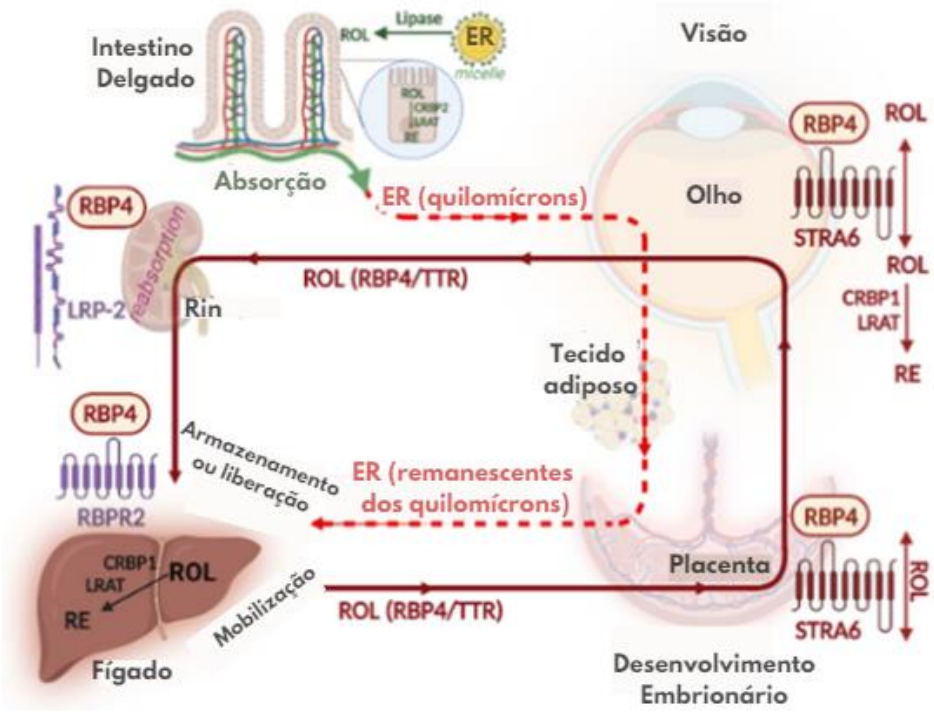
Dietary molecules with VA activity exist in two forms: preformed VA and provitamin A. Preformed VA molecules are mainly retinol and retinyl esters, usually obtained from animal-derived foods, while provitamin A carotenoids are obtained from plant-derived foods, which are later converted to the active form (CHEN et al, 2023; YADAV, 2022; CARAZO et al, 2021; TANUMIHARDJO et al, 2016)

ABSORPTION

The illustrative schematization of the absorption, transport and metabolism of the AV is shown in Figure 1. In the lumen of the intestine preformed VA and provitamin A carotenoids are released from the food matrix and emulsified with dietary fatty acids and bile acids, forming mixed micelles that reach the border membrane in intestinal brush (O'CONNOR, 2022; EFSA, 2015).

Retinol is absorbed by enterocytes and esterified with fatty acids to generate retinyl esters (ER) (CHEN et al, 2023; YADAV, 2022; MOLTEDO et al, 2021). The most important enzyme involved in this synthesis in the gut, as well as in other tissues, is lecithin: retinol acyltransferase (LRAT) (O'CONNOR, 2022), along with cellular retinol-binding protein 2 (CRBP2). Retinyl esters are then incorporated into chylomicrons through the activity of microsomal triglyceride transfer protein (MTP) and transported in the lymph and blood. In peripheral tissues, chylomicrons undergo remodeling, and retinyl esters are hydrolyzed by lipoprotein lipase (LPL) and taken up by target organs, such as the eye, placenta, and adipose tissue, which retains 10 to 20% of the body's AV. However, most retinyl esters remain associated with chylomicron remnants and are metabolized by the liver (CHEN et al, 2023; YADAV, 2022; O'CONNOR, 2022; MOLTEDO et al, 2021; EFSA, 2015).

Figure 1- Scheme of vitamin A absorption, transport and metabolism. Enterocytes of the intestinal membrane absorb retinol and carotenoids from mixed micelles from the action of gastrointestinal lipases in the food matrix and convert them into ER by the action of the enzymes CRBP2 and LRAT, ER is incorporated into chylomicrons by MTP, where it circulates until it is captured by the target organs through the hydrolyzation of the enzyme LPL, the remaining ER is metabolized by the liver and converted into retinol that is associated with CRBP1, and can be released into the bloodstream bound to RBP4 (later forming the RBP4/TTR complex), or transported to the EHS where it is converted back into ER by LRAT for storage. The organ also produces the enzyme RBPR2, which catalyzes hepatic absorption of excessive circulating RBP4 and regulates its biliary excretion. In the kidneys, the elimination of retinoids is mediated by the reabsorption of RBP4 by the LRP-2 enzyme. In peripheral organs such as the eyes and placenta, retinol absorption is mediated by the enzyme STRA6, the interaction between STRA6 and RBP4 allows the bidirectional transport of retinoids to the intra- and extracellular medium. ER: Retinol ester, ROL: retinol, CRBP2: cellular retinol-binding protein 2, LRAT: lecithin: retinol acyltransferase. TTR: transthyretin, LRP-2: lipoprotein receptor-related protein 2 complex, RBP4: retinol-binding protein type 4, RBPR2:Retinol transporter protein receptor 2, CRBP1: retinol-binding cellular protein 1, STRA6: retinoic acid-stimulated receptor 6, CEH: hepatic stellate cell.



SOURCE: Adapted from O'CONNOR, 2022.

HEPATIC METABOLISM OF VITAMIN A

The liver is the main organ responsible for the storage, metabolism, and distribution of AV to peripheral tissues. Most of the AV (80-90%) is stored in the liver (CHEN et al, 2023; YADAV, 2022; CARAZO et al, 2021). Chylomicron-associated retinyl esters are taken up by hepatocytes via hepatic LPL and hydrolyzed to retinol, which is associated with cellular retinol-binding protein 1 (CRBP1). CRBP1 plays important roles in fine-tuning AV metabolism, including protecting retinol from degradation and ensuring its delivery to retinoid enzymes for oxidation or esterification (O'CONNOR, 2022). Hepatocytes are also responsible for RBP production and AR synthesis and catabolism (EFSA, 2015).

The retinol thus formed can follow different paths: a) bind to RBP and be released into the bloodstream; b) be oxidized to AR for cell signaling; c) be metabolized, in more polar forms, by the cytochrome P450 (CYP26) enzyme system, and conjugated with bile salts for excretion by bile; d) or else be transported to the CEH, where it will be stored. The individual's AV nutritional status determines the route to be followed (O'CONNOR, 2022; CARAZO et al, 2021).

CRBP1-bound retinol is transported to the HECs by hepatocytes, where it is converted by LRAT into retinyl esters and stored in large cytoplasmic lipid droplets of different sizes (Figure 1). The main storage site for AVs is the CEH (CZUBA, 2024; CHEN et al, 2023; YADAV, 2022). In the healthy liver, the bidirectional retinoic acid-stimulating receptor 6 (STRA6) transports the AV between the extra and intracellular retinoid-binding proteins (figure 1). The interaction of RBP4 with STRA6 allows for the bidirectional transfer of retinol into and out of cells (O'CONNOR, 2022).

EXTRA-LIVER METABOLISM OF VITAMIN A

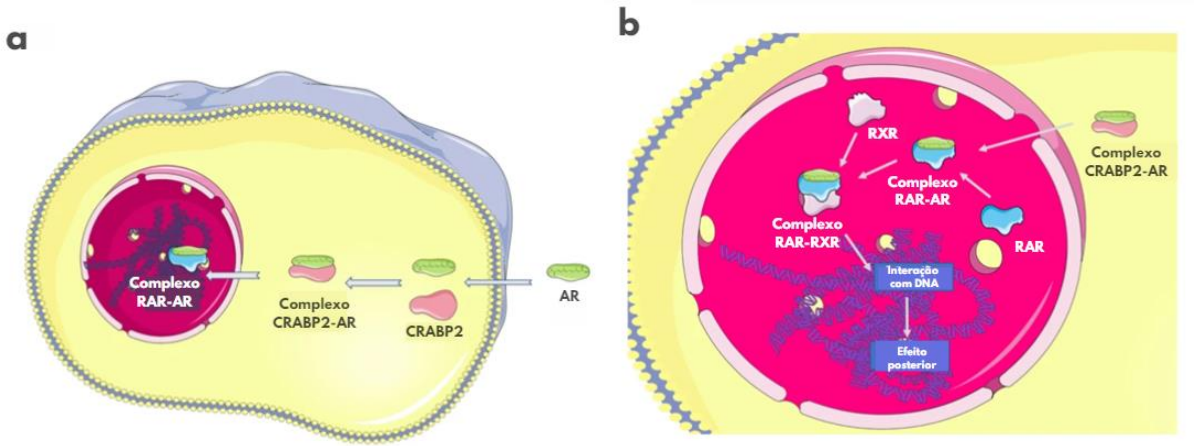
Retinol storage is under strict AR feedback regulation. The expression of LRAT and RBP1 in the liver is induced by RA, thus acting to direct the flow of retinol for storage in times of AV sufficiency. AV metabolism also responds to regulators of liver lipid metabolism (O'CONNOR, 2022). As demand increases, stocks of hepatic retinol are mobilized. As required, retinyl esters from CEH are hydrolyzed by various hepatic lipases to retinol and transferred to hepatocytes. Hepatocytes secrete retinol bound to retinol-binding protein (encoded by RBP4) (O'CONNOR, 2022; YADAV, 2022). This retinol-RBP4 complex is designated holo-RBP4 or holo-RBP, in contrast to apo-RBP4 which is not bound to retinol (YADAV, 2022). Holo-RBP4 circulates as a complex with transthyretin (TTR) (O'CONNOR, 2022; YADAV, 2022). Blood VA levels are homeostatically regulated to maintain a narrow range, through hepatic co-secretion of RBP-bound retinol (LOUNDER et al, 2017)

Retinol-bound RBP4 interacts with specific receptors expressed by target tissues (O'CONNOR, 2022; YADAV, 2022). Retinol uptake in tissues can be mediated by passive diffusion or active uptake via STRA6 (YADAV, 2022). STRA6 is a high-affinity holo-RBP4 receptor expressed by many blood tissue barrier sites, such as pigmented cells of the retina, placenta, yolk sac, choroid plexus, and Sertoli cells (O'CONNOR, 2022). In addition to protein-mediated transport, a considerable fraction of VA can be transported by lipoproteins that deliver retinoids to many target tissues, including the placenta (YADAV, 2022). The elimination of retinoids occurs through the kidneys or liver into the bile. RBP4 is reabsorbed from the proximal tubule of the kidney via the lipoprotein receptor-related protein 2 (LRP-2) complex (figure 1) (O'CONNOR, 2022).

VITAMIN A CELL SIGNALING

Active retinoids can be generated in tissues from retinyl esters, retinol, or β-carotene. All-trans-retinoic acid, or AR, is the major bioactive metabolite of retinol (CZUBA, 2024; CHEN et al, 2023; YADAV, 2022; O'CONNOR, 2022). AR is transported from the cytosol to the nucleus by binding to retinoic acid binding protein type 2 (CRABP2) (Figure 2a), where it binds to members of the retinoic acid nuclear receptors (RAR), forming an AR-RAR complex that stimulates the narrowing of RAR binding with the retinoid X receptor (RXR), forming RAR/RXR heterodimers, which subsequently bind to specific retinoic acid response elements (RARE), thus initiating the transcription of target genes and promoting the regulatory effects of AV (figure 2b), acting on lipid metabolism, fatty acid oxidation, gluconeogenesis, and extracellular matrix remodeling, among other functions (CZUBA, 2024; BURZYŃSKI et al, 2023; CHEN et al, 2023).

Figure 2 - Retinoic acid signaling. a) Transport of retinoic acid through the membrane and cytoplasm. b) Retinoic acid signaling in the nucleus. a) AR is transported from the cytosol to the nucleus by binding with CRABP2, where it binds to RAR, forming the AR-RAR complex, b) this complex stimulates the narrowing of the RAR bond with RXR, forming RAR/RXR heterodimers, which subsequently bind to RARE, promoting the regulatory effects of RAR. AR: RA retinoic acid, CRABP2: retinoic acid type 2 binding protein, RAR: retinoic acid receptor, RXR: retinoid X receptor, RARE: specific elements of response to retinoic acid.



FONTE: Adaptado de BURZYŃSKI et al, 2023.

MAIN FUNCTIONS OF VITAMIN A

Retinal and AR are the two major metabolites that mediate the physiological functions of AV. The retinal is the chromophore of visual pigments, a critical component of the visual cycle. On the other hand, AR is an activator of nuclear receptors, which are transcription factors that respond to variations in ligand levels, so VA acts on several cellular factors that influence growth, immunity, among other aspects (CHEN et al, 2023)

GROWTH AND DEVELOPMENT

AV is an essential micronutrient for human beings, especially in times of intense growth and development (DALLAZEN et al, 2023; ZHAO et al, 2022). Findings from experimental studies suggest that VA may affect growth through the regulation of growth hormone (GH) and thyroid-stimulating hormone beta genes. RA deficiency is associated with reduced GH secretion by the pituitary gland, resulting in somatic growth failure, particularly in preschool-aged children (SSENTONGO et al, 2020).

Children who do not achieve their full development do not achieve adequate learning, behavior, and mental and physical well-being; perform worse in school; and earn lower wages as adults. This perpetuates a cycle of poverty and continuously undermines human development (CORREIA et al, 2019). In low- and middle-income countries, 36.8% of children aged three to four years performed poorly on developmental tests (CORREIA et al, 2019). It is estimated that, worldwide, more than 200 million preschool children are not developing properly (CORREIA et al, 2019). Short stature, weight loss, and low weight are responsible for more than 45% of mortality in children under five years of age and impaired

cognitive development and are associated with multiple risk factors, including fetal growth restriction, enteric and systemic infections, diarrheal diseases, and poverty, highly concomitant factors in individuals with VAD (SSENTONGO et al, 2020).

IMMUNITY AND OXIDATIVE STRESS

Another aspect that deserves to be highlighted is the fact that AV is closely linked to the immune system (CHEN et al, 2023; GURGEL et al, 2018). Considered among all micronutrients as most closely associated with infectious diseases (RAMALHO, 2017). AV plays a key role in maintaining mucosal integrity, differentiation, growth and function of neutrophils, Natural Killer (NK) cells, monocytes, dendritic cells and T and B lymphocytes, modulation of phagocytic cell response, stimulation of phagocytosis, expression of mucin, keratin and cytokines, production of immunoglobulins, participation in hematopoiesis, oxidation-reduction reaction, healing, in the apoptosis process and in the regulation of genes that influence immunity (CHOOBDAR et al, 2023; CARAZO et al, 2021; ZHANG et al, 2019; LOUNDER et al, 2017; EFSA, 2015) and also participates in the activation of cell-mediated cytotoxicity and the increase in the response of thymocytes to specific mitogens (RAMALHO, 2017).

AR increases the percentage of lymphoid cells expressing T-helper lymphocyte surface markers, while β-carotene increases lymphoid cells expressing NK cell markers, which suggests a differentiated action of the various retinoids on specific cellular immunity (CHOOBDAR et al, 2023).

In the inflammatory state, the AV is significantly reduced in approximately 72 hours. This fact can be explained by the deviation of protein synthesis, prioritizing the production of acute phase proteins to the detriment of the reduction of the pool of circulating visceral proteins (including the retinol transporter protein - RBP), high consumption of antioxidants, exacerbation of oxidative stress caused by inflammation and infection; and increased urinary excretion during the acute phase of infection, which causes depletion of the stores of this vitamin (TANUMIHARDJO et al, 2016).

VA is a fat-soluble antioxidant, carried in conjunction with LDL cholesterol (LDL-c) and protects the polyunsaturated fatty acid against oxidation. When there is depletion of antioxidants in the LDL-c molecule, lipid chain peroxidation occurs, so that the presence of antioxidants in this lipoprotein delays the onset of this process (O'CONNOR, 2022; CARAZO et al, 2021). Retinol through its antioxidant activity combines with peroxyl radicals preventing the formation of hydroperoxides (CARAZO et al, 2021).

Carotenoids are efficient in fighting free radicals and act as singlet oxygen deactivators and peroxyl radical scavengers, reducing DNA and lipid oxidation (MIZAEK et al, 2022), in addition to protecting LDL-c molecules from oxidation (O'CONNOR, 2022; CARAZO et al, 2021), with β-carotene being the most well-known and studied carotenoid due to its antioxidant potential, especially in relation to the protection of LDL-c molecules (MIZAEK et al, 2022; BOHN et al, 2019). As an anti-infective vitamin, VA adequacy is necessary to support rapid growth and resistance to infections in the pediatric public, where this condition can lead to critical consequences (CHOOBDAR et al, 2023).

VAD affects the immune system on several levels, including destroying the integrity of the mucosal epithelial membrane, which acts as a protective barrier in the gastrointestinal, respiratory, and urinary systems. It causes metaplasia and destruction of the defense mechanism of the squamous layer of the airways, epithelium, and microbial invasion. DVA also leads to weakened immunity by dysfunction of macrophages and natural killer cells, monocytes, neutrophils, and dendritic cells. It also increases the severity of enterovirus infections by reducing the concentration of interferon alpha and IgM (CHOOBDAR et al, 2023; ZHANG et al, 2019)element.

VISUAL CYCLE

In the eye, the retina is the structure responsible for visual perception, including its transmission to the brain. This perception is mediated by specific structures in the retina: rods and cones. Rods are sensitive to low light and are therefore crucial for vision in dark situations (e.g., night vision), while cones are responsible for high-intensity light (color vision) (YADAV, 2022; CARAZO et al, 2021; TANUMIHARDJO et al, 2016). This important function of the rods is linked to the size of the pupil, which opens in the dark to allow light to reach the back of the eye and becomes smaller in bright light (TANUMIHARDJO et al, 2016).

VA has a role in the regeneration of visual pigment. The active derivative of VA 11-cis-retinal is associated with the protein opsin, a G-coupled protein receptor in the retina. The complex is known as rhodopsin, which is the crucial pigment for light perception. Under light stimuli, the 11-cis-retinal is transformed into all-trans-retinal and initiates a chain of reactions whose final consequence is the transmission of optical perceptions through the optic nerve to the brain. After this reaction, part of the *all-trans-retinal* can be transformed back into 11-cis-retinal , allowing the recycling of this key molecule. The remaining *all-trans-retinal* can be transformed into retinol, which can be

stored in the epithelial cells to be later reused or converted into AR (HODGE, 2023; YADAV, 2022; CARAZO et al, 2021)

The visual system requires a constant supply of retinol precursor to maintain vision (O'CONNOR, 2022) otherwise, a lack of retinol supply can lead to night blindness, due to poor regeneration of visual pigment in the retinal rods (HODGE, 2023; O'CONNOR, 2022). In individuals with VAD, the ability of the rods to adapt in the dark and for the pupils to properly measure light inside and outside the eye may be impaired (TANUMIHARDJO et al, 2016). As the severity of the deficiency worsens, signs of xerophthalmia develop with Bitot's spots (conjunctival, triangular, or oval, foamy lesions) and conjunctival xerosis (appears as conjunctival wrinkling). If VAD persists, its later stages present as corneal xerosis, corneal ulceration, and eventually keratomalacia as the corneal ulcers heal, resulting in corneal scarring and blindness (HODGE, 2023; WHO, 2009).

EVALUATION OF THE NUTRITIONAL STATUS OF VITAMIN A

The nutritional status of AV is defined by the balance between the proportion of the micronutrient ingested and its use by the body (MCLAREN, 2012). Its evaluation can be made through dietary, biochemical, functional and clinical indicators. Each method has its strengths and limitations, for the choice of use, its usefulness must be evaluated according to the purpose and target group established (TANUMIHARDJO et al, 2016; MCLAREN, 2012).

DIETARY ASSESSMENT

Dietary assessment methods include dietary records, 24-hour food recall, food frequency questionnaires, brief dietary assessment instruments, and dietary history (TANUMIHARDJO et al, 2016; MCLAREN, 2012). Deficiency is considered when the intake does not meet the needs established for the population, on the other hand, if the consumption remains above the recommendations, especially the pre-formed AV, it is possible to form reserves and maintain concentrations (TANUMIHARDJO et al, 2016).

Dietary assessment has the advantage of being non-invasive, inexpensive, and uncomplicated, so that many individuals can be readily seen and a profile of a population can be drawn, aiding possible subsequent dietary interventions. (MCLAREN, 2012). They also have great applicability, being widely used worldwide by professionals in governments, academia, health services and the food industry for a wide range of purposes, such as assessing the level of inadequacy by sex and age groups and assessing the potential of a food supply to meet the nutritional needs of a country (MOLTEDO et al, 2021).

However, it is important for the elaboration and application of these questionnaires to be aware of which foods are sources of AV available and consumed in the country or population of study, which are enriched, especially with preformed AV, as well as the seasonality of different fruits and vegetables sources of carotenoids (MOLTEDO et al, 2021; TANUMIHARDJO et al, 2016). Potential confounding factors such as self-report and use of supplementation should be considered, as well as methodological challenges such as inconstancy regarding the unit used to quantify consumption (International units 'IU' or Recommended mean estimate 'EAR') and the absence of a consensus regarding the system of conversion of provitamin A carotenoids into RAS (MOLTEDO et al, 2021; TANUMIHARDJO et al, 2016; MCLAREN, 2012).

FUNCTIONAL ASSESSMENT

Some measurements are able to assess the functional impact of AV, reflecting its influence on specific biological systems. These measurements seek to identify night blindness, which is the first functional indicator of VAD (CARAZO et al, 2021; WHO, 2009). Ocular symptoms associated with VAD have been shown to develop at concentrations less than <0.7 µmol/L (HODGE, 2023).

Among the main ones are dark adaptation tests, electroretinography, pupillary threshold test and conjunctival impression cytology (TANUMIHARDJO et al, 2016).

The dark adaptation tests and the pupillary threshold test are based on the conversion time of the rod to cone retinal receptors in the dark adaptation process, consisting of exposing the individual to lighting and then to a dark room for ten minutes. Although they are direct tests and do not require associated biomarkers, they have limitations due to the high degree of attention required by the test subject, and due to the set of factors that can cause confounding such as eye diseases, protein or zinc deficiency and age, being inappropriate for children and the elderly (TANUMIHARDJO et al, 2016).

Electroretinography measures the number of photoreceptors in the retina and their ability to regenerate rhodopsin after an exposure to bright, discolorating light. For this, the pupil dilation of the analyzed subject and direct contact with a measuring electrode are required. Conjunctival impression cytology, on the other hand, consists of taking a sample of the conjunctiva of the eye and staining the cells, in search of abnormality defined as absence of goblet cells and hyperplasia of epithelial cells. In addition to the limitations mentioned above, these methods are more restricted because they are invasive, being used only in clinical or research settings (TANUMIHARDJO et al, 2016).

A pilot study in 1980 proved the validity of the interview in relation to the objective test of night vision – scotopic vision and serum retinol (SOMMER et al, 1980). In view of the above, the World Health Organization (WHO) proposed a standardized interview, which is an algorithm to increase sensitivity and reduce the misclassification of night blindness, and which should be used prioritizing local language. For its application, the use of expensive equipment and specialized ophthalmological knowledge is not required (WHO, 1996). The proposed interview, in addition to being easy to apply, allows the detection of the problem in the population segment most vulnerable to nutritional deficiencies (ZHAO et al, 2022; YISAK et al, 2020).

Pereira et al. compared the diagnosis of night blindness through the proposed interview with electroretinography and the association of these diagnoses with serum retinol concentrations. Night blindness diagnosed by both methods showed an association with VAD according to serum retinol concentrations. The authors conclude that the standardized interview for the diagnosis of night blindness can be a good strategy to assess the nutritional status of AV, being a simple, non-invasive, and low-cost method (PEREIRA et al, 2020).

CLINICAL EVALUATION

In the clinical evaluation, some procedures can help estimate the status of AV, including the patient's historical survey, in the search for risk factors such as malabsorption, infectious diseases, impaired immunity, cirrhosis, pancreatic insufficiency, prematurity, low socioeconomic status, and current pregnancy or lactation in a context of malnutrition (HODGE, 2023). Likewise, it is of great value to perform the physical examination due to the possible identification of signs of deficiency such as conjunctival xerosis, keratinization of the mucous membranes of the respiratory, gastrointestinal, and urinary tracts, dryness, desquamation, and follicular thickening of the skin, and growth retardation in children (HODGE, 2023).

However, the most commonly used aspect to determine AV status is xerophthalmia, which titles the clinical spectrum of ocular manifestations of VAD; these range from the mildest stages of night blindness, Bitot's spots to the potentially permanent stages of xerosis, ulceration, and necrosis of the cornea (keratomalacia) (HODGE, 2023; WHO, 2009). The various stages of xerophthalmia are considered disorders and clinical indicators of VAD (WHO, 2009).

It is observed that the clinical manifestation of VAD occurs late, when the deficiency is already installed and the AV reserves are already seriously depleted, so its evaluation is

not effective to diagnose it previously, highlighting the importance of the subclinical diagnosis of VAD to minimize its consequences in the population. In addition, the identification of clinical signs can be influenced by factors such as the professional's interpretation and the population's access to the health service (MCLAREN, 2012; WHO, 2009).

BIOCHEMICAL EVALUATION

The most commonly used forms of biochemical measurement of AV status are the quantification of serum retinol and retinol transporter protein (RBP). VAD is defined as its concentration less than <0.7 µmol/L (HODGE, 2023; TANUMIHARDJO et al, 2016).

However, these two parameters are not sensitive indicators of the nutritional status of AV and do not reflect hepatic reserve. This is because serum retinol is homeostatically controlled by liver reserves and only falls when liver reserves are very low (MEZZANO et al, 2022; TANUMIHARDJO et al, 2016; McCauley et al., 2015). Serum retinol and RBP tend to be lower in infants and young children than in adults, even in populations with adequate serum VA levels (TANUMIHARDJO et al, 2016). Difficulties also arise when assessing micronutrient deficiencies in countries where there is a high burden of infection as these biomarkers are altered by inflammation (MEZZANO et al, 2022; SHEFTEL et al, 2021; TANUMIHARDJO et al, 2016). In addition, there may be interference due to drugs, alcohol, and physiological conditions (CARAZO et al, 2021; SHEFTEL et al, 2021).

The retinol concentration of breast milk is an indicator of the vitamin status of both the mother and the infant, and has been shown to be a more sensitive marker of maternal nutritional status than the respective blood concentrations (MACHADO et al, 2019; SOUZA et al, 2015). The cut-off points adopted to identify VAD and adequate formation of hepatic reserve are <1.05 and >2.3 µmol/L, respectively (SOUZA et al, 2015; STOLTZFUS, 1995). However, the measurement by this method is hampered by the difficulty of standardizing the collection of breast milk samples, since the AV content of breast milk is very variable. Among the factors that cause this variability are: breastfeeding period, breast to be pumped, time of day, time elapsed since the last feeding, collection at the beginning or end of the feeding, and the mother's pre- or post-prandial state (DEMINICE et al, 2018; TANUMIHARDJO et al, 2016).

Hepatic AV reserves are considered a reference of excellence for the evaluation of this vitamin (CHEN et al, 2023; TANUMIHARDJO et al, 2016). Hepatic stellate cells store 50-80% of the total AV in the body in the form of retinyl palmitate in lipid droplets in the cytoplasm, being responsible for regulating the transport and storage of AV. A normal

reserve of the vitamin in these cells represents an adequate supply for most individuals for several weeks or months (TANUMIHARDJO et al, 2021; SENOO et al, 2017).

Hepatic reserve of AV can be measured indirectly through retinol *isotope dilution* (RID) or dose-response tests, such as *relative-dose-response* (RDR) and *modified-relative-dose-response* (MRDR), or they can be quantified directly from liver tissue, through biopsy or autopsy (SURI et al, 2023; TANUMIHARDJO et al, 2016). Direct measurement is the most reliable way to estimate the hepatic reserve of AV. It is not realistic to perform biopsies in living people, being used to evaluate retinol concentrations in humans only in special cases. Autopsy samples, on the other hand, should be considered for population monitoring, given that VAD is not considered a primary cause of death and its concentrations in the liver remain unchanged up to 48 hours postmortem (MEZZANO et al, 2022; TANUMIHARDJO et al, 2016; OLSON et al, 1984). Hepatic retinol reserve is considered *adequate* when the values are equal to or greater than 20µg/g (or 0.07µmol/g) of liver (OLSON et al, 1979).

VITAMIN A DEFICIENCY

VAD is a public health problem worldwide (ZHAO et al, 2022; DING et al, 2021; MIRANDA et al, 2018; HANSON et al, 2017; CRUZ et al, 2017a) that can increase maternal/perinatal mortality (CRUZ et al, 2018; 2017a; WHO, 2011a). The main causes of VAD include an insufficient intake of VA-rich foods, malabsorption, and loss of AV due to disease (ZHAO et al, 2022; GURGEL et al, 2018).

The most characteristic consequence of VAD is impaired vision. In the long term, VAD can cause xerophthalmia and, eventually, total blindness, which can be permanent. This circumstance is the most common cause of preventable blindness in developing countries. VAD is also characterized by epithelial modifications that directly affect various body systems, including respiratory, urogenital, reproductive, gastrointestinal, nervous, and skin systems, as well as increasing the risk of infections, malnutrition, and anemia (CARAZO et al, 2021; GURGEL et al, 2018).

The main victims of VAD are pregnant women, newborns, and children under five years of age who are males, in countries with a low sociodemographic development index (HODGE, 2023; ZHAO et al, 2022; MEZZANO et al, 2022; MIRANDA et al, 2018; HANSON et al, 2017). Many populations in these countries rarely eat meat, dairy, or carotenoid-rich vegetables, which makes it difficult to obtain sufficient amounts of VA (HODGE, 2023). Maternal and infant VAD not only affects individuals at these biological times, but also extends to long-term health in adulthood (ALMEIDA et al, 2022)

In the gestational period, VAD increases the risk of complications during pregnancy and in the postpartum period and has been positively associated with maternal infections, anemia, and birth defects (THOENE et al, 2020). The increased need for the vitamin, especially in women in the third trimester of pregnancy, when fetal growth is faster, can also lead to night blindness, a risk marker for pregnancy that is able to identify VAD in its subclinical stage (MACHADO et al, 2016). In addition, maternal VAD can lead to embryonic malformations, which are manifested by deficiencies of the cardiovascular and nervous system and less developed tissues, among other defects (CARAZO et al, 2021).

In children, VAD can cause growth and developmental deficits, vision loss, and be a potential risk factor for cognitive impairment and mental illness, as well as increase susceptibility to respiratory, parasitic infections, and diarrhea (ZHAO et al, 2022). The greater vulnerability of this age group to VAD is attributed to the rapid growth and development, characteristic of this phase of life and, consequently, the increase in the need for AV, which is often not met due to insufficient intake. This is coupled with greater susceptibility to diseases that reduce absorption, increase metabolic demands, and excretion of this vitamin. In this way, repeated infections further reduce the absorption of AV, resulting in a vicious cycle in this population (DALLAZEN et al, 2023; ZHAO et al, 2022).

There is a downward trend in the worldwide prevalence of VAD, with significant reductions reported since 1990 (ZHAO et al, 2022; MIRANDA et al, 2018). However, in 2019 its values remained high, reaching more than four hundred and eighty-nine million people (ZHAO et al, 2022). According to a WHO report, 190 million preschool-aged children and 19 million pregnant women have been exposed to VAD globally (ZHAO et al, 2022; THOENE et al, 2020). In several Latin American countries, VAD is still considered a serious public health problem (ZHAO et al, 2022).

In Brazil, studies have identified prevalences of 10% to 20% of serum retinol levels below 0.70 µmol/L, a condition that characterizes VAD as a moderate to severe public health problem (MIRANDA et al, 2018). According to the Pan American Health Organization (PAHO) and the WHO, the country is considered to be an area of severe subclinical shortage of AV (ZHAO et al, 2022).

For children and infants, the recommended daily intake of VA ranges around 400-500 retinol activity equivalents (RAE), while for women, pregnant and breastfeeding women, the recommended levels range between 700 and 1300 RAE, with the highest for lactating women (HODGE, 2023; CARAZO et al, 2021). The minimum requirement to prevent symptomatic AVD in children from one to five years of age is about 200 micrograms/day (HODGE, 2023). There are no specific guidelines for increasing β-carotene intake or

indications for supplementation in breastfeeding mothers. The typical intake of β-carotene in a Western diet is six to eight mg per day (NICHH, 2022).

MATERNAL VITAMIN A TRANSFER

MATERNAL VITAMIN A TRANSFER DURING PREGNANCY

In the early intrauterine period, the developing embryo is totally dependent on maternal circulation for its AV supply (THOENE et al, 2020; QUADRO et al, 2020). The maternal/fetal retinol concentration is about 2:1 in mothers in the absence of severe retinol deficiency (TEKGÜNDÜZ et al, 2022). Maternal-fetal transport of retinoids relies on RBP4 (maternal- and fetal-derived) as well as lipoprotein-mediated pathways, both of which respond to AV status (O'CONNOR, 2022). The AV reaches the embryo by crossing the maternal-fetal barrier (placenta and yolk sac) (DEMINICE et al, 2018). Placental homeostasis plays a key role in the delivery of retinol to the fetus and is responsible for the storage of retinoids until fetal liver maturation is complete (TEKGÜNDÜZ et al, 2022).

Depending on the maternal dietary regimen, different metabolic pathways appear to be activated to maintain retinoid homeostasis in the placenta and control the amount of preforms and provitamin A that is transferred to the developing embryo, a process that the literature has recently reported to be possibly involved with lipid metabolism (QUADRO et al, 2020).

The literature also demonstrates relatively stable fetal AV levels , despite fluctuations in maternal retinol levels, this is justified by the transplacental passage of retinol that increases in cases of maternal retinol deficiency (TEKGÜNDÜZ et al, 2022; THOENE et al, 2020), which can increase even more when comparing retinol-deficient mothers compared to insufficient ones (THOENE et al, 2020). In addition, it appears that maternal RBP levels, and in turn placental retinol release, increase or decrease according to the intensity of the transplacental retinol passage to protect the fetus from a sudden change in retinol levels. Some factors can reduce maternal and umbilical cord RBP during pregnancy, such as malnutrition, gestational diabetes, preeclampsia, and anemia (TEKGÜNDÜZ et al, 2022).

Dietary AV appears to sufficiently support adequate embryogenesis if maternal hepatic stores are depleted or cannot be adequately mobilized, this may occur through a compensation with increased transport of retinyl esters in the absence of RBP-bound retinol induced by increased expression of placental LPL (QUADRO et al, 2020). It has been observed in animal models that even if maternal liver storage is inadequate, adequate dietary retinol intake may allow for normal fetal development (TEKGÜNDÜZ et al, 2022).

In cases of inadequate intake, serum retinol is maintained at the expense of the hepatic reserve to ensure adequate regulation of fetal transfer until the reserve is depleted, with depletion there is a decrease in serum concentrations and consequently fetal supply is impaired (TEKGÜNDÜZ et al, 2022; THOENE et al, 2020; AHMAD et al, 2018). Newborns born to mothers with deficient retinol concentrations have significantly lower retinol concentrations in their umbilical cord blood compared to those born to mothers with adequate concentrations (THOENE et al, 2020).

However, it has been suggested that the adequacy of maternal hepatic retinol may not guarantee the adequacy of fetal transfer, and consequently, prevention against all possible neonatal nutritional deficiencies is not guaranteed (THOENE et al, 2020).

Due to the physiological changes of pregnancy, such as increased blood volume and AV demand, there is a decrease in serum retinol levels in pregnant women, especially in the third trimester. This, together with a selective placental barrier that aims to avoid teratogenic effects, causes newborns to have a lower storage capacity for hepatic retinol, with a low reserve at birth (TEKGÜNDÜZ et al, 2022).

The transfer of AV to the fetus also influences other factors that affect the development of the fetus after birth, such as the placental transfer of antibodies from mother to baby, the control of maternal hormone expression signaling, and longitudinal growth, especially in the third trimester (AHMAD et al, 2018; GAMLIEL et al, 2016).

TRANSFER OF VITAMIN A VIA BREASTFEEDING

After birth, most serum retinol is transported to the breast by the RBP, reaching breast milk. From then on, the transport of VA into breast milk in the first six months of life provides 60 times more VA when compared to the placental route throughout pregnancy, increasing the physiologically low hepatic reserve of newborns. In addition, breast milk also transports active provitamin A carotenoids, which serve as additional nutrients for the baby (GAMLIEL et al, 2016).

The AV plays a role in mammary gland metabolism throughout lactation. RA is essential for the development of the mammary gland and in the secretory epithelium to achieve adequate milk production. Retinoids, through the RARα-dependent signaling pathway, have also been shown to regulate, at least in part, the weaning process, where epithelial cell death is coupled with tissue remodeling (CABEZUELO et al, 2020).

After the initial support by colostrum milk (<72 hours postpartum), the transitional milk (up to 15 days) supports the newborn, and milk production increases considerably to meet the nutritional and developmental needs of the rapidly growing baby, after 16 days,

the mature milk starts to support the infant. The bright yellow color of human colostrum reflects the rich carotenoid content, compared to transitional and mature milk.

The amount of VA that neonates receive from colostrum and milk depends significantly on the mother's AV nutritional status. VA levels in breast milk reflect the mother's recent diet or supplementation status more than her long-term stores (HOMBALI et al, 2019). The fat content of breast milk can be a useful vehicle to improve the bioaccessibility and bioavailability of carotenoids (MESQUITA et al, 2021). β-carotene is a normal component of human colostrum and mature milk, contributing to the antioxidant defenses of the newborn (NICHHD, 2022).

VITAMIN A IN THE EARLY STAGES OF LIFE

The beginning of life is a window of opportunities for special professional attention, with a focus on ensuring the child's present and future health (ALMEIDA et al, 2022). Recently, the Brazilian Association of Nutrology recommended extending this window from 1,000 to 2,200 days, encompassing 100 days in preconception and from the first to the fifth year of life (ALMEIDA et al, 2022). Adequate nutritional intervention is essential in care during this moment of life, especially in relation to the nutritional status of AV, in view of the increase in its demand, but for this it is necessary to consider the particularities of each phase of early life in relation to this micronutrient (ALMEIDA et al, 2022; CRUZ et al, 2017b).

PRECONCEPTION PHASE

The proper development of the embryo influences the health of the offspring in the long term, being dependent on the good quality of the gametes, which is directly related to the health condition of the parents. A series of health situations and/or behaviors of women in the preconception period have been shown to be associated with a worse prognosis for the health of their offspring, including psychological factors, stress, smoking, alcoholism, and especially poor food quality and exaggerated energy intake, in addition to obesity and malnutrition (ALMEIDA et al, 2022).

AV is essential in the process of female germ cell development. The maternal status of this micronutrient at the time of conception influences the reproductive outcome. VAD in women of reproductive age can impair the processes of fertilization, implantation, and fetal formation, impairing health, pregnancy outcomes, and the growth and development of offspring, in addition to favoring the intergenerational transmission of this condition in the long term (CLAGET-DAME et al, 2011)

FETAL PHASE

The literature has consolidated that maternal behavior during pregnancy influences the baby's health through the provision of an adequate intrauterine environment for fetal development, which favors birth conditions. (ALMEIDA et al, 2022; NEVES et al, 2015). Pregnancy is a unique period of the life cycle in which cell differentiation occurs rapidly, the presence of retinol, is essential for proper fetal growth and development and maternal metabolism, playing an important role in full-term pregnancy and birth weight (MEZZANO et al, 2022; CARAZO et al, 2021; NEVES et al, 2020; THOENE et al, 2020).

During the gestational period, there is an increase of about 40% in the daily requirements of the vitamin for the maintenance of the placenta and fetal development (CRUZ et al, 2018). During this period, the concentration of retinol in maternal plasma decreases during the first trimester and slowly increases again, again reaching normal values before delivery (CARAZO et al, 2021).

There are specific recommendations on the need to assess the nutritional status of AV of all pregnant women during prenatal care (CRUZ et al, 2018). Serum retinol concentrations tend to decrease during the trimesters of pregnancy and serum levels are intensely needed in the last trimesters when compared to the first trimester (CRUZ et al, 2017b). In pregnant women, AV may decrease more intensely in the third trimester, a period considered to have greater transfer of this vitamin to the fetus, which may be aggravated by reduced stores, gestational hemodilution, and the inability of the fetus to synthesize AV (CRUZ et al, 2018; MACHADO et al, 2016)

Nutritional intervention is one of the five axes of intervention recommended by the WHO for prenatal care (ALMEIDA et al, 2022; WHO, 2016). However, few women have access to this follow-up (HOLAND et al, 2021).

NEONATAL PHASE

The neonatal period comprises the day of birth to the first month of life of the newborn (ALMEIDA et al, 2022). Most childhood deaths are concentrated in the first year of life, especially in the first month (WHO, 2024; BUGELLI et al, 2021; FRANÇA et al., 2017). AV has been shown to be important in preventing a variety of neonatal diseases (HUANG et al, 2021).

Birth, by itself, represents an oxidative stress to the newborn. The transition from an intrauterine environment, which is relatively oxygen-poor, to the extrauterine one, which is significantly richer in oxygen, is a toxic transition and exposes the infant to increased free

radical production, leading to an imbalance in the antioxidant system (SOUZA et al, 2015). Thus, the importance of the antioxidant function of AV is highlighted.

The role of AV as an anti-inflammatory and in the immune system are also fundamental in this age group, since newborns have an immature immune system and, consequently, their functional impairment, in addition to having antigenic inexperience, which favors microbial invasion, making this group highly susceptible to infection and reinfection (SOUZA et al, 2015). In newborns, VAD increases the risk of death from infectious and respiratory diseases (GURGEL et al, 2018).

The nutritional status of the newborn is closely linked to the intake of breast milk during the first week of life (SOUZA et al, 2015). Therefore, the importance of adequate nutrition for mother-infant dyads at all times between preconception and postpartum is highlighted (THOENE et al, 2020). There is currently no consensus in the scientific literature on the cutoff value for adequate retinol concentration for newborns, or whether adult values should be chosen for this age group (DEMINICE et al, 2018).

PRESCHOOL PHASE

Globally, preschool-aged children are the population groups most at risk for VAD. The population in this group is at risk for xerophthalmia due to relatively high growth requirements and relatively low body storage. The general picture of food consumption patterns in this population is a monotonous cereal-based diet, devoid of the necessary amount of AV sources (LIMA et al, 2018; DALLAZEN et al, 2018).

In this period, the outcomes of VAD to be highlighted are dry eyes, night blindness, impaired immune system, anemia and increased mortality in children suffering from infectious diseases such as measles or diarrhea. Another important factor to note is the marginal deficiency of AV, which is usually ignored, but has a higher prevalence than VAD in this population, leading to an inadequate level of AV, which can cause anemia, respiratory and digestive tract infections, in addition to affecting the growth and development of children (CHEN et al, 2021).

Evidence shows that the chances of survival of preschool children increase when VA status improves, reducing the risk of all-cause mortality by 23-34% (YISAK et al, 2020). High levels of prevalence of VAD were also found in preschool children, especially those under three years of age, in addition to high rates of marginal VAD, which were shown to increase with age (CHEN et al, 2021; YISAK et al, 2020).

VITAMIN A DEFICIENCY PREVENTIVE STRATEGIES

With the worldwide effort to reduce the problem of VAD, strategies have been developed to prevent and treat it in populations. Among the adopted conducts are encouraging increased AR intake, industrial and homemade food fortification, and periodic supplementation of high doses with AV capsules or tablets (FAYE et al, 2021; HOMBALI et al, 2019).

BREASTFEEDING

Souza et al. point out that the hepatic concentration of retinol in newborns may be sufficient to meet daily requirements only during the first days of life, since it is a period of increased nutritional demands (SOUZA et al, 2015). Breast milk is considered the most important AV source to increase the hepatic reserves of the newborn (NEVES et al, 2015), favoring rapid growth and acting as an antioxidant and immune barrier; however, many factors modulate the composition of this nutrient in breast milk, such as diet, economic situation, and maternal nutritional status (MESQUITA et al, 2021; GURGEL et al, 2018).

The WHO recommends six months of exclusive breastfeeding and partial breastfeeding up to two years or more (MINISTRY OF HEALTH, 2019). According to the *National Study of Child Food and Nutrition (ENANI-2019).* Breastfeeding rates have been growing in Brazil, however, we are still far from the WHO goals (ENANI, 2021).

While VA stores during pregnancy are important for fetal development, healthy breast milk production needs a greater boost from diet or liver stores. Increased uptake of retinoids by the mammary gland is necessary for its production (MESQUITA et al, 2021; CRUZ et al, 2017a). The literature indicates a significant increase of approximately 90% in the need for AV during lactation (CRUZ et al, 2017a). Breastfeeding women can quickly deplete their stores of the vitamin if dietary intake is not increased during this time (TANUMIHARDJO et al, 2021; CARAZO et al, 2021).

The Dietary Reference Intake specifies the value of 4.6 IU of daily retinol for the infant in the first months of life as the amount necessary for the child to meet daily requirements, accumulate liver stores and prevent the development of clinical symptoms of deficiency (CRUZ et al, 2017a; IOM, 2001). It has been found that if maternal VA concentrations are not adequate, the mature milk of infants may not reach the adequate amount of this nutrient and they may develop VAD (CRUZ et al, 2017a).

The WHO classifies VAD as a public health issue for mothers and babies as mild (equal to or less than 10% of the population), moderate (10 to 25% of the population) and severe (equal to or greater than 25% of the population), according to the concentration of

VA in breast milk. In populations with adequate concentrations of VA, the average concentration of this vitamin in breast milk is 1.75–2.45 mol/L, while the average values are below 1.4 mol/L in populations with deficiency (SOUZA et al, 2015). The inadequacy of AV in milk can result in the maintenance of low hepatic reserves in the infant, increasing their susceptibility to severe respiratory infections, pneumonia, and diarrhea, which contributes to increased rates of infant morbidity and mortality (SOUZA et al, 2015).

Newborns rely on breast milk, infant formula, or other external sources of retinol to meet essential needs after birth. Therefore, adequate dietary intake also remains important during pregnancy to prevent deficiency in early lactation. The recommended dietary intake for maternal intake of RAE increases from 770 to 1300 µg/day from pregnancy to lactation to support the transfer of retinol through the human milk supply. Retinol stores are expected to be further depleted during lactation for retinol-deficient or under-retaining mothers with persistently inadequate dietary intake. Similarly, mothers with lower serum retinol concentrations produce milk with lower retinol content for their babies, which increases the risk of infant deficiency (THOENE et al, 2020; DEMINICE et al, 2018).

FOOD INTRODUCTION

Adequate food introduction is one of the most important factors in early life, as at this stage the individual's eating habits are established (MINISTRY OF HEALTH, 2019). After six months, breastfeeding is no longer exclusive and water and fresh food sources must be added, adapting the amount and consistency according to age, from one year onwards the child's diet is already similar to the rest of the family (MINISTRY OF HEALTH, 2019; 2014).

At this time, all the foods necessary to maintain the child's nutritional status should be introduced, including the foods that are the source of VA (MINISTRY OF HEALTH, 2019). Important factors related to eating behavior are also stimulated, such as a sense of satiety and adaptation of the food reward system, which will influence eating throughout life (MINISTRY OF HEALTH, 2019; 2014).

The child's taste is influenced by the mother's diet at the time of lactation (MINISTRY OF HEALTH, 2019; 2005). The consumption of complementary food together with breastfeeding improves the absorption of AV. Children whose mothers have adequate concentrations of AV in their breast milk reach, with relative ease, the daily requirements of the vitamin through adequate complementary foods (MINISTRY OF HEALTH., 2005).

However, an unfavorable complementary feeding pattern is observed in Brazilian children . Feeding is introduced early and in a monotonous way, the use of bottles is very frequent, even among breastfed children, complementary foods do not meet the needs of

VA, especially for low-income families. There are still many beliefs and taboos related to young children's diet, which contribute to the infrequent use of sources of vitamins and minerals, even when they are available and consumed in the family (ENANI, 2021; MINISTRY OF HEALTH, 2005).

MATERNAL AND CHILD VITAMIN A SUPPLEMENTATION

WHO and PAHO classify some countries as having severe subclinical disability and an AV supplementation program targeting children aged 6 to 59 months has been implemented since 1983. In 2005, this program was extended to postpartum women and residents in higher-risk areas, consisting of the administration of a single dose of AV with 200,000 IU orally in the immediate postpartum period (MESQUITA et al, 2021; MIRANDA et al, 2018; CRUZ et al, 2017a).

Postnatal supplementation is performed to minimize reversible damage to the newborn and partially recover the maternal state of AV before lactation, being an emergency measure, not the resolution of the central problem (GURGEL et al, 2018). Despite significantly increasing the VA in colostrum, concentrations seem to decrease in mature milk, reaching insufficiency 30 days after calving. There is still contradiction in the literature regarding the ideal dose of postnatal supplementation (CRUZ et al, 2017a).

In 2011, the WHO began to recommend supplementation with daily or weekly doses with daily or weekly doses for pregnant women from vulnerable groups in areas with endemic deficiency, due to the benefits achieved in this population group, a recommendation reaffirmed in 2013 (CRUZ et al, 2017a; NEVES et al, 2015). The recommended dose is 10,000 IU daily or 25,000 IU weekly for four to eight weeks for prevention and treatment of gestational night blindness, without risk of teratogenicity (SOUZA et al, 2015; NEVES et al, 2015).

Despite having lower serum retinol levels compared to adult populations, the WHO currently does not recommend VA supplementation for infants aged one to five months, stating that supplementation offers no benefit in reducing infant morbidity and mortality (THOENE et al, 2020). However, the literature points to AV supplementation as a way to increase AV stores in the newborn and improve infant survival (CHOOBDAR et al, 2023). A review in 2021 indicated a positive effect on oral supplementation of newborns, without adverse effects such as Hypervitaminosis or increased intracranial pressure (HUANG et al, 2021).

AV supplementation has been implemented in some regions and countries, but full implementation of periodic high-dose interventions is difficult in countries with large

populations; thus, the coverage rate remains low (ZHAO et al, 2022). Despite its importance, there are a small number of studies available on AV supplementation during the gestational period, mainly studies on the reduction and prevention of maternal-neonatal morbidity and mortality (CRUZ et al, 2017a).

FOOD ENRICHMENT

Fortification, enrichment or simply addition is a process in which one or more nutrients, whether or not naturally contained in it, are added to the food, within the legal parameters, with the aim of reinforcing its nutritional value and preventing or correcting any nutritional deficiencies presented by the general population or groups of individuals. Food fortification has been used as a low-cost strategy to prevent nutritional deficiencies in many countries, both developed and developing (HOMBALI et al, 2019).

It is proposed that food fortification with VA works by increasing daily intake and absorption of the vitamin to sufficiently high levels, aiming to close the existing intake gap and significantly increase liver stores to correct VAD and its implications on health and survival (HOMBALI et al, 2019). Staple food vehicles potentially suitable for AV fortification in public health programs include refined or crude sugar, edible vegetable oils, fats, and cereal grains (rice); wheat flour, corn flour or corn flour; condiments and seasonings; and powdered or liquid milk (WHO, 2006).

Some countries have implemented mandatory programs at the national level to fortify staple foods with VA. A global review concluded that fortifying staple foods with VA and other micronutrients may not improve vitamin status. However, for children and adolescents in low- and middle-income populations, this conduct may lead to a lower risk of subclinical AV deficiency (HOMBALI et al, 2019).

VITAMIN A AND CAUSES OF INFANT DEATH

PREMATURITY

Prematurity is the leading cause of death and disability in children under five years of age worldwide (YE et al, 2022). The AV plays a vital role in full-term pregnancy, providing fetal reserves and maintaining maternal metabolism during pregnancy, in addition to its role in the immune system (MEZZANO et al, 2022; SOUZA et al, 2015). Preterm infants represent a population that inspires concern about AV, as the vitamin is transmitted primarily from the mother through the placenta to the fetus in the third trimester. Therefore, VAD is prevalent in preterm infants (YE et al, 2022; SUN et al, 2022; DING et al, 2021; TAO et al, 2016). As a result, it is expected that preterm birth will reflect negatively on the nutritional

status of this vitamin, causing low concentrations of serum retinol and retinol-binding protein (RBP), in addition to low hepatic reserve (SUN et al, 2022; SOUZA et al, 2015).

At the same time, the nutritional needs of AV in a premature infant are higher than at any other time in life. This is due to the intense catabolism during the first few weeks after birth with the low supply of retinol in the liver at birth, the low concentrations of plasma retinol, and the low concentrations of RBPs, compared to full-term infants (SOUZA et al, 2015).

In addition, hepatic storage of VA is not as efficient in extremely preterm infants, which contributes to low plasma retinol concentrations (SUN et al, 2022). Studies show that the lower the gestational age, the lower the weight and the more severe the VAD (HUANG et al., 2021; DING et al, 2021). VAD in premature infants can cause retinopathy due to prematurity, in addition to making them predisposed to the development of various diseases (YE et al., 2022; SUN et al, 2022).

However, the milk of breastfeeding women who had preterm delivery tends to be inadequate from a quantitative point of view, since fetal needs were not fully met with the interruption of maternal-fetal transfer. In case of absence of breast milk, the baby can stay for several weeks on enteral feeding, whose composition does not meet its needs adequately (SUN et al, 2022; MESQUITA et al, 2021; SOUZA et al, 2015). Thus, low VA level in preterm infants at birth can last throughout childhood (TAO et al, 2016).

If the hepatic reserves of the newborn remain low, it can favor the installation, maintenance and/or worsening of OLD, forming a vicious cycle of infection/OLD/infection, in addition to the occurrence of long-term episodes (SOUZA et al, 2015). The risks of developing diseases related to AV status that are of most concern to premature infants are respiratory distress syndrome, chronic lung disease, retinopathy of prematurity, necrotizing enterocolitis, patent ductus arteriosus, and infections in general (TAO et al, 2016).

Due to the fragility of this population, when it comes to premature babies, not only the effectiveness but also the safety of the intervention must be considered. Despite the need for deeper checks, the use of clinical VA has been shown to be safe for premature infants, free from adverse reactions such as pain and sepsis (DING et al, 2021). There is still a lack of evidence to determine the most appropriate AV treatment method for premature infants (DING et al, 2021; TAO et al, 2016)

CONGENITAL ANMALIES

The composition of the maternal diet during pregnancy has metabolic importance for the health of the offspring, even before conception, and can permanently program their

offspring (MESQUITA et al, 2021). Once VA is deficient, it will not only affect the normal growth and development of the embryo, but it can also cause congenital diseases, including pulmonary hypoplasia, central nervous system malformations, and bone deformity of the fetus (MA et al, 2021). VAD predisposes pregnant women to miscarriage, as well as brain, macular, renal, and vascular congenital defects (MESQUITA et al, 2021).

Two periods during pregnancy are more critical and should be treated with the utmost care, the first trimester of pregnancy (up to 14 weeks), when the vital parts of the body are formed and the end of pregnancy, when the maturation of the hypothalamic-pituitary axis occurs (MESQUITA et al, 2021). Unfortunately, the initial window of development occurs before many women can be aware of pregnancy, and VAD is chronic among women of childbearing age, which is compounded by the increased demand of this critical period (Gilbert et al., 2023; IBGE, 2020; MICHIKAWA et al, 2019).

The relationship between maternal nutrition and fetal programming is informed through endocrine signals, epigenetics, and oxidative stress. During pregnancy, carotenoids play an important role in promoting communication between cells (gap junctions), regulating hormonal imbalances, and increasing the immune response, which prevents gestational complications. The fetal and neonatal periods have considerable epigenetic plasticity. Altering VA signaling through dietary and genetic disruptions can create birth defects (Gilbert et al., 2023; MESQUITA et al, 2021)element. Findings in the literature suggest a crucial role of pro-AV carotenoids and preformed AV in the epigenetic programming of offspring, possibly influencing the phenotype and the development of diseases in adulthood. It has been suggested that the performance of carotenoids as antioxidants can reduce oxidative stress, infection, inflammation, and damage to the placenta during pregnancy, thus conferring a healthy life to the offspring (MESQUITA et al, 2021). The type of congenital anomaly most associated with AV in the literature are those of bone origin (ROCKE et al, 2022; MICHIKAWA et al, 2019).

RESPIRATORY DISEASES

Respiratory tract infections (RTIs) are the most widespread infectious diseases in children, promoting high morbidity and mortality. Preschool children who have experienced more than eight episodes of airway infections per year are considered to have recurrent respiratory tract infections (IRTRs) (ZHANG et al, 2024; ABDELKADER et al, 2022; SUN et al, 2022; WANG et al, 2021). Respiratory diseases such as asthma, pneumonia, and bronchiolitis are the most common reasons for hospitalization in the pediatric population (GOTH et al, 2022; WANG et al, 2021). Infection from TRRIs can, over the course of

occurrences, migrate to other organs, in addition to harming the child's physical and mental health in the long term, and increasing health care expenses (ZHANG et al, 2024; HURWITZ et al, 2017)

The mechanisms by which AV aids in the prevention of respiratory diseases include: regulation and promotion of the proliferation and differentiation of various lung cells, thereby maintaining the integrity of the airway epithelium; improvement of immune function, further enhancing resistance to disease and damage; promotion of the synthesis of active substances on the lung surface; antioxidant effect; and promotion of repair after lung injury (WEI et al, 2024; HUANG et al, 2021). VA can regulate the content of mRNAs and reduce the expression of fatty acid synthase genes, affecting the synthesis of phospholipid precursors. Thus, protein synthesis of phospholipids and pulmonary surfactants is increased, promoting lung development and maturity. (DING et al, 2021). Pulmonary surfactant is essential for maintaining alveolar stability and reducing surface tension during breathing (WEI et al, 2024). In addition, the vitamin promotes antioxidant protection and the functioning of repair mechanisms after lung injury (DING et al, 2021).

AV is recognized for its role in lung maturation and function during pregnancy and lactation (CRUZ et al, 2017a) and is required in the fetal lung for cell differentiation and surfactant synthesis (SUN et al, 2022). Studies in animal models have observed that it can improve alveolar formation and alveolar hair growth, reduce the expression of elastin messenger ribonucleotides from the lung parenchyma and the accumulation of elastic fibers, and promote better gas exchange (DING et al, 2021). VA consumption is exceptionally high as the lungs grow and develop during the last trimester and shortly after birth due to its role in lung maturation (GOTH et al, 2022; SUN et al, 2022). In addition, free radicals produced by oxidative stress from childbirth increase vitamin requirement and have been associated with damage to the respiratory system (SOUZA et al, 2015).

In preterm infants, this issue is even more concerning due to the immaturity of antioxidant systems and inadequate AV reserves (SOUZA et al, 2015). In animal experiments, lower plasma concentrations and hepatic retinol reserve were found in preterm infants who developed bronchopulmonary disease, compared to those who did not, corroborating the hypothesis that VAD contributes to the development of chronic lung disease and/or respiratory tract infections in this type of population (SUN et al, 2022). Wei et al. studied the relationship between cord blood AV and neonatal lung diseases, cord blood VAD and preterm birth were independent risk factors for neonatal lung diseases, and the lower the level of AV in umbilical cord blood, the more susceptible newborns were to neonatal respiratory infections (WEI et al, 2024).

Childhood-acquired lung function predicts adult lung function, so maternal and neonatal AV levels are predictive of future lung function and respiratory morbidity (GOTH et al., 2022). It was found that administering VA supplementation before and during pregnancy and postpartum in women with VAD had an influence on their children's lung function in the long term. This benefit is likely due to the effects of in utero supplementation (CRUZ et al, 2017a).

SEPTICEMIA

Sepsis is the dysfunction of one or more organs resulting from the host's dysregulated response to an infection, severe or not, that has not been treated correctly. The inflammatory response originates in one organ and can extend and affect others, causing inflammation in different parts of the body, endothelial and mitochondrial vascular dysfunction, and life-threatening (DOLIN et al, 2023; LOU et al, 2023; FIOCRUZ, 2021; ZHANG et al, 2019; CHERUKURI et al, 2019). The intrinsic factors of sepsis refer to the immaturity of the immune system and the barrier functions of the skin, mucous membranes, and gastrointestinal tract. (FIOCRUZ, 2021; SOUZA et al, 2015).

With a mortality rate of more than 25%, sepsis represents a significant burden on public health resources. A steady increase in the incidence of severe sepsis has been reported in recent decades (LOU et al, 2023; ZHANG et al, 2019; CHERUKURI et al, 2019).

Notably, sepsis is a common cause of death in children (CHOOBDAR et al, 2023; ZHANG et al, 2019). Mortality from severe sepsis has been reported to be as high as 34.6% in children. It was revealed that more than 50% of deaths in preschool children were due to serious infectious diseases that can result in sepsis (ZHANG et al, 2019).

Newborn patients and those with immunosuppression are among the most affected by sepsis. In this age group, the risk of developing the disease is inversely proportional to gestational age (FIOCRUZ, 2021; SOUZA et al, 2015), and the lack of specific symptoms hinders early diagnosis, which is essential for survival (CHOOBDAR et al, 2023; FIOCRUZ, 2021. In developing countries, neonatal sepsis is a leading cause of death and morbidity in infants, accounting for 44% of all deaths. Lower levels of VA in newborns and their mothers have been associated with increased risk of sepsis (CHOOBDAR et al,2023).

AV is an immunomodulator and its deficiency can cause an imbalance between pro- and anti-inflammatory factors and impaired immune function, which are found in sepsis. VAD is also associated with a worsening of the inflammatory response, generating an unfavorable situation for patients with sepsis in the early stages (CHOOBDAR et al, 2023; ZHANG et al, 2019). In addition, sepsis is known to increase urinary retinol loss by more

than five times the reference dietary intake, contributing to deficiency of this micronutrient and greater fragility to recurrent infections (CHERUKURI et al, 2019). Lower incidence of sepsis in children can be attributed to improved immune function after VA administration (CHOOBDAR et al, 2023; CHERUKURI et al, 2019). It has been suggested that RA may aid in the treatment of sepsis through the activation of RAR/RXR by promoting the expression of mitogen-activated protein kinase phosphatase 1 (MKP-1), which reduces inflammation by inhibiting the production of pro-inflammatory cytokines by phosphorylation of the mediators p65 and JNK (DOLIN et al, 2023). VAD may play another role in sepsis by dysregulating the total platelet count, in addition to playing a specific role in the post-disease period through immune system dysfunction and the epithelial barriers that cover the digestive, respiratory, and urinary tracts, leading to a higher risk of clearance of bacteria in the blood and overlapping infection (ZHANG et al, 2019).

MENINGOENCEPHALIC DISEASES

Meningoencephalitis, inflammation of the brain and the membranes that surround it (meninges), is usually caused by a viral, bacterial or fungal infection (MARFIN et al, 1994). Children under five years of age are among the most vulnerable population for these diseases, in which the prevalence of the infectious agent is associated with previous immune status. Among the main symptoms are nausea, vomiting and food refusal, thus highlighting the importance of nutritional status in the occurrence, duration and outcome of meningoencephalitis (MINISTRY OF HEALTH, 2017). There are few studies on AV and meningoencephalic diseases. It has been suggested that VA supplementation may contribute to reducing the severity and mortality associated with certain meningoencephalic diseases (MARFIN et al, 1994). AV supplementation has been shown to be effective in the treatment of measles-induced encephalitis. A dose of 200,000 IU per day for two days can lead to reduced inflammation and reduced mortality from the disease in children (DIWAN et al, 2022; AL-QAYOUDHI et al, 2016)

DISEASES OF THE DIGESTIVE TRACT

Intestinal inflammatory disorders have been recognized to stimulate the production of tumor necrosis factor-alpha (TNF-α), a key etiological mediator of intestinal barrier dysfunction. Reduced numbers of regulatory T cells (Tregs) in the intestinal mucosa of patients with this pathology have been associated with disrupted epithelial junctions. The strong exposure linked to the high susceptibility to infections characteristic of this age group makes it a crucial moment of intervention for these diseases (MEDEIROS et al, 2018).

Studies have shown that AV is associated with diseases of the gut microbiota and gastrointestinal tract, due to its physical barrier functions (CHENG et al, 2021; LOUNDER et al, 2017). Supplementing with VA helps relieve diarrhea and improves intestinal damage (CHENG et al, 2021). Retinoids are also essential micronutrients to improve malnutrition and enteric diseases and related infant mortality and morbidity (MEDEIROS et al, 2018).

AV modifies intestinal permeability, and is essential for the development of mucosal permeability due to the regulation of lymphocyte traffic to the intestine. AR promotes the secretion of interleukin 22 (IL-22), known to promote the proliferation and healing of epithelial cells, restore tight junctions, and increase the mucus production of goblet cells (MEDEIROS et al, 2018; LOUNDER et al, 2017; LOUNDER et al, 2017).

In addition, gastrointestinal pathologies by themselves are associated with malnutrition, due to their malabsorptive character, impairing the state of AV. Children with diarrheal disease were more malnourished than those without diarrhea, as diarrheal disease disrupted luminal mucosal function and resulted in metabolic dysfunction, malabsorption, and nutrient loss, loss that impaired growth, development, and nutritional status (CHANIE et al, 2021). A double causal relationship was observed between VAD and intestinal villus impairment (HOSSAIN et al, 2016).

Although widely associated with VAD, mortality rates from diarrheal diseases have declined in recent decades, on the other hand, there is increasing morbidity from non-diarrheal environmental enteric dysfunctions, associated with enteric pathogens in early life (MEDEIROS et al, 2018). In this context, studies have addressed the concept of environmental enteropathy, a usually subclinical disorder that usually occurs among residents of low- and middle-income (developing) countries where sanitation is often poor and hygiene practice is inadequate. Persistent contact/exposure to fecal pathogens can trigger inflammation and structural changes in the small intestine, which ultimately result in functional changes. It is manifested by increased intestinal permeability, malabsorption, and inadequate growth in individuals without evident diarrhea (MEDEIROS et al, 2018; HOSSAIN et al, 2016).

Although VAD is associated with a higher risk of occurrence and aggravation of enteric infections, it was pointed out that supplementation may not protect against reinfections, highlighting the need for long-term follow-up. Studies have demonstrated the impact of environmental enteropathy on the maternal and child population. This condition has been linked to impaired intestinal barrier function, leading to malnutrition, impaired intestinal absorption, vaccine response failure, and cognitive deficits in children (MEDEIROS et al, 2018).

CONCLUSION

The metabolism of VA is finely regulated in the body. Absorption, excretion and transport are carried out in order to promote constant serum concentrations, being mediated by the available hepatic reserve and its mobilization into the bloodstream. In view of the important roles played by AV in growth and development, maintenance of the visual cycle, and strengthening of the immune system, as well as the relationship between VAD and increased mortality in children under five years of age due to inflammatory and infectious diseases, the importance of promoting the adequacy of this micronutrient during early life is emphasized in order to improve health in the maternal and child context. In this sense, interventions aimed at improving the status of AV, such as supplementation, nutritional education, and promotion of breastfeeding, can have a positive outcome in the formation and maintenance of infant hepatic reserve, playing an important role in the prevention and management of childhood diseases and in the reduction of mortality. In addition, public health policies that aim to improve access to VA-rich foods and quality health services can have a significant impact on children's health and well-being, especially in vulnerable communities.

REFERENCES

1. Abdelkader, A., et al. (2022). Recurrent respiratory infections and vitamin A levels: a link? It is cross-sectional. *Medicine, Baltimore*, 101(33), 19 ago.

2. Ahmad, S., et al. (2018). Vitamin A supplementation during pregnancy enhances pandemic H1N1 vaccine response in mothers, but enhancement of transplacental antibody transfer may depend on when mothers are vaccinated during pregnancy. *J Nutr*, Epub, 148(12), 1968-1975. https://doi.org/10.1093/jn/nxy228

3. Almeida, C., et al. (2022). First 2,200 days of life as a window of opportunity for multidisciplinary action regarding the developmental origin of health and disease: positioning of the Brazilian Association of Nutrology. *Int J of Nutrology*, Epub, 15(3).

4. Al-Qayoudhi, A., et al. (2016). Acute measles encephalitis in an immigrant Syrian child: Case report and review of the literature. *Oman Med J*, Epub, 31(2), 150-153. https://doi.org/10.5001/omj.2016.30

5. Bohn, T., et al. (2019). β-Carotene in the human body: metabolic bioactivation pathways - from digestion to tissue distribution and excretion. *Proc Nutr Soc*, Epub, 78(1), 68-78. https://doi.org/10.1017/S0029665118002787

6. Secretaria de Vigilância em Saúde e Ambiente. (2022). Painéis de Saúde Brasil: Mortalidade na infância e componentes. Disponível em: <https://svs.aids.gov.br/daent/centrais-de-conteudos/paineis-de-monitoramento/saude-brasil/mortalidade-na-infancia/>. Acesso em: 19 abril. 2024.

7. Bugelli, A., et al. (2021). The determinants of infant mortality in Brazil, 2010-2020: A scoping review. *Int J Environ Res Public Health*, Epub, 18(12), 6464. https://doi.org/10.3390/ijerph18126464

8. Burzyński, J., Fichna, J., & Tarasiuk, A. (2023). Putative molecular targets for vitamin A in neutralizing oxidative stress in acute and chronic pancreatitis - A systematic review. *Naunyn Schmiedebergs Arch Pharmacol*, Epub, 396(7), 1361-1370. https://doi.org/10.1007/s00210-023-02353-2

9. Cabezuel, M., et al. (2020). Role of vitamin A in mammary gland development and lactation. *Nutrients*, Epub, 12(1), 80. https://doi.org/10.3390/nu12010080

10. Carazo, A., et al. (2021). Vitamin A update: Forms, sources, kinetics, detection, function, deficiency, therapeutic use and toxicity. *Nutrients*, Epub, 13(5), 1703. https://doi.org/10.3390/nu13051703

11. Chanie, E. (2021). The effect of timely initiation of complementary feeding and vitamin A supplementation on acute malnutrition among children aged 6-59 months attending Hamusit Health Centre, Northwest Ethiopia, 2021: A cross-sectional study. *Heliyon*, Epub, 7(11). https://doi.org/10.1016/j.heliyon.2021.e08317

12. Chen, G., Weiskirchen, S., & Weiskirchen, R. (2023a). Vitamin A: too good to be bad? *Front Pharmacol*, Epub, 14. https://doi.org/10.3389/fphar.2023.1168987

13. Chen, Q., et al. (2021). Vitamin A levels among pre-school children of Central and Western China. *Front Public Health*, Epub, 9, 694106. https://doi.org/10.3389/fpubh.2021.694106

14. Cheng, B., et al. (2021). Vitamin A deficiency increases the risk of gastrointestinal comorbidity and exacerbates core symptoms in children with autism spectrum disorder. *Pediatr Res*, Epub, 89(1), 211-216. https://doi.org/10.1038/s41390-020-01151-5

15. Cherukuri, L., et al. (2019). Vitamin A treatment for severe sepsis in humans: a prospective randomized double blind placebo-controlled clinical trial. *Clin Nutr. ESPEN*, Epub, 29, 49-51. https://doi.org/10.1016/j.clnesp.2018.12.005

16. Choobdar, F., et al. (2023). Association of lower vitamin A levels in neonates and their mothers with increased risk of neonatal late-onset sepsis: A case-control study. *J Mother Child*, Epub, 26(1), 78-86. https://doi.org/10.34763/jmotherandchild.2023260115

17. Hodge, C., & Taylor, C. (2023). Vitamin A deficiency. In *StatPearls*. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK448092/

18. Clagett-Dame, M., & Knutson, D. (2011). Vitamin A in reproduction and development. *Nutrients*, Epub, 3(4), 385-428. https://doi.org/10.3390/nu3040385

19. Correia, L., et al. (2019). Interaction between vitamin A supplementation and chronic malnutrition on child development. *Cien Saude Colet*, Epub, 24(8), 3037-3046. https://doi.org/10.1590/1413-81232018248.21062017

20. Cruz, P., et al. (2018). Roux-en-Y gastric bypass aggravates vitamin A deficiency in the mother-child group. *Obes Surg*, Epub, 1, 114-121. https://doi.org/10.1007/s11695-017-2879-6

21. Cruz, S., & Ramalho, A. (2017a). Impact of vitamin A supplementation on pregnant women and on women who have just given birth: A systematic review. *J Am Coll Nutr*, Epub, 37(3), 243-250. https://doi.org/10.1080/07315724.2017.1378283

22. Cruz, S., et al. (2017b). Relationship between the nutritional status of vitamin A per trimester of pregnancy with maternal anthropometry and anemia after Roux-en-Y gastric bypass. *Nutrients*, Epub, 9(9), 989. https://doi.org/10.3390/nu9090989

23. Czuba, L., & Isoherranen, N. (2024). LX-2 stellate cells are a model system for investigating the regulation of hepatic vitamin A metabolism and respond to tumor necrosis factor α and interleukin 1 β. *Drug Metab Dispos*, Epub, 52(5), 442-454. https://doi.org/10.1124/dmd.122.0012

24. Dallazen, C., et al. (2018). Introduction of inappropriate complementary feeding in the first year of life and associated factors in children with low socioeconomic status. *Cad. Saúde Pública*, 34(2). https://doi.org/10.1590/0102-311X00202816

25. Dallazen, C., et al. (2023). Vitamin A deficiency and associated risk factors in children aged 12-59 months living in poorest municipalities in the South Region of Brazil. *Public Health Nutr*, Epub, 1, 132-142. https://doi.org/10.1017/S1368980022003098

26. Deminice, T., et al. (2018). Vitamin A intake of Brazilian mothers and retinol concentrations in maternal blood, human milk, and the umbilical cord. *J Int Med Res*, Epub, 46(4), 1555-1569. https://doi.org/10.1177/0300060518757454

27. Dhage, V., & Nagtode, N. (2024). Health problems among under-five age group children in developing countries: A narrative review. *Cureus*, Epub, 16(2). https://doi.org/10.7759/cureus.4329

28. Ding, Y., Chen, Z., & Lu, Y. (2021). Vitamin A supplementation prevents bronchopulmonary dysplasia in premature infants: A systematic review and meta-analysis. *Medicine, Baltimore*, 100(3). https://doi.org/10.1097/MD.0000000000024391

29. Diwan, M., et al. (2022). Measles-induced encephalitis: Recent interventions to overcome the obstacles encountered in the management amidst the COVID-19 pandemic. *Diseases*, Epub, 10(4), 104. https://doi.org/10.3390/diseases10040104

30. Dolin, H. (2023). Retinoic acid-induced regulation of inflammatory pathways is a potential sepsis treatment. *Infect Immun*, Epub, 91(4). https://doi.org/10.1128/iai.00317-23

31. United States National Institute of Child Health and Human Development (NICHHD). (2022). Drugs and lactation database (LactMed®): Beta-carotene. Bethesda (MD): StatPearls Publishing. Disponível em: https://www.ncbi.nlm.nih.gov/books/NBK501906/. Acesso em: 27 ago. 2022.

32. Estudo Nacional de Alimentação e Nutrição Infantil (ENANI-2019). Universidade Federal do Rio de Janeiro - UFRJ. (2021). Prevalência e práticas de aleitamento materno em crianças brasileiras menores de 2 anos. Disponível em: https://enani.nutricao.ufrj.br/wp-content/uploads/2021/11/Relatorio-4_ENANI-2019_Aleitamento-Materno.pdf. Acesso em: 15 ago. 2023.

33. European Food Safety Authority (EFSA). (2015). EFSA panel on dietetic products, nutrition, and allergies (NDA). Scientific opinion on dietary reference values for vitamin A. *EFSA Journal*, 13(3), 4028. https://doi.org/10.2903/j.efsa.2015.4028

34. Faye, M., et al. (2021). Adequate vitamin A liver stores estimated by the modified relative dose response test are positively associated with breastfeeding but not vitamin A supplementation in Senegalese urban children 9-23 months old: A comparative cross-sectional study. *PLoS One*, Epub, 16(1). https://doi.org/10.1371/journal.pone.0246071

35. França, E., Lansky, S., & Rego, M. (2017). Leading causes of child mortality in Brazil, in 1990 and 2015: estimates from the Global Burden of Disease study. *Rev Bras Epidemiol*, Epub, 20(Suppl 01), 46-60. https://doi.org/10.1590/1980-5497201700050005

36. Fundação Osvaldo Cruz (FIOCRUZ). (2021). Sepse: a maior causa de morte nas UTIs. Rio de Janeiro. Disponível em: https://portal.fiocruz.br/noticia/sepse-maior-causa-de-morte-nas-utis. Acesso em: 27 maio. 2024.

37. Gamliel, M., et al. (2016). The oxytocin-CD38-vitamin A axis in pregnant women involves both hypothalamic and placental regulation. *J Matern Fetal Neonatal Med*, Epub, 29(16), 2685-2690. https://doi.org/10.3109/14767058.2015.1057817

38. Gilbert, R., & Gleghorn, J. (2023). Connecting clinical, environmental, and genetic factors point to an essential role for vitamin A signaling in the pathogenesis of congenital diaphragmatic hernia. *Am J Physiol Lung Cell Mol Physiol*, Epub, 324(4), L456-L467. https://doi.org/10.1152/ajplung.00087.2023

39. Goth, F., et al. (2022). Cohort profile: the vitamin A and D and nitric oxide (AD-ON) observational cohort on lung development and symptoms in premature and mature children in North Zealand, Denmark. *BMJ Open*, Epub, 12(2). https://doi.org/10.1136/bmjopen-2021-053210

40. Gurgel, C., et al. (2018). Vitamin A nutritional status in high- and low-income postpartum women and its effect on colostrum and the requirements of the term newborn. *J Pediatr, Rio de Janeiro*, 94(2), 207-215. https://doi.org/10.1016/j.jped.2017.05.007

41. Hanson, C., et al. (2017). Status of vitamin A and related compounds and clinical outcomes in maternal-infant pairs in the Midwestern United States. *Ann Nutr Metab*, Epub, 71(3-4), 175-182. https://doi.org/10.1159/000481500

42. Holand, B., et al. (2021). Adequacy of prenatal care considering nutritional assistance in Southern Brazil: Maternar Cohort Study. *Cad. Saúde Pública*, Epub, 37(6). https://doi.org/10.1590/0102-311x00054420

43. Hombali, A., et al. (2019). Fortification of staple foods with vitamin A for vitamin A deficiency. *Cochrane Database Syst Rev*, Epub, 5(5). https://doi.org/10.1002/14651858.CD012156.pub2

44. Hossain, M., et al. (2016). Undernutrition, vitamin A and iron deficiency are associated with impaired intestinal mucosal permeability in young Bangladeshi children assessed by lactulose/mannitol test. *PLoS One*, Epub, 1(12). https://doi.org/10.1371/journal.pone.0164447

45. Huang, L., Zhu, D., & Pang, G. (2021). The effects of early vitamin A supplementation on the prevention and treatment of bronchopulmonary dysplasia in premature infants: A systematic review and meta-analysis. *Transl Pediatr*, Epub, 10(12), 3218-3229. https://doi.org/10.21037/tp-21-470

46. Hurwitz, J., et al. (2017). Low retinol-binding protein and vitamin D levels are associated with severe outcomes in children hospitalized with lower respiratory tract infection and respiratory syncytial virus or human metapneumovirus detection. *J Pediatr*, Epub, 187, 323-327. https://doi.org/10.1016/j.jpeds.2017.04.035

47. Instituto Brasileiro de Geografia e Estatística (IBGE). (2020). Pesquisa de orçamentos familiares 2017-2018: Análise do consumo alimentar pessoal no Brasil. Rio de Janeiro. Disponível em: <https://edisciplinas.usp.br/pluginfile.php/7222745/mod_resource/content/2/relatorio%20publicado%20IBGE_POF_2017_2018.pdf>. Acesso em: 27 maio. 2024.

48. Institute of Medicine (IOM). (2001). U.S. Panel on Micronutrients. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academies Press (US). Washington, DC. Disponível em: <https://www.ncbi.nlm.nih.gov/books/NBK222310/>. Acesso em: 27 maio. 2024.

49. Lima, D., Damiani, L., & Fujimori, E. (2018). Vitamin A deficiency in Brazilian children and associated variables. *Rev Paul Pediatr*, Epub, 36(2), 176-185. https://doi.org/10.1590/1984-0462/;2018;36;2;00008

50. Lou, C., et al. (2023). Causal effects of genetically vitamins and sepsis risk: A two-sample Mendelian randomization study. *BMC Infect Dis*, 23(1), 766. https://doi.org/10.1186/s12879-023-07729-2

51. Lounder, D., et al. (2017). Lower levels of vitamin A are associated with increased gastrointestinal graft-versus-host disease in children. *Blood*, Epub, 129(20), 2801-2807. https://doi.org/10.1182/blood-2016-10-748061

52. Ma, H., et al. (2021). The relationship between changes in vitamin A, vitamin E, and oxidative stress levels, and pregnancy outcomes in patients with gestational diabetes mellitus. *Ann Palliat Med*, Epub, 10(6), 6630-6636. https://doi.org/10.21037/apm-21-290

53. Machado, M., et al. (2019). Breast milk content of vitamin A and E from early- to mid-lactation is affected by inadequate dietary intake in Brazilian adult women. *Nutrients*, Epub, 11(9), 2025. https://doi.org/10.3390/nu11092025

54. Machado, S., et al. (2016). Influence of Roux-en-Y gastric bypass on the nutritional status of vitamin A in pregnant women: A comparative study. *Obes Surg*, Epub, 26(1), 26-31. https://doi.org/10.1007/s11695-015-1755-2

55. McLaren, D., & Kraemer, K. (2012). Assessment of vitamin A status. *World Rev Nutr Diet*, Epub, 103, 52-64. https://doi.org/10.1159/000336594

56. Marfin, A., et al. (1994). Infectious disease surveillance during emergency relief to Bhutanese refugees in Nepal. *JAMA*, 272(5), 377-381. https://doi.org/10.1001/jama.1994.03520050051034

57. Medeiros, P., et al. (2018). Modulation of intestinal immune and barrier functions by vitamin A: Implications for current understanding of malnutrition and enteric infections in children. *Nutrients*, Epub, 10(9), 1128. https://doi.org/10.3390/nu10091128

58. Mesquita, L., et al. (2021). The role of vitamin A and its pro-vitamin carotenoids in fetal and neonatal programming: Gaps in knowledge and metabolic pathways. *Nutr Rev*, Epub, 79(1), 76-87. https://doi.org/10.1093/nutrit/nuaa028

59. Mezzano, J., et al. (2022). Effects of iron and vitamin A levels on pregnant women and birth outcomes: Complex relationships untangled using a birth cohort study in Uganda. *Matern Child Health J*, Epub, 26(7), 1516-1528. https://doi.org/10.1007/s10995-022-03475-0

60. Michikawa, T., et al. (2019). Maternal dietary intake of vitamin A during pregnancy was inversely associated with congenital diaphragmatic hernia: The Japan Environment and Children's Study. *Br J Nutr*, Epub, 122(11), 1295-1302. https://doi.org/10.1017/S0007114519002503

61. UNICEF. (2007). Cadernos de atenção básica: Carência de micronutrientes. Brasília. Disponível em:

<https://bvsms.saude.gov.br/bvs/publicacoes/cadernos_atencao_basica_carencias_micronutrientes.pdf>. Acesso em: 27 maio, 2024.

62. Ministério da Saúde. (2019). Guia alimentar para crianças brasileiras menores de 2 anos. Disponível em: <https://www.gov.br/saude/pt-br/assuntos/saude-brasil/eu-quero-me-alimentar-melhor/Documentos/pdf/guia-alimentar-para-criancas-brasileiras-menores-de-2-anos.pdf/view>. Acesso em: 15 ago. 2023.

63. Ministério da Saúde. (2014). Guia alimentar para população brasileira. Disponível em: <https://bvsms.saude.gov.br/bvs/publicacoes/guia_alimentar_populacao_brasileira_2ed.pdf>. Acesso em: 27 maio, 2024.

64. Ministério da Saúde. (2017). Guia de vigilância em saúde (v.1, 1ª ed. atualizada). Brasília-DF. Disponível em: <https://bvsms.saude.gov.br/bvs/publicacoes/guia_vigilancia_saude_volume_1.pdf>. Acesso em: 27 maio, 2024.

65. Ministério da Saúde, & Organização Pan-Americana da Saúde. (2005). Guia alimentar para crianças menores de 2 anos (1ª ed.). Disponível em: <https://bvsms.saude.gov.br/bvs/publicacoes/guia_alimentar_criancas_menores_2anos.pdf>. Acesso em: 27 maio, 2024.

66. Miranda, W., et al. (2018). Vitamin A supplementation program in Brazil: Evaluability assessment. *Rev Panam Salud Publica*, Epub, 42. https://doi.org/10.26633/RPSP.2018.152

67. Mizaek, K., et al. (2022). The effect of β-carotene, tocopherols, and ascorbic acid as antioxidant molecules on human and animal in vitro/in vivo studies: A review of research design and analytical techniques used. *Biomolecules*, Epub, 12(8), 1087. https://doi.org/10.3390/biom12081087

68. Moltedo, A., et al. (2021). The complexity of producing and interpreting dietary vitamin A statistics. *J Food Compost Anal*, Epub, 100. https://doi.org/10.1016/j.jfca.2021.103935

69. Moura, E., et al. (2022). Mortality in children under five years old in Brazil: Evolution from 2017 to 2020 and the influence of COVID-19 in 2020. *J. Pediatr*, Rio de Janeiro, 98(6), 626-634. https://doi.org/10.1016/j.jped.2021.10.008

70. Neves, P., et al. (2020). Effect of vitamin A status during pregnancy on maternal anemia and newborn birth weight: Results from a cohort study in the Western Brazilian Amazon. *Eur J Nutr*, Epub, 59(1), 45-56. https://doi.org/10.1007/s00394-019-01913-6

71. Neves, P., et al. (2015). Vitamin A supplementation in Brazilian pregnant and postpartum women: A systematic review. *Rev Bras Epidemiol*, Epub, 18(4), 824-836. https://doi.org/10.1590/1980-5497201500040011

72. O'Connor, C., Varshosaz, P., & Moise, A. (2022). Mechanisms of feedback regulation of vitamin A metabolism. *Nutrients*, Epub, 14(6), 1312. https://doi.org/10.3390/nu14061312

73. Olson, J. (1979). Liver vitamin A reserves of neonates, preschool children and adults dying of various causes in Salvador, Brazil. *Arch Latinoam Nutr*, 29(4), 521-545.

74. Olson, J., Gunning, D., & Tilton, R. (1984). Liver concentrations of vitamin A and carotenoids, as a function of age and other parameters, of American children who died of various causes. *Am J Clin Nutr*, 39(6), 903-910. https://doi.org/10.1093/ajcn/39.6.903

75. Pereira, S., et al. (2020). Diagnosis of night blindness through standardized interview and electroretinography. *Nutr Hosp*, Epub, 37(1), 155-159. https://doi.org/10.20960/nh.02940

76. Quadro, L., & Spiegler, E. (2020). Maternal-fetal transfer of vitamin A and its impact on mammalian embryonic development. *Subcell Biochem*, Epub, 95, 27-55. https://doi.org/10.1007/978-3-030-33543-8_2

77. Ramalho, A. (2017). *Função plenamente reconhecida de nutrientes: Vitamina A* (2ª ed.). São Paulo: International Life Science Institute - ILSI.

78. Rocke, A., et al. (2022). Low maternal vitamin A intake increases the incidence of teratogen-induced congenital diaphragmatic hernia in mice. *Pediatr Res*, Epub, 91(1), 83-91. https://doi.org/10.1038/s41390-021-01324-0

79. Senoo, H., Mezaki, Y., & Fujiwara, M. (2017). The stellate cell system (vitamin A-storing cell system). *Anat Sci Int*, Epub, 92(4), 387-455. https://doi.org/10.1007/s12565-016-0365-3

80. Sharrow, D., et al. (2022). Global, regional, and national trends in under-5 mortality between 1990 and 2019 with scenario-based projections until 2030: A systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. *Lancet Glob Health*, Epub, 10(2), e195-e206. https://doi.org/10.1016/S2214-109X(21)00365-4

81. Sheftel, J., & Tanumihardjo, S. (2021). Systematic review and meta-analysis of the relative dose-response tests to assess vitamin A status. *Adv Nutr*, Epub, 12(3), 904-941. https://doi.org/10.1093/advances/nmaa119

82. Sommer, A., et al. (1980). History of nightblindness: A simple tool for xerophthalmia screening. *Am J Clin Nutr*, 33(4), 887-891. https://doi.org/10.1093/ajcn/33.4.887

83. Souza, G., et al. (2015). Vitamin A concentration in human milk and its relationship with liver reserve formation and compliance with the recommended daily intake of vitamin A in pre-term and term infants in exclusive breastfeeding. *Arch Gynecol Obstet*, Epub, 291(2), 319-325. https://doi.org/10.1007/s00404-014-3562-1

84. Ssentongo, P., et al. (2020). Association of vitamin A deficiency with early childhood stunting in Uganda: A population-based cross-sectional study. *PLoS One*, Epub, 15(5). https://doi.org/10.1371/journal.pone.0233065

85. Stoltzfus, R., & Underwood, B. (1995). Breast-milk vitamin A as an indicator of the vitamin A status of women and infants. *World Health Organ*, 73, 703-711.

86. Sun, M., et al. (2022). Dynamic monitoring and a clinical correlation analysis of the serum vitamin A, D, and E levels in children with recurrent respiratory tract infections. *Am J Transl Res*, Epub, 14(5), 3533-3538. https://doi.org/10.1007/pmc8440847

87. Suri, D., et al. (2023). Association between biomarkers of inflammation and total liver vitamin A reserves estimated by 13C-retinol isotope dilution among preschool children in 5 African countries. *J Nutr*, Epub, 153(3), 622-635. https://doi.org/10.1093/jn/nxac335

88. Tanumihardjo, S., et al. (2016). Biomarkers of nutrition for development (BOND)-Vitamin A review. *J Nutr*, Epub, 146(9), 1816S-1848S. https://doi.org/10.3945/jn.116.233331

89. Tanumihardjo, S. (2021). Biological evidence to define a vitamin A deficiency cutoff using total liver vitamin A reserves. *Exp Biol Med*, Maywood, 246(9), 1045-1053. https://doi.org/10.1177/15353702211020277

90. Tao, E., et al. (2016). [Vitamin A level and diseases of premature infants]. *Zhongguo Dang Dai Er Ke Za Zhi*, Epub, 18(2), 177-182. https://doi.org/10.7499/j.issn.1008-8830.2016.02.012

91. Tekgündüz, K., et al. (2022). Factors that affect placental retinol transfer in preterm infants and mothers with retinol deficiency. *Turk J Med Sci*, Epub, 52(2), 294-302. https://doi.org/10.55730/1300-0144.5538

92. Thoene, M., et al. (2020). Effect of maternal retinol status at time of term delivery on retinol placental concentration, intrauterine transfer rate, and newborn retinol status. *Biomedicines*, Epub, 8(9), 321. https://doi.org/10.3390/biomedicines8090321

93. UN. (n.d.). Millennium Development Goals. Goal 4: Reduce child mortality. Retrieved May 27, 2024, from <https://www.un.org/millenniumgoals/childhealth.shtml>

94. UN. (2024b). Inter-agency Group for Child Mortality Estimation. The World Bank Data. Mortality rate, under-5 (per 1,000 live births) - Brazil. Retrieved May 23, 2024, from <https://data.worldbank.org/indicator/SH.DYN.MORT?contextual=default&end=2020&locations=BR&start=1960&view=chart>

95. UNICEF. (2021). United Nations Inter-Agency Group for Child Mortality Estimation (UN IGME). Levels and trends in child mortality. Retrieved March 27, 2024, from <http://data.unicef.org/resources/levels-and-trends-in-child-mortality-2024/>

96. Wang, X., et al. (2021). Association between serum vitamin A levels and recurrent respiratory tract infections in children. *Front Pediatr*, Epub, 9. https://doi.org/10.3389/fped.2021.775669

97. Wei, Y., et al. (2024). Correlation of vitamin A levels in umbilical cord blood with neonatal pulmonary diseases. *Pediatr Neonatol*, Epub. https://doi.org/10.1016/j.pedneo.2024.03.003

98. World Health Organization (WHO). (1996). *Indicators for assessing vitamin A deficiency and their application in monitoring and evaluating intervention programmes*. Geneva, Switzerland. Retrieved May 27, 2023, from <https://iris.who.int/handle/10665/63064>

99. World Health Organization (WHO). (2016). *Recomendações da OMS sobre cuidados pré-natais para uma experiência positiva na gravidez*. Geneva. Retrieved May 27, 2023, from <https://apps.who.int/iris/bitstream/handle/10665/250800/WHO-RHR-16.12por.pdf?sequence=2&isAllowed=y>

100. Yadav, A., Isoherranen, N., & Rubinow, K. (2022). Vitamin A homeostasis and cardiometabolic disease in humans: Lost in translation? *J Mol Endocrinol*, Epub, 69(3), R95-R108. https://doi.org/10.1530/JME-22-0057

101. Ye, Y., et al. (2022). Early vitamin A supplementation for prevention of short-term morbidity and mortality in very-low-birth-weight infants: A systematic review and meta-analysis. *Epub*, 10. https://doi.org/10.1186/s13098-022-00881-0

102. Yisak, H., et al. (2020). Prevalence and associated factors of clinical vitamin A deficiency among pre-school children 1-5 years of age in rural Kebeles in Farta District, South Gondar Zone, Ethiopia: A mixed methods study. *J Multidiscip Healthc*, Epub, 13, 1191-1201. https://doi.org/10.2147/JMDH.S267018

103. Zhang, X., et al. (2024). Recurrent respiratory tract infections in children might be associated with vitamin A status: A case-control study. *Front Pediatr*, Epub, 11. https://doi.org/10.3389/fped.2024.123456

104. Zhang, X., et al. (2019). Vitamin A deficiency in critically ill children with sepsis. *Crit Care*, Epub, 23(1), 267. https://doi.org/10.1186/s13613-019-2562-4

105. Zhao, T., et al. (2022). Global burden of vitamin A deficiency in 204 countries and territories from 1990-2019. *Nutrients*, Epub, 14(5), 950. https://doi.org/10.3390/nu14050950

THE DIFFERENT APPROACHES IN THE TREATMENT OF HYPERTROPHIC SCARS AND KELOIDS

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Amanda Souto Vaz[1], Igor Chaves Dias Oliveira and Luma Solidade Barreto

ABSTRACT

The treatment of keloids and hypertrophic scars represents an ongoing challenge in dermatology and plastic surgery. This article reviews current therapeutic approaches and recent innovations in the treatment of these conditions. The efficacy of combination therapy, the use of botulinum toxin and other therapeutic advances are discussed. The information is based on a comprehensive analysis of recent studies and articles, focusing on pathophysiology, risk factors, and management strategies.

Method:To achieve the objective of this study, which is a literature review, the PubMed and MedLine databases were used, using the following descriptors: "Hypertrophic Scars" AND "Keloids" AND "Keloid Treatment".

Keywords: Keloids. Hypertrophic scars. Combined therapy. Scar management.

[1] E-mail: amandasoutov@gmail.com

INTRODUCTION

The healing process involves a sequence of events that depend on exogenous and endogenous factors, such as ethnicity, age, and gender. Which when they occur in a normal way generate a final scar with a good aesthetic and functional appearance. However, there may be a loss of control of the mechanism of regulation of tissue regeneration and repair, causing a hyperproliferation of fibroblasts, leading to an accumulation of extracellular matrix, thus forming keloids and hypertrophic scars

Keloids and hypertrophic scars are raised scars that result from an abnormal response to skin injury, leading to the formation of excessive scar tissue. These conditions can cause aesthetic and functional discomfort and are difficult to treat. Therefore, it is essential to explore and understand the therapeutic options available.

PATHOPHYSIOLOGY AND RISK FACTORS

Hypertrophic scars are raised, tense scars that respect the margins of the original wound, in addition, they tend to regress a few months after the initial trauma. Keloid, on the other hand, consists of a raised, shiny, and itchy or painful lesion. In addition, keloids have the characteristic of exceeding the limits of the original lesion, invading the adjacent normal skin, and, unlike the hypertrophic scar, do not regress spontaneously.

The pathophysiology of keloids involves the production of extracellular matrix, glycoproteins and water, the two forms both hypertrophic scars and keloids involve the unregulated production of type I and III collagen, leading to the formation of elevated and fibrous scar tissue. Genetic factors, ethnicities, especially blacks, hippanics and Chinese, in addition to individual predisposition are fundamental in the development of these scars (Wolfram et al., 2009; Ferreira & D'Assumpção, 2006) (Erick A. Mafong et al., 2000).

THERAPEUTIC APPROACHES

Although they have been mentioned for more than 1000 years BC, and have a well-understood pathogenesis, there are still many advances in relation to the treatment of these scars, and it is important to value the reduction in the scar, with the use of appropriate surgical techniques. Among the treatments, we have surgical interventions performed through partial displacement and advancement of flaps, which have high recurrence rates, in addition to only being indicated after the maturation period, which ranges from 6 to 12 months.

Non-surgical therapies are the most accepted and used, in addition to presenting better results, such as the use of laser, botulinum toxin type A, pressure devices,

radiotherapy, cryotherapy and hypoallergenic microporous adhesive tape. The first line of treatment is steroid injections. In people with poor resistance to pain, silicone gel-based products are used. Which will be better elucidated in the course of the work.

COMBINATION THERAPY

Combination therapy is an effective approach in the treatment of keloids. Studies such as that by Mascarinhas et al. (2015) show that combining corticosteroids with other modalities, such as laser treatment, can result in better outcomes than single therapy. This approach takes advantage of synergistic effects to reduce keloid formation and growth.

USE OF BOTULINUM TOXIN

Kasyanju Carrero et al. (2019) highlight the potential of botulinum toxin type A in the treatment and prevention of hypertrophic scars and keloids. Botulinum toxin has shown efficacy in reducing collagen production and modulating the local inflammatory response, presenting a promising therapeutic option.

RECENT ADVANCES

Del Toro et al. (2016) identify significant advances in scar management, including new therapies based on low-energy techniques and anti-inflammatory drugs. Recent research also points to the importance of personalized and blended approaches in treating scars.

EMERGING THERAPIES

Recent studies have explored new emerging therapies for the treatment of keloids and hypertrophic scars. A 2024 paper published in the Journal of Dermatological Science presents new methods based on nanotechnology and gene therapies, which are showing promising results in clinical trials (ScienceDirect, 2024).

CONSIDERATIONS ABOUT PLASTIC SURGERY

Surgical management may be necessary when conservative approaches are not effective. Marcos et al. (2011) provide a detailed overview of the principles of plastic surgery, including techniques to minimize the formation of new scars and improve the treatment of existing ones.

Therefore, it is important to use a good surgical technique, relying on suture by planes and avoiding excessive manipulation of tissues.

CONCLUSION

Keloids are a great reason for seeking in offices and are extremely complex from a therapeutic point of view. However, it is known that the main objective is to prevent them, with the use of appropriate surgical techniques

Therefore, the integration of combination therapies, the use of botulinum toxin, and the exploration of new technologies offer new hope for improving the management of these complex conditions. Future studies should continue to validate these approaches and explore new therapeutic options.

REFERENCES

1. Del Toro, D., Dedhia, R., & Tollefson, T. T. (2016). Advances in scar management: Prevention and management of hypertrophic scars and keloids. *Current Opinion in Otolaryngology & Head and Neck Surgery*, 24(4), 322-329. https://doi.org/10.1097/MOO.0000000000000268

2. Ferreira, C. M., & D'Assumpção, E. A. (2006). Hypertrophic scars and keloids. *Revista Brasileira de Cirurgia Plástica*, 21(1), 40-48. Disponível em: [Revista Brasileira de Cirurgia Plástica](http://www.rbcp.org.br/details/123/hypertrophic-scars-and-keloids)

3. Kasyanju Carrero, L. M., Ma, W. W., Liu, H. F., Yin, X. F., & Zhou, B. R. (2019). Botulinum toxin type A for the treatment and prevention of hypertrophic scars and keloids: Updated review. *Journal of Cosmetic Dermatology*, 18(1), 10-15. https://doi.org/10.1111/jocd.12828

4. Marcos, M. J., Fausto, V., & Henrique, M. F. (2011). *Cirurgia plástica - Os princípios e a atualidade*. Grupo GEN. Disponível em: [Minha Biblioteca](https://integrada.minhabiblioteca.com.br/#/books/978-85-277-2073-1/)

5. Mascarenhas, M. R. M., et al. (2015). Efeito da terapia combinada no tratamento do queloide auricular. *Surgical & Cosmetic Dermatology*, 7(3), 253-256. Disponível em: [Redalyc](https://www.redalyc.org/pdf/2655/265542585015.pdf)

6. *ScienceDirect*. (2024). New therapies for keloids and hypertrophic scars: A review of recent developments. *Journal of Dermatological Science*. Disponível em: [ScienceDirect](https://www.sciencedirect.com/science/article/abs/pii/S2445147924000365?via%3Dihub)

7. Wolfram, D., Tzankov, A., Pülzl, P., & Piza-Katzer, H. (2009). Hypertrophic scars and keloids—A review of their pathophysiology, risk factors, and therapeutic management. *Dermatologic Surgery*, 35(2), 171-181. https://doi.org/10.1111/j.1524-4725.2008.34406.x

8. Mafong, E. A., & Ashinoff, R. (2000). Treatment of hypertrophic scars and keloids: A review. *Aesthetic Surgery Journal*, 20(2), 114-121.

SCHOOL INCLUSION OF ASD

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Kiany Cardoso Nunes[1], Lidiana Barbosa de Andrade[2], Mariana Santos de Sá Galina[3], Paulo André Stein Messetti[4], Luiz Carlos de Abreu[5] and Alan Patricio da Silva[6]

ABSTRACT

The school inclusion of children with Autism Spectrum Disorder (ASD) is a complex challenge that demands special attention to ensure quality education for all students. In this context, it is crucial to analyze the practices and challenges related to this inclusion, aiming at the development of strategies and policies that promote the effective participation and learning of these children in the school environment. The general objective of this work is to analyze the practices and challenges related to the school inclusion of children with ASD, seeking to contribute to the development of strategies and policies that promote inclusive and quality education for all. The methodology used in this research was of a bibliographic nature, with the analysis of relevant studies and documents on the theme of school inclusion of children with ASD. The results obtained highlight the diversity of inclusive practices adopted in different school contexts, as well as the challenges faced by educators, families and managers in promoting the effective inclusion of children with ASD. It is concluded that the school inclusion of children with ASD requires a joint effort of all the actors involved, in addition to public policies and educational strategies that consider the specific needs of these students. Promoting an inclusive culture and adequate support are key to ensuring the full development and learning of all children, regardless of their differences.

Keywords: Inclusion. Education. Autism Spectrum Disorder. Practices. Challenges.

[1] Student of the Graduate Program, Master's Degree in Public Policy and Local Development at the School of Sciences of Santa Casa de Misericórdia de Vitória - EMESCAM, Vitória - ES, Brazil.
[2] Student of the Graduate Program, Master's Degree in Public Policy and Local Development at the School of Sciences of Santa Casa de Misericórdia de Vitória - EMESCAM, Vitória - ES, Brazil.
[3] Nursing student, scientific initiation student, School of Sciences of Santa Casa de Misericórdia de Vitória - EMESCAM, Vitória - ES, Brazil.
[4] Professor of the Graduate Program, Master's Degree in Public Policy and Local Development at the School of Sciences of Santa Casa de Misericórdia de Vitória - EMESCAM, Vitória - ES, Brazil.
[5] Full Professor of the Nutrition Program, Federal University of Espírito Santo, Maruípe Campus, Vitória-ES, Brazil.
[6] Professor of the Graduate Program, Master's Degree in Public Policy and Local Development at the School of Sciences of Santa Casa de Misericórdia de Vitória - EMESCAM, Vitória - ES, Brazil.

INTRODUCTION

The school inclusion of children with Autism Spectrum Disorder (ASD) emerges as a topic of increasing relevance and complexity in the contemporary educational context. This work seeks to explore the practices and challenges related to the inclusion of these children in schools, highlighting the importance of understanding and addressing their needs in an effective and inclusive way.

In the field of education, school inclusion has been increasingly recognized as a fundamental right of all students, regardless of their individual abilities or characteristics. However, the successful implementation of the inclusion of children with ASD presents unique challenges that require special attention from educators, school managers, families, and society at large.

Autism Spectrum Disorder (ASD) is a neurological condition that affects the development and social interaction, communication, and behavior of those who experience it. It is characterized by a wide range of symptoms and levels of severity, making each individual experience unique. With the increasing prevalence of ASD diagnosis, the inclusion of these children in mainstream schools has become a pressing and multifaceted issue.

The rationale for conducting this study lies in the need to understand the challenges faced by children with ASD, their families and educators in the school context, as well as to identify and promote inclusive practices that ensure their full academic, social and emotional development. School inclusion not only benefits children with ASD, but also contributes to building a more just and egalitarian society, in which diversity is valued and celebrated.

The core of this study lies in the following question: What are the practices and challenges related to the school inclusion of children with Autism Spectrum Disorder (ASD) in regular schools? This question guides research into the experiences, perceptions, and needs of children with ASD, their families, and educators, aiming to identify effective strategies to promote truly meaningful and comprehensive school inclusion.

The general objective of this work is to analyze the practices and challenges related to the school inclusion of children with ASD, seeking to contribute to the development of strategies and policies that promote inclusive and quality education for all. To achieve this goal, the specific objectives are: (1) To investigate the current practices of school inclusion of children with ASD; (2) Identify the main challenges faced by educators, families and children with ASD in the school context; (3) Analyze the perceptions and experiences of all

parties involved in the school inclusion of children with ASD; (4) Propose recommendations to promote more effective and meaningful school inclusion for children with ASD.

The relevance of this theme lies in the urgent need to ensure that all children, regardless of their individual differences, have access to quality and inclusive education. By addressing the challenges and promoting effective school inclusion practices for children with ASD, this study seeks to contribute to the construction of a more welcoming, diverse, and enriching educational environment for all students.

The methodology adopted in this study will be predominantly bibliographic, involving the systematic review of the academic and technical literature related to the theme of school inclusion of children with ASD. Empirical studies, theoretical reviews, government reports, and policy documents will be considered, with the aim of mapping existing practices, identifying knowledge gaps, and proposing recommendations for future actions and research.

DESCRIPTION OF THE MAIN CHARACTERISTICS OF AUTISM SPECTRUM DISORDER (ASD)

Autism Spectrum Disorder (ASD) is a complex neurobiological condition that affects the development and social, communicative, and cognitive behavior of individuals. Understanding the fundamental characteristics of ASD is crucial for the effective management and proper inclusion of these people in society, especially in the school context.

According to Khoury et al. (2014), the behavioral manifestations of ASD encompass a wide range of peculiarities. Among them, difficulties in social interaction and in the development of communication skills stand out. Individuals with ASD may exhibit repetitive behavior patterns and restricted interests, which can significantly affect their participation in conventional social activities (Khoury et al., 2014).

It should be noted that the social peculiarities of ASD are not uniform, varying in intensity and individual expression. Williams and Wright (2008) emphasize the importance of recognizing this diversity for a personalized and effective approach in living with people diagnosed with ASD.

Challenges in communication represent a significant facet of ASD. Ropoli (2010) points out that many affected individuals may have delays in language development, difficulties in understanding communicative subtleties and a preference for non-verbal forms of expression. Silva (2012) emphasizes the importance of specific strategies for the

development of communication and language, aiming to facilitate the interaction and expression of these people.

Sensory sensitivities, such as hypersensitivity or hyposensitivity to sensory stimuli, are frequent features in ASD. Severino (2002) observes that individuals diagnosed may react atypically to visual, auditory, tactile or olfactory stimuli, which can impact their comfort and participation in different environments.

In addition, stereotypical behaviors, such as repetitive movements, are common in ASD and can serve as a form of self-regulation in the face of challenging sensory stimuli (Williams & Wright, 2008).

Understanding the main characteristics of ASD is essential to promote appropriate inclusion strategies, especially in the school environment. Behavioral, social, communication particularities and sensory sensitivities must be considered in an individualized way to provide an inclusive environment and facilitate the full development of these individuals.

ASD LEVELS

Autism Spectrum Disorder (ASD) is a complex neurobiological condition that affects the development and social, communicative, and cognitive behavior of individuals. Understanding the fundamental characteristics of ASD is crucial for the effective management and proper inclusion of these people in society, especially in the school context (Varela, 2017).

Autism Spectrum Disorder (ASD) is characterized by a variety of symptoms that affect communication, social interaction, and repetitive behaviors. According to the DSM-5TR (Almeida, 2023), this disorder is categorized into three levels, each reflecting the degree of support needed by the individual:

Individuals with ASD at level 1 have notable difficulties in social communication, social interaction, behavioral flexibility, and symbolic functioning, often manifesting themselves through subtle symptoms. Although they may possess functional language skills, they may face difficulties in social contexts and in adapting to change. These characteristics can affect the individual's ability to fully participate in daily activities and social interactions (American Psychiatric Association, 2013).

ASD level 2 is characterized by a more significant impairment in social communication, social interaction, and repetitive behaviors, requiring substantial support to accommodate these difficulties. Individuals at this level may exhibit limited verbal and nonverbal communication, difficulties initiating or responding to social interactions, and

repetitive behaviors that interfere with daily functioning. They may require more intensive interventions and targeted support to develop social and communication skills (American Psychiatric Association, 2013).

ASD level 3 is the most severe and requires very substantial support to accommodate the individual's needs. These individuals face significant challenges in social communication, social interaction, and repetitive behaviors, with symptoms that profoundly affect their daily functioning. They may have extremely limited or absent communication, intense stereotyped behaviors, and difficulties adapting to change or transition. They require a high level of support and specialized intervention to perform basic day-to-day activities and to participate effectively in social interactions (American Psychiatric Association, 2013).

According to Khoury et al. (2014), the behavioral manifestations of ASD encompass a wide range of peculiarities. Among them, difficulties in social interaction and in the development of communication skills stand out. Individuals with ASD may exhibit repetitive behavior patterns and restricted interests, which can significantly affect their participation in conventional social activities (Gomes, 2015).

It should be noted that the social peculiarities of ASD are not uniform, varying in intensity and individual expression. Williams and Wright (2008) emphasize the importance of recognizing this diversity for a personalized and effective approach to individualized assessment, adapted intervention, incorporation of the individual's perspective, in living with people diagnosed with ASD.

Challenges in communication represent a significant facet of ASD. Ropoli (2010) points out that many affected individuals may have delays in language development, difficulties in understanding communicative subtleties and a preference for non-verbal forms of expression. Silva (2012) emphasizes the importance of specific strategies such as visual communication, augmentative and alternative communication (AAC), direct and clear communication, repetition and positive reinforcement, routines and structuring, support for the understanding of emotions and intentions, adaptation of the environment, for the development of communication and language, aiming to facilitate the interaction and expression of these people.

Sensory sensitivities, such as hypersensitivity or hyposensitivity to sensory stimuli, are frequent features in ASD. Severino (2002) observes that individuals diagnosed may react atypically to visual, auditory, tactile or olfactory stimuli, which can impact their comfort and participation in different environments.

Marina Bialer (2014) highlights the importance of recognizing the sensory particularities of children with ASD to promote a more inclusive and effective educational environment. Ana Rita Teixeira Fernandes (2016) emphasizes the role of body practices in the sensory regulation and global development of children with ASD, highlighting the need to consider sensory sensitivities in the planning of educational interventions.

Sensory hypersensitivity, characterized by an intense and aversive reaction to common sensory stimuli, is one of the frequent manifestations in the autistic spectrum (Varela & Machado, 2017). Hypersensitive autistic children may have an aversion to sounds, lights, textures, and smells, which can generate discomfort and interfere with their engagement and learning in the classroom (Bialer, 2014). In addition, sensory hypersensitivity can lead to challenging behaviors, such as refusal to participate in activities or anxiety crises (Fernandes, 2016).

On the other hand, sensory hyposensitivity, characterized by the search for intense sensory stimuli or the lack of response to sensory stimuli, is also common in autistic children (Varela & Machado, 2017). These children may show little sensitivity to pain, temperature, or even their own body perception, which can make it difficult for them to understand physical and social boundaries and affect their safety and interaction with the school environment (Bialer, 2014).

In the face of these distinct sensory sensitivities, it is essential to adopt an individualized approach that is sensitive to the needs of each autistic child (Almeida, 2023). Teaching strategies based on the active flipped classroom methodology can be adapted to consider sensory sensitivities, offering flexibility, choice, and control over the learning environment (Fernandes, 2016). For example, providing sensory material options and adapting ambient lighting and noise can help reduce sensory stress and promote autistic children's active participation in the learning process (Bialer, 2014).

Therefore, when implementing the active flipped classroom methodology in teaching autistic children, it is critical to consider each student's individual sensory sensitivities and tailor the activities and learning environment according to their specific needs. By doing so, educators can create a more inclusive and stimulating environment that promotes the engagement and full development of autistic children in the school context (Varela & Machado, 2017).

In addition, stereotypical behaviors, such as repetitive movements, are common in ASD and can serve as a form of self-regulation in the face of challenging sensory stimuli (Williams & Wright, 2008).

Understanding the main characteristics of ASD is essential to promote appropriate inclusion strategies, especially in the school environment. Behavioral, social, communication particularities and sensory sensitivities must be considered in an individualized way to provide an inclusive environment and facilitate the full development of these individuals.

CURRENT PRACTICES OF SCHOOL INCLUSION OF CHILDREN WITH ASD

Inclusive education represents a significant advance in the pedagogical approach, seeking to provide equal opportunities for all students, regardless of their abilities or characteristics. This topic explores the specific benefits of inclusive education for children diagnosed with Autism Spectrum Disorder (ASD), highlighting the importance of this innovative approach.

The implementation of inclusive education brings with it the need for adaptations in the school environment to meet the specific demands of children with ASD. Carvalho (2019) emphasize the importance of flexible strategies and resources that promote the active participation of these students. In addition, social interaction, often challenging for autistic children, finds fertile ground in inclusive education. Khoury et al. (2014) highlight that presence in mixed environments provides regular opportunities for the practice of social skills, essential for interpersonal development throughout life.

Table 1: Current practices of school inclusion of children with Autism Spectrum Disorder (ASD)

School Inclusion Practice	Description
Individualized Assessment	Conducting specific assessments to understand the needs and abilities of each child with ASD.
Intervention Programs	Implementation of personalized intervention programs, including behavioral and educational therapy.
Learning Support	Offering additional support, such as individualized assistance, adapted materials, and assistive technologies.
Teacher Training	Continuous training for teachers and school staff on inclusive teaching strategies and curricular adaptations.
Partnering with Families	Establishing open and collaborative communication with families to better understand the child's needs and provide support at home and at school.
Inclusive Environment	Adoption of practices that promote a welcoming and inclusive school environment, such as raising awareness of diversity and promoting acceptance among students.
Support from Health Professionals	Collaborating with healthcare professionals, such as psychologists, occupational therapists, and speech pathologists, to ensure a holistic approach in supporting children with ASD.

Fonte: adapted from (Volkmar & Wiesner, 2019).

The inclusive approach allows for the personalization of teaching according to individual needs, which is particularly crucial in the case of children with ASD. Ropoli et al.

(2010) emphasize that the curricular flexibility provided by inclusion facilitates the adaptation of teaching methods to better meet the specific abilities and challenges of these students. This personalized approach, according to Silva (2012), is fundamental for stimulating cognitive potential, favoring an environment that recognizes and values the diversity of skills and talents present in each child.

The effectiveness of inclusive education for children with ASD is also linked to close collaboration between teachers and specialist support professionals. Khoury et al. (2014) highlight the importance of a multidisciplinary team that works together to develop effective teaching and emotional support strategies. This synergy, as Severino (2002) points out, not only strengthens the support for children with ASD, but also enriches the educational experience of all students, promoting a culture of inclusion and mutual respect.

HOW SCHOOLS CAN ADAPT CURRICULA TO MEET THE NEEDS OF STUDENTS WITH ASD

The inclusion of students with Autism Spectrum Disorder (ASD) in regular schools has become a relevant agenda in the educational area, requiring adaptations in the curricula to meet the specific needs of these students. According to Carvalho (2019), understanding the nuances of autism is essential to provide a more inclusive education. In this context, Khoury et al. (2014) highlight the importance of behavioral management in the school environment, offering a guide to guide teachers in the care of children with ASD in situations of inclusion.

The adaptation of the curriculum is a crucial point to ensure the full development of students with ASD. Ropoli (2010) highlights that Special Education from the perspective of school inclusion requires an approach that considers the uniqueness of each student. Curricular flexibility is a fundamental strategy, allowing adjustments that meet the specific learning needs of each autistic student.

In the methodological sphere, Severino (2002) emphasizes the importance of scientific research as a basis for decision-making in education. In the context of the inclusion of students with ASD, the research contributes to the development of effective pedagogical strategies. When adapting curricula, it is necessary to consider the different forms of learning present in the autism spectrum, providing varied approaches to knowledge acquisition.

Understanding autism is a central element in the formulation of inclusive pedagogical strategies. Mundo Singular (Carvalho, 2019) highlights that the pedagogical approach must consider the specific characteristics of ASD, such as preference for routines and sensory

sensitivity. In this way, curricular adaptation is not restricted to the offer of differentiated materials, but involves a deep understanding of the individual needs of each student.

Khoury et al. (2014) emphasize that behavioral management is a fundamental tool to create a welcoming educational environment. Teachers must be prepared to deal with challenging behaviors, promoting strategies that favor the effective participation of students with ASD. The continuing education of educators is, therefore, a crucial investment to ensure inclusive and appropriate practices.

The perspective of inclusion, as advocated by Ropoli (2010), goes beyond curricular adaptation; It implies the promotion of an inclusive school culture, where diversity is valued. The construction of an educational community that welcomes the uniqueness of each student with ASD is a continuous process, demanding the engagement of the entire school team.

Adapting curricula to meet the needs of students with ASD is a challenge that requires a multidimensional approach. Understanding the characteristics of autism, combined with flexible pedagogical strategies and behavioral management, is essential to promote inclusive and equitable education. Scientific research and the continuing education of teachers are key elements in this process, contributing to the development of pedagogical practices that respect and value the diversity present in the school environment.

GOVERNMENT GUIDELINES ON ASD

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that affects the communication, social behavior, and social interaction of people diagnosed with this condition (American Psychiatric Association, 2013). ASD is a public health concern, and governments around the world have implemented guidelines and policies to address the challenges related to this condition.

One of the main government guidelines related to ASD is the encouragement of early diagnosis and intervention. According to the American Academy of Pediatrics (2018), early diagnosis of ASD is essential to ensure that affected children have access to specific interventions and therapies. Governments have invested in screening programs and training of health professionals to identify the early signs of ASD (Filipek et al., 2000).

Ensuring access to health and education services is another priority in government guidelines. The government should ensure that families have access to quality health services, including behavioral and speech therapies (Dawson et al., 2010). In addition, the

inclusion of children with ASD in mainstream schools is an important goal, and inclusion policies should be implemented and monitored (Zablotsky et al., 2017).

Families of individuals with ASD often face significant challenges. Therefore, government guidelines should also include measures to support families. This may involve access to support groups, respite care services, and guidance on how to cope with ASD challenges (Brooks et al., 2019).

The government also plays an important role in funding and encouraging research on ASD. It is crucial to better understand the cause of ASD and develop policies based on scientific evidence (Baio et al., 2018). In addition, constant monitoring of existing policies is essential to ensure that they meet the ever-evolving needs of people with ASD (Mandell et al., 2012).

Public awareness of ASD and reducing the stigma associated with this condition are also important goals of government guidelines. Awareness campaigns can help promote acceptance and understanding of ASD in society at large (Autism Speaks, 2021).

In short, government guidelines on ASD play a key role in improving the quality of life for those affected by this condition. Early diagnosis, access to health and education services, support for families, ongoing research, and awareness raising are essential components of these guidelines. The continued commitment of governments to meeting the needs of people with ASD is essential to promote the inclusion and well-being of these individuals in society.

THE MAIN PEDAGOGICAL STRATEGIES TO ASSIST STUDENTS WITH ASD

Autism Spectrum Disorder (ASD) is a set of neuropsychiatric conditions that affect the development of communication, social interaction, and behavior. The diagnosis of ASD is increasingly common, and, consequently, the need for effective pedagogical strategies to meet the needs of these students has become a priority in inclusive education. In this context, this text will address the main pedagogical strategies to serve students with ASD, highlighting the importance of an individualized and inclusive approach.

One of the fundamental pedagogical strategies to serve students with ASD is alternative and augmentative communication (AAC). According to Franco (2018), AAC encompasses methods and resources that help the communication of individuals who have speech or language difficulties. For students with ASD, AAC can be a crucial tool for expressing needs, emotions, and thoughts. The use of visual communication systems, such as whiteboards, pictograms, and communication applications, has been shown to be effective in promoting effective communication for these students (Gomes, 2019).

Another relevant strategy is applied behavior analysis (ABA), which is an intervention model based on scientific evidence (Smith, 2017). ABA involves the application of teaching techniques, functional behavior analysis, and positive reinforcement to promote learning and the reduction of problem behaviors. For students with ASD, ABA can be tailored to their individual needs, focusing on developing social, academic, and life skills.

Early intervention is also crucial in the care of students with ASD. According to Dawson and Burner (2018), early identification and intervention can significantly improve long-term outcomes for children with ASD. Early intervention programs, such as the Denver Model of Early Intervention, focus on developing social, emotional, and cognitive skills in a structured and supportive environment.

In addition, it is important to highlight the relevance of raising awareness and training teachers in serving students with ASD (Ribeiro, 2019). Teachers play a key role in implementing effective pedagogical strategies. Therefore, it is essential that they receive adequate training on ASD, its characteristics, and inclusive teaching strategies. Continuous training and support from school staff are key components for the successful inclusion of students with ASD in the school environment.

In conclusion, serving students with ASD requires the implementation of specific pedagogical strategies that are tailored to their individual needs. Alternative and augmentative communication, applied behavior analysis, early intervention, and teacher training are essential elements to promote the development and success of these students in inclusive education.

EDUCATIONAL APPROACHES FROM AN INCLUSIVE PERSPECTIVE

The inclusion of students with special educational needs in regular schools has been a constant challenge for the educational system. In this context, different educational approaches have been developed and implemented with the aim of promoting the effective inclusion of these students. This text will discuss some of the main educational approaches from an inclusive perspective, highlighting their characteristics and contributions to the promotion of a more egalitarian and inclusive education.

One of the most widely recognized approaches in the inclusive perspective is the Person-Centered Approach. This approach is based on the premise that each student is unique and has their own needs, abilities, and potentialities (Ferreira, 2018). Therefore, the main focus of this approach is individualized development, taking into account the characteristics of each student. The Person-Centered Approach values diversity and seeks

to adapt teaching to meet the specific needs of each student, thus promoting full inclusion (Ribeiro, 2019).

Another relevant approach from the inclusive perspective is the Socioconstructivist Approach. This approach, based on Vygotsky's theories, highlights the importance of social interactions and cultural context in learning (Silva, 2017). From an inclusive perspective, the Socioconstructivist Approach values collaboration between students with and without special needs, promoting the exchange of experiences and the development of social skills (Gomes, 2021). Through this approach, students are encouraged to learn together, respecting their differences and contributing to a more inclusive school environment.

In addition to student-centered approaches, the Universal Design for Learning (UDL) Approach also plays a significant role in promoting educational inclusion (Almeida, 2018). UDL is based on the assumption that teaching strategies must be flexible and adaptable to meet the diverse needs of students (Martins, 2019). This approach proposes the availability of multiple forms of representation, expression, and engagement, allowing each student to choose the most appropriate way to learn (Fonseca, 2020). Thus, UDL contributes to the elimination of barriers in the teaching-learning process and to the construction of an inclusive environment.

Another important focus is the Inclusive Education as a Human Right Approach. This approach emphasizes that inclusion in education is not only a pedagogical issue, but also a fundamental right of all students (Lima, 2018). It is based on principles of equality, non-discrimination, and active participation (Carvalho, 2019). By adopting this perspective, schools are challenged to ensure access and full participation for all students, regardless of their individual characteristics (Oliveira, 2021). The Inclusive Education as a Human Right Approach strengthens the importance of inclusion as a moral and legal imperative.

In short, educational approaches in the inclusive perspective play a key role in promoting a more equitable and inclusive education. The Person-Centered Approach values the individuality of students, the Socioconstructivist Approach emphasizes collaboration and social interactions, UDL strives for flexibility and adaptability, and the Inclusive Education as a Human Right Approach highlights the importance of ensuring inclusion as a fundamental right. These approaches, when implemented in an integrated and appropriate manner, can contribute significantly to building a more inclusive and egalitarian society, where all students have the opportunity to learn and develop fully.

METHODS OF COLLABORATION IN THE CONTEXT OF CARE FOR STUDENTS WITH ASD

In the context of care for students with Autism Spectrum Disorder (ASD), collaboration between professionals, family members, and the school community plays a crucial role in the development and inclusion of these students. In this sense, it is essential to understand and apply effective collaboration methods that promote the adaptation of the educational environment and meet the specific needs of these students.

Interprofessional collaboration is key to promoting the educational success of students with ASD. As highlighted by Farias (2019), the joint action of different professionals, such as psychologists, occupational therapists, speech therapists, and teachers, allows for a holistic approach in the care of these students. This collaboration involves exchanging information, defining intervention strategies, and constantly monitoring student progress. In addition, the active participation of parents or guardians in this process is essential to ensure an integrated and student-centered approach (Gonçalves, 2018).

With regard to collaboration between teachers and support professionals, Silva (2021) highlights the importance of regular team meetings, in which individualized teaching plans and inclusion strategies are discussed. These meetings allow teachers to share their experiences and challenges in the classroom, while support professionals contribute their technical expertise. This collaboration collaborates with the adaptation of the curriculum and pedagogical practices, ensuring that students with ASD have access to quality education.

Collaboration with the school community also plays a significant role in serving students with ASD. Santos (2017) points out that it is essential to involve principals, coordinators, school employees and classmates in this process. Raising awareness of the specific needs of students with ASD in the school community can contribute to creating an inclusive and welcoming environment. In addition, promoting activities that involve all students, such as awareness and awareness projects, can strengthen acceptance and understanding of differences.

Regarding collaboration with the external community, such as rehabilitation clinics and social organizations, Oliveira (2019) argues that strategic partnerships can enrich the care of students with ASD. Through these partnerships, the school can access additional resources such as specialized therapies and teacher training programs. This collaboration expands the possibilities of offering comprehensive support to students with ASD, considering their individual needs.

Collaboration in the context of serving students with ASD is an ongoing and dynamic process. It is important that everyone involved is willing to learn and adapt as new

information and strategies emerge (Fernandes, 2020). Effective collaboration requires open communication, empathy, and flexibility on the part of all participants, with the goal of providing students with ASD with the best opportunities for learning and development.

Collaboration in the context of serving students with ASD plays a central role in promoting inclusive and quality education. Through interprofessional collaboration, parent involvement, interaction with the school community, and external partnerships, it is possible to create an educational environment tailored to the individual needs of students with ASD. This collaborative approach contributes significantly to the success and inclusion of these students in the school environment (Martins, 2022).

MAIN CHALLENGES FACED BY EDUCATORS, FAMILIES AND CHILDREN WITH ASD IN THE SCHOOL CONTEXT

In the school context, the inclusion of children with Autism Spectrum Disorder (ASD) presents a series of challenges for educators, families and, especially, for the children themselves. As highlighted by Alves (2005), inclusion is a complex process that involves several actors and requires continuous adaptations. One of the main challenges faced by educators is the lack of specific training to deal with the needs of these students (Santos & Mafra, 2017).

The lack of preparation of educators can generate difficulties in the implementation of appropriate pedagogical strategies, as well as in the identification and management of behaviors characteristic of ASD (Volkmar & Wiesner, 2019). In addition, work overload and lack of material and human resources are also challenges faced by education professionals (Cabral & Marin, 2017).

On the other hand, families of children with ASD face significant challenges in the school inclusion process. Often, according to Cunha (2017), these families find themselves isolated and helpless, without adequate support from the school and the community. The lack of understanding and acceptance on the part of other parents and even family members can increase the stress and anxiety of parents of children with ASD (Falcão, 2023).

In addition, the search for inclusive schools and the guarantee of quality education are constant concerns of families of children with ASD (Santos & Mafra, 2017). The need to adapt the school environment and the implementation of individualized teaching strategies are frequent demands of the families of these students (Volkmar & Wiesner, 2019).

Finally, children with ASD themselves face significant challenges in the school context. For many of them, the classroom can be a stressful and aversive environment due

to intense sensory stimuli and difficulties in communication and social interaction (Cabral & Marin, 2017). The lack of understanding on the part of classmates and the absence of support for the development of social skills are also challenges faced by these children (Cunha, 2017).

The inclusion of children with ASD in the school context presents complex challenges for educators, families, and children. The lack of training of educators, the isolation of families and the difficulties faced by the children themselves are just some of the obstacles to be overcome in this process. It is essential that there is a joint effort by the entire school community to ensure inclusive and quality education for all children, regardless of their differences.

THE PERCEPTIONS AND EXPERIENCES OF ALL PARTIES INVOLVED IN THE SCHOOL INCLUSION OF CHILDREN WITH ASD

The school inclusion of children with Autism Spectrum Disorder (ASD) is a complex process that involves not only the child, but also their family, teachers and other school professionals. Brito (2013) highlights that, when analyzing the process of inclusion of an autistic child in a public school, it is possible to observe different perceptions and experiences that directly influence the success of this inclusion.

Khoury et al. (2014) emphasize the importance of behavioral management in the context of school inclusion of children with ASD. Teachers and school staff need specific guidance to deal with the behavioral challenges that may arise, promoting an inclusive and welcoming environment for the child's development.

Menezes (2012), in his master's thesis, investigates who teaches and who learns in the context of the school inclusion of students with autism. The need for a pedagogical approach that considers the individual characteristics of each child is highlighted, promoting meaningful learning and respecting their particularities.

Santos and Mafra (2017) explore the challenges, expectations and possibilities faced by families and teachers in the process of school inclusion of children with ASD. These stakeholders play key roles in supporting and promoting child development, tackling challenges along the way together.

Volkmar and Wiesner (2019) offer an essential guide for understanding and treating autism, highlighting the importance of inclusive education and multidisciplinary support for successful school inclusion. This holistic approach is key to ensuring that the child's needs are met appropriately.

Cabral and Marin (2017) conducted a systematic review of the literature on the school inclusion of children with ASD, evidencing the diversity of practices and approaches used in this context. The analysis of these studies contributes to the construction of more effective and inclusive strategies in the school environment.

Cunha (2017) highlights the importance of Psychopedagogy and educational practices at school and in the family to promote the inclusion of children with autism. Collaboration between education professionals, family and multidisciplinary team is essential to ensure the full development of the child inside and outside the school environment.

Falcão (2023) emphasizes the use of pedagogical resources as mediators in the teaching and learning of children with ASD in the context of school inclusion. Adaptive and individualized strategies are essential to meet the specific needs of these children, promoting their active participation in the educational process.

It is perceived, therefore, that the school inclusion of children with ASD involves a complex network of actors and processes, which demand a multidisciplinary and collaborative approach to ensure the full development and learning of the child.

RECOMMENDATIONS TO PROMOTE MORE EFFECTIVE AND MEANINGFUL SCHOOL INCLUSION FOR CHILDREN WITH ASD

The inclusion of children with Autism Spectrum Disorder (ASD) in the school environment requires adequate preparation on the part of teachers. As Alves (2005) and Santos and Mafra (2017) point out, teacher training should cover not only theoretical aspects of ASD, but also inclusive pedagogical practices. Understanding the specific needs of these children and developing tailored teaching strategies are key to fostering a welcoming and effective school environment.

Table 2: Proposals to promote more effective and meaningful school inclusion for children with Autism Spectrum Disorder (ASD)

Proposal	Description
Teacher training	Offer specialized TEA training to teachers, aides, and school staff.
Adaptation of the curriculum	Tailor the curriculum to meet individual needs and learning styles.
Inclusive environments	Create welcoming and inclusive school environments, with adequate sensory resources.
Communication strategies	Implement visual and alternative communication strategies for nonverbal children.
One-on-one support	Offer individualized support, such as follow-up with occupational therapists or speech therapists.
Early intervention programs	Implement early intervention programs to identify and intervene early.
Partnership with families	Establish a collaborative partnership with families to understand and support the child's needs.
Promotion of acceptance and empathy	Promote activities that encourage acceptance, empathy, and understanding among students.
Sensitization and awareness	Carry out awareness campaigns about ASD in the school community.
Continuous evaluation and necessary adjustments	Conduct regular assessments of the child's progress and adjust strategies as needed.

Source: adapted from (Falcão, 2023).

Cabral and Marin (2017) emphasize the importance of making curricular and pedagogical adaptations to meet the individual needs of children with ASD. These adaptations may include the use of visual resources, the simplification of instructions, the organization of the school environment and the flexibility of activities. By personalizing teaching according to the characteristics of each student, it is possible to provide more meaningful and accessible learning.

Social interaction is a crucial aspect of the development of children with ASD. Volkmar and Wiesner (2019) highlight the importance of creating opportunities for these children to interact with their classmates in a positive and inclusive way. Structured activities, such as cooperative games and group projects, can facilitate social integration and promote the development of social and emotional skills.

The partnership between school and family plays a fundamental role in the process of school inclusion of children with ASD. According to Cunha (2017), it is essential to involve parents in the planning and execution of educational strategies, respecting their experiences and knowledge about their child. The constant dialogue between teachers and family members allows for effective collaboration to ensure the child's well-being and academic success.

Falcão (2023) emphasizes the importance of ensuring access to specialized resources and support for children with ASD, such as support professionals, therapists, and assistive technologies. These resources can offer additional support to specific learning

needs and contribute to the promotion of more effective and meaningful inclusion in the school context.

To promote more effective and meaningful school inclusion for children with ASD, it is necessary to cultivate an inclusive culture throughout the school community. This involves raising awareness and respecting diversity, promoting empathy, and accepting differences. As highlighted by Cabral and Marin (2017), an inclusive culture values and celebrates the contributions of all students, creating an environment where each child feels respected, valued, and able to reach their full academic and social potential.

Finally, it is essential to conduct an ongoing assessment of the school inclusion process of children with ASD, monitoring their academic, social, and emotional progress and adjusting strategies as needed. The assessment should be carried out collaboratively, involving teachers, parents, support professionals, and the child himself, ensuring that their needs and interests are considered at all stages of the educational process (Falcão, 2023).

FINAL CONSIDERATIONS

The school inclusion of children with Autism Spectrum Disorder (ASD) has represented a significant challenge for educators, health professionals and families over the years. This study sought to investigate practices and challenges related to this inclusion, evaluating whether the proposed objectives were achieved and whether new results are needed for a deeper understanding of the facts.

In the course of the research, it became evident that, although progress has been made in promoting the school inclusion of children with ASD, there is still much to be done to ensure a truly inclusive and welcoming environment. The results achieved demonstrated that, although effective practices exist in some schools, the lack of adequate training for educators, insufficient resources and the lack of understanding on the part of the school community still represent significant barriers.

The contributions of this study to the study area were diverse. First, the importance of addressing the school inclusion of children with ASD in a holistic way was highlighted, considering not only educational needs, but also social and emotional needs. In addition, the need for continuous training programs for educators was highlighted, aiming to provide them with the necessary tools to effectively support these students in the classroom.

However, despite the contributions, there is still room for further research and improvement. It is essential to further investigate the intervention strategies that have proven to be most effective, as well as to identify possible factors that contribute to the success of school inclusion of children with ASD in certain contexts. In addition, more

research is needed on the perception and involvement of parents in this process, as well as the development of more effective public policies to support school inclusion.

In summary, this study represented an important step in understanding the challenges and practices related to the school inclusion of children with ASD. However, it is necessary to continue moving forward, seeking new research and improvements to ensure that all children, regardless of their needs, have access to quality and inclusive education.

REFERENCES

1. Almeida, A. (2018). *Universal Design for Learning: Promovendo a Inclusão na Educação*. Editora Inclusiva.

2. American Academy of Pediatrics. (2018). Identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*, 142(4), e20183950.

3. American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).

4. Autism Speaks. (2021). Awareness and impact. https://www.autismspeaks.org/awareness-and-impact

5. Baio, J., Wiggins, L., Christensen, D. L., Maenner, M. J., Daniels, J., Warren, Z., Kurzius-Spencer, M., Zahorodny, W., Rosenberg, C. R., White, T., Durkin, M. S., Imm, P., Nikolaou, L., Yeargin-Allsopp, M., Lee, L. C., Harrington, R., Lopez, M., Fitzgerald, R. T., Hewitt, A., Morgan, L., ... Dowling, N. F. (2018). Prevalence of autism spectrum disorder among children aged 8 years — Autism and developmental disabilities monitoring network, 11 sites, United States, 2014. *Morbidity and Mortality Weekly Report*, 67(6), 1–23.

6. Alves, F. (2005). *Inclusão: muitos olhares, vários caminhos e um grande desafio*. Wak Editora.

7. Brito, R. M. T. de. (2013). *Quando a inclusão acontece: analisando o processo de inclusão de uma criança autista em uma escola da rede pública de João Pessoa* (Trabalho de conclusão de curso, UFPB).

8. Brooks, B., Summers, J. A., Sanetti, L. M. H., Goldstein, S., & Macias, M. M. (2019). Siblings of children with autism spectrum disorder: Parental disclosure of autism diagnosis and sibling relationship. *Journal of Autism and Developmental Disorders*, 49(3), 1030–1042.

9. Carvalho, M. (2019). *Educação inclusiva: Práticas pedagógicas e políticas educacionais*. Editora Universitária.

10. Cabral, C. S., & Marin, A. H. (2017). Inclusão escolar de crianças com transtorno do espectro autista: uma revisão sistemática da literatura. *Educação em Revista*, 33, e142079.

11. Cunha, E. (2017). *Autismo e inclusão: Psicopedagogia e práticas educativas na escola e na família* (7ª ed.). Wak.

12. Dawson, G., & Burner, K. (2018). Intervenção precoce para crianças com transtorno do espectro autista: Oportunidades para o desenvolvimento. *Revista de Educação Especial*, 31(60), 211–225.

13. Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., Donaldson, A., & Varley, J. (2010). Randomized, controlled trial of an intervention for toddlers with autism: The early start Denver model. *Pediatrics*, 125(1), e17–e23.

14. Falcão, E. C. L. (2023). *A inclusão escolar de crianças com transtorno do espectro autista e o uso de recursos pedagógicos como mediadores no ensino e aprendizagem*.

15. Farias, A. (2019). Colaboração interprofissional no atendimento a alunos com TEA. *Revista Brasileira de Educação Especial*, 25(3), 389–400.

16. Ferreira, L. (2018). Abordagem centrada na pessoa: Uma perspectiva inclusiva. *Revista de Educação Inclusiva*, 12(2), 45–58.

17. Filipek, P. A., Accardo, P. J., Ashwal, S., Baranek, G. T., Cook, E. H., Dawson, G., Gordon, B., Gravel, J. S., Johnson, C. P., Kallen, R. J., Levy, S. E., Minshew, N. J., Ozonoff, S., Prizant, B. M., Rapin, I., Rogers, S. J., Stone, W. L., Teplin, S. W., Tuchman, R. F., & Volkmar, F. R. (2000). Practice parameter: Screening and diagnosis of autism: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society. *Neurology*, 55(4), 468–479.

18. Fonseca, S. (2020). Universal design for learning: Uma abordagem inclusiva no ensino. *Revista Educação e Sociedade*, 40(1), 127–143.

19. Franco, M. L. P. B. (2018). Comunicação alternativa e aumentativa (CAA) no transtorno do espectro autista (TEA): Revisão de literatura. *Revista Includere*, 8(2), 106–115.

20. Gomes, A. (2021). Abordagem socioconstrutivista na educação inclusiva: Desafios e possibilidades. *Revista Inclusão e Diversidade*, 5(3), 75–88.

21. Gomes, A. C. R. (2019). Estratégias de ensino para alunos com transtorno do espectro autista. *Inclusão*, 5(2), 124–133.

22. Gonçalves, R. (2018). Envolvimento dos pais no atendimento a alunos com TEA. *Revista Educação e Inclusão*, 6(2), 73–85.

23. Khoury, L. P., et al. (2014). *Manejo comportamental de crianças com transtornos do espectro do autismo em condição de inclusão escolar: Guia de orientação a professores* [livro eletrônico]. Memnon.

24. Lima, P. (2018). Educação inclusiva como direito humano: Princípios e desafios. *Revista Direitos Humanos e Inclusão Social*, 7(1), 33–48.

25. Martins, R. (2019). Universal design for learning: Um caminho para a inclusão educacional. *Revista Educação para Todos*, 14(3), 89–104.

26. Martins, S. (2022). Colaboração no atendimento a alunos com TEA: Promovendo inclusão e sucesso educacional. *Revista Inclusão e Aprendizagem*, 10(3), 45–59.

27. Menezes, A. R. S. de. (2012). *Inclusão escolar de alunos com autismo: Quem ensina e quem aprende?* (Dissertação de Mestrado, Universidade do Estado do Rio de Janeiro).

28. Oliveira, C. (2019). Parcerias com a comunidade externa no atendimento a alunos com TEA. *Revista Inclusão Social*, 7(2), 120–134.

29. Oliveira, C. (2021). *Educação inclusiva e direitos humanos: Interfaces e desafios*. Editora Inclusão Social.

30. Ribeiro, E. (2019). Abordagem centrada na pessoa e inclusão escolar: Práticas e reflexões. *Revista Educação Inclusiva e Cidadania*, 6(2), 112–127.

31. Ribeiro, M. S. (2019). Formação de professores para a inclusão de alunos com transtorno do espectro autista: Desafios e perspectivas. *Revista Educação e Emancipação*, 13(2), 42–56.

32. Ropoli, E. A., et al. (2010). *A educação especial na perspectiva da inclusão escolar: A escola comum inclusiva*. Ministério da Educação, Secretaria de Educação Especial; Universidade Federal do Ceará.

33. Severino, A. J. (2002). *Metodologia do trabalho científico* (22ª ed.). Cortez.

34. Silva, A. B. B. (2012). *Mundo singular - Entenda o autismo*. Rio de Janeiro: ED. Fontanar.

35. Santos, R. V., & Mafra, J. F. (2017). A inclusão escolar de crianças com transtorno do espectro autista: Família e professores entre desafios, expectativas e possibilidades. *Cadernos de Pós-graduação*, 145–169.

36. Santos, P. (2017). Colaboração com a comunidade escolar no atendimento a alunos com TEA. *Inclusão e Diversidade*, 4(1), 65–78.

37. Silva, M. (2021). Colaboração entre professores e profissionais de apoio para alunos com TEA. *Revista Educação Inclusiva*, 9(1), 120–135.

38. Smith, J. C. (2017). Análise do comportamento aplicada: Uma abordagem eficaz para o ensino de crianças com transtorno do espectro autista. *Psicologia em Pesquisa*, 11(1), 123–137.

39. Volkmar, F. R., & Wiesner, L. A. (2019). *Autismo - Guia essencial para compreensão e tratamento* (1ª ed.). Porto Alegre: Artmed.

40. Williams, C., & Wright, B. (2008). *Convivendo com autismo e síndrome de Asperger: Estratégias práticas para pais e profissionais*. São Paulo: M. Books do Brasil.

SYSTEMIC SCLEROSIS

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Gabriela Cortines Blanc[1] and Bruna Lima Eiras de Araújo[2]

ABSTRACT

Systemic sclerosis (SSc) is a rare connective tissue disease of unknown etiology, heterogeneous clinical manifestations, and chronic evolution, often progressive.1,6 It is characterized by inflammatory, fibrotic, and atrophic changes.6 The onset of the disease is more common in the age group of 30 to 50 years, and is more prevalent in women. SSc has been reported in all geographic areas and in all races, but it has been observed that the black race has a higher chance of developing it.[1.4]

SSc can compromise the connective tissue of various organs such as the skin, lungs, heart, gastrointestinal, renal and musculoskeletal tracts.8 In addition, it is classified into two subtypes, the diffuse and limited forms, and it is the extent of skin thickening that differentiates these two. In 10% of patients, the skin is normal, no thickening occurs, and it is called scleroderma sine sclero.[4]

As it is a disease that affects multiple systems, it imposes limitations on the affected individual and affects their quality of life. Proper diagnosis is very important, since the manifestations can be varied and with some possible differential diagnoses.[4]

Keywords: Sclerosis. Connective tissue. Sickness.

[1] Complete higher education
Education: Unigranrio Barra University
[2] Complete higher education
Education: Unigranrio Barra University

INTRODUCTION

EPIDEMIOLOGY

Systemic sclerosis (SSc) is a rare diffuse connective tissue disease of unknown cause. Its prevalence is higher among females, about 3-14 times higher than in men, and is more common in the reproductive age group, declining after menopause (suggesting the influence of sex hormones). It is a pathology that can present at all ages, but its onset occurs more in the 30 to 50 age group, both in limited and diffuse cutaneous form. In addition, it can affect all races, although it is higher in blacks. It has been observed that this group is more likely to develop a diffuse cutaneous form, associated with interstitial pulmonary involvement, characterizing a worse prognosis.[1,2]

Its distribution is worldwide, with incidence varying according to countries. In the United States, 19 to 75 cases per 100,000 inhabitants were estimated, while in England, Japan and Australia the rates were lower. England had the most similar percentage, about 1 patient for every thousand inhabitants.[1,3] According to some analyses, it has been observed that regional genetic variations and environmental exposures can influence prevalence and incidence rates.[3]

There are no published data on the predominance of systemic sclerosis in the Brazilian population,[1,3] but a specific study analyzed the incidence of this disease in the city of Campo Grande, capital of the state of Mato Grosso do Sul. A total of 166 patients with SSc were treated in the city's outpatient clinics and rheumatology services, among which 89 lived in the city, only 10 were new cases and 79 had already been previously diagnosed. Thus, the prevalence in 2014 in this region of Brazil was 105.6 per million inhabitants. Furthermore, it is curious that among these 89 patients, 86 were women, and 58 were white, 20 brown, 8 black and 3 yellow.[3]

A genetic contribution to susceptibility to the disease has already been observed, as 1.6% of patients with SSc have a first-degree relative with SSc, thus observing a higher prevalence than in the general population. The risk of other autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis, is also higher.[1]

ETIOLOGY AND PATHOPHYSIOLOGY

Systemic sclerosis is a disease of unknown etiology with a probable multifactorial cause, including environmental and genetic factors.[2] Some possible factors involved in the pathogenesis of this disease are: solvents (e.g., benzene), toxic oil and silica, drugs, breast reconstruction with silicone prosthesis, viruses (retrovirus, human parvovirus B19, and

cytomegalovirus), and genetics. It is believed that some viruses have the same sequence as the topoisomerase 1 protein, which is targeted by SSc.[1,4]

The pathophysiology of systemic sclerosis can be explained through three important aspects: vascular dysfunction, immune and fibroblast activation, with excessive collagen production.[1,5] The heterogeneity in the clinical characteristics of SSc patients is probably a reflection of the variable contributions of each of these pathogenic factors.

Vasculopathy is very important in the clinical practice of systemic sclerosis, and its origin is due to the injury and activation of endothelial cells, due to unknown factors. Raynaud's phenomenon is an example of an early manifestation, which is characterized by an altered blood flow response brought on by cold.[1,5]

With the injured endothelium, there is a dysregulation of vasodilatory substances (such as nitric oxide and prostacyclin) and vasoconstrictors (endothelin-1). The increase in serum endothelin stimulates collagen synthesis, increases leukocyte adhesion to the endothelium, promotes migration and proliferation of smooth muscle cells to the intimal layer of the vessels, activating fibroblasts. This process leads to the synthesis of extracellular matrix molecules, leading to fibrosis with loss of elasticity and reduction of the vascular lumen, causing hypoxemia and tissue necrosis. The increase in nitric oxide, in turn, helps to maintain muscle tone, as it counterbalances the action of endoletin-1.[4] In this way, there is a greater expression of the intracellular adhesion molecule-1 (ICAM-1) and others.[1,4]

In the microvessels, an increase in leukocyte permeability and diapedesis, activation of the coagulation and fibrinolytic cascade, as well as platelet aggregation, are observed. This, in turn, stimulates the release of serotonin and platelet granules (such as thromboxane). In addition, the process of vasculopathy also affects the great vessels in various organs, resulting in reduced blood flow and tissue ischemia.[1]

Another factor is the involvement of both the humoral and cellular immune systems, in which mediators make the link between vasculopathy and tissue fibrosis. In the early stages of the disease, activated T cells, monocytes, and macrophages accumulate in lesions of the skin, lungs, and other affected organs. These in turn show a TH2 polarized immune response, and secrete IL-4 and IL-13, these cytokines induce TGF-beta production, promote collagen synthesis and other pro-fibrosis responses.[1,4] Approximately 95% of patients with systemic sclerosis have circulating autoantibodies against one or more antigens, these include anticentromere, antitopoisomerase I, antifibrillaryn, anti-PM-Scl, or anti-RNA polymerase I or III. Although antitoisomerase-I antibodies are not very sensitive,

they are highly specific for SSc (98-100%) and are related to a higher risk of interstitial lung disease and skin lesion.[6]

The last process is the most striking due to the intense deposit of collagen, fibronectin and glycosaminoglycans in the tissues involved.[4] Fibroblasts are mesenchymal cells responsible for maintaining the functional and structural integrity of connective tissue. With the production of TGF-beta, these proliferate, migrate, and secrete collagens, extracellular matrix, growth factors, and cytokines, in addition to differentiating into myofibroblasts. Fibroblasts in SSc exhibit an abnormally cultured phenotype and have an increased rate of collagen gene transcription, thus having large amounts of this substance.[1.4]

CLINICAL PICTURE

Systemic sclerosis has two forms of presentation, limited cutaneous and diffuse cutaneous. The limited form is marked by a slower evolution, characterized by skin thickening restricted to the extremities of the limbs and face, and is typically associated with the presence of anti-centromere antibody.[4,8] Pulmonary arterial hypertension is an expected complication. In the diffuse form, the thickening occurs early and extends to the proximal region of the limbs, trunk and abdomen. Pulmonary fibrosis and scleroderma renal crisis are more frequent in this case, and the predominant antibodies are anti-Scl70 and anti-RNA polymerase III.[8] A minority presents typical signs and symptoms of SSc, but without cutaneous involvement, and is classified as sine scleroderma.[8]

The clinical picture will be divided according to the classification of the disease, and the main manifestations are:

Cutaneous: the onset of the disease is associated with the first phases of cutaneous involvement, marked by edema (puffy fingers) representing the inflammation generated and by hardened regions (after regression of edema), and there may be intense itching. Fibrosis is characterized by thickening of the skin, being the mark that most distinguishes systemic sclerosis from other connective tissue pathologies.[1,8] Usually this process begins in the extremities, fingers and toes. As the disease progresses, there may be thinning of the lips and retraction of the gums, leading to microstomia and dental prominence.[8] The modified Rodnan score is used to measure the extent, degree of skin involvement, and prognosis of the disease. Finally, skin atrophy occurs. Due to the accumulation of collagen, obliteration of the hair follicles, sweat glands, eccrine and sebaceous glands can occur, resulting in hair loss, decreased sweating and dry skin.[1] Among the most common alterations, it is possible

to observe hyperchromia lesions in the extremities and trunk, or hypopigmented, especially in dark-skinned patients, known as salt and pepper lesions. In addition, telangiectasias and calcinosis may occur.[1,6,8]

Vascular: Raynaud's phenomenon is an episodic vasoconstriction in the fingers and toes, which occurs in practically all patients with systemic sclerosis (95%), and is caused by cold and stress.[1,6] Generally in the limited forms of the disease, this process precedes the cutaneous or visceral manifestations by years, while in the diffuse forms, it occurs together. This phenomenon, when associated with SSc, can bring complications, such as scars, digital ulcers, and even amputation of the fingers.[6]

Gastrointestinal: involvement of the entire gastrointestinal tract (from the oropharynx to the anus) may occur, and affects about 90% of patients with SSc.[6] The esophagus is the most affected organ (esophagitis), and therefore complaints of dysphagia, odynophagia, retrosternal burning pain, and regurgitation are common.[4] Abnormal peristalsis and relaxation of the lower esophageal sphincter aggravate esophagitis due to reflux, facilitating Barrett's metaplasia, and follow-up with upper gastrointestinal endoscopy is extremely important.[4,8] Intestinal and gastric involvement are less frequent.[6]

Musculoskeletal system: arthralgias, arthritis, and morning stiffness are the most frequent symptoms, especially in the early stages of the disease.[4] Muscle weakness and tendon friction occur due to the inflammation generated, and are more present in the diffuse cutaneous form. In addition, joint contractures can lead to the classic scleroderma claw hand.[8]

Pulmonary: pulmonary involvement is the main cause of morbidity and mortality in systemic sclerosis. It is very common, even in asymptomatic individuals, being present in approximately 90% of patients with SSc without respiratory symptoms, and changes are observed by computed tomography.[8]

Cardiac: cardiac involvement occurs in two ways, when it is primary, inflammation and fibrosis are observed, leading to myocardial ischemia, fibrosis, myositis, pericarditis and heart failure. When it is secondary to pulmonary arterial hypertension, there is right and left heart failure, tricuspid regurgitation, diagnosed by transesophageal Doppler echocardiography.[6] It usually occurs in the diffuse and asymptomatic form.[4]

Renal: it is rare to happen, and can present a difficult prognosis. Scleroderma renal crisis is characterized by the development of thrombotic microangiopathy and a sudden

onset of severe arterial hypertension, associated with progressive renal failure.[4,8] Some symptoms that may occur are headache, visual disturbances, encephalopathy, seizures, pulmonary edema, and pericardial effusion.[6]

DIAGNOSIS

Systemic sclerosis is a disease in which anamnesis and physical examination are essential, and in 90% of cases it is necessary for diagnosis. For this, it is necessary to be aware of the varied range of cutaneous, vascular and visceral manifestations. Laboratory and imaging tests are important for the evaluation, monitoring of the disease, and therapeutic planning of the patient.[4.3]

There are some ways of stratifying SSc through classification criteria. The most used in clinical practice are those of the American Rheumatism Association (ACR), which was proposed in 1890, and from this it is possible to make a standard definition of the disease, in which it considers SSc in the presence of a major criterion or at least two minor criteria.[2.3]

- Major criterion: proximal scleroderma (symmetrical fibrosis of the skin proximal to the metacarpophalangeal (MCF) or metatarsophalangeal (MTF).
- Minor criteria: sclerodactyly, ulcerations of digital pulps or resorption of distal phalanges, fibrosis in the lung bases (present on chest X-ray).

In patients with the disease in the initial phase, the above criteria do not detect adequately, and for this reason others have been created to facilitate the diagnosis of early forms: [2,3]

- Objective evidence (physician-observed) of Raynaud's phenomenon plus standard scleroderma on nailfold capillaroscopy or SSc-specific autoantibodies (anticentromere, antitopoisomerase I, antifibrillaryn, anti-PM-Scl, or anti-RNA polymerase I or III).
- Subjective evidence (at anamnesis) of Raynaud's phenomenon plus scleroderma pattern on nailfold capillaroscopy or SSc-specific autoantibodies.

To help, some complementary tests can be requested, including laboratory tests, in order to evaluate autoantibodies (ANA and disease-specific tests). ANA is an antinuclear antibody, and its positive value is expected in most patients (95%),[4,6] its most common pattern in immunofluorescence is nucleolar. Its absence imposes a differential diagnosis with diseases that simulate SSc, such as: eosinophilic fasciitis, nephrogenic systemic fibrosis, and scleromyxedema.[6] The disease-specific antibodies are: anticentromere

antibody (ACA), antitopoisomerase 1 antibody (Scl-70), antibodies against RNA polymerase I, II, and III, and fibrillarin.[4]

Antibodies against topoisomerase I are detected in 31% of patients with diffuse cutaneous SSc, but in only 13% of patients with limited cutaneous SSc, while anticentromere antibodies are the opposite, they are detected in 38% of patients with limited cutaneous SSc and only in 2% of patients with diffuse cutaneous SSc. [1.8]

In addition, autoantibodies are related to the patient's clinical practice, such as anticentromere antibodies are commonly associated with limited cutaneous SSc and pulmonary arterial hypertension, and rarely with cardiac and renal involvement, presenting a better survival (Figure 2). Patients positive for topoisomerase I have reduced survival compared to those without this antibody.[1.2]

Laboratory tests are also useful for the evaluation of the disease and the patient, for which the erythrocyte sedimentation rate, C-reactive protein, for example, and the characterization of systemic involvement are analyzed.[6]

Imaging tests help early recognition, adequate classification and extension of the involvement of different organs in patients with SSc. Examples of what can help are pulmonary function tests that show whether there is a progressive decrease in total lung capacity and reduced carbon monoxide diffusion. The reduction in carbon monoxide diffusion in the absence of restriction on spirometry is very suggestive of pulmonary hypertension. High-resolution chest tomography is the most sensitive test to detect interstitial lesions. Ground-glass images of the lung bases are the most common lesions, but in addition, honeycomb images, reticular opacities, and cysts can be observed. Transthoracic echocardiogram should be done to investigate pulmonary hypertension. Upper GI endoscopy is important to evaluate the gastrointestinal tract, especially the esophagus.[4.6]

The presence of skin hardening with a characteristic symmetrical distribution pattern is very common in cutaneous systemic sclerosis, for this reason a full-thickness skin biopsy is necessary to establish the diagnosis.[1] Nailfold capillaroscopy (CPU) is a non-invasive, low-cost imaging method that is of great help in this approach. This allows an evaluation of the structural alterations of the peripheral microcirculation, and is used mainly to differentiate between primary and secondary Raynaud's phenomenon and in the diagnosis of SSc. Approximately 90% of patients with SSc have the SD (scleroderma pattern) in the CPU, characterized by the presence of variable intensity of capillary dilations and devascularization.[8]

Figure 1: Autoantibodies and clinical correlation in SSc.

Autoanticorpos	Correlação clínica
Acometimento cutâneo difuso	
Anti-DNA topoisomerase I (Scl-70)	Doença intersticial pulmonar. Pior prognóstico
Anti-RNA polimerase III	Crise renal esclerodérmica e neoplasia. Pior prognóstico
Antifibrilarina (U3 RNP)	HAP e miosite
Anti-Pm/Scl	Doença intersticial pulmonar, síndrome de sobreposição e miosite
Acometimento cutâneo limitado	
Antiproteínas centroméricas	Úlcera digital, telangiectasias e HAP
Anti-U1 RNP	DMTC, HAP

Source: Zarur, 2020

TREATMENT

The therapeutic approach to systemic sclerosis should be based on the extent and severity of the manifestations presented. General measures should be adopted by the in a multidisciplinary manner, among them we have smoking cessation, protection from exposure to cold, vaccination for influenza and pneumococcus, anti-reflux measures, nutritional support and physical activity.[6]

Advanced diagnosis has provided early identification of cases, and this is very valid for cases of diffuse cutaneous SSc, in which treatment with immunosuppressants would help prevent progression to cutaneous and pulmonary fibrosis.[6]

In general, treatment for cutaneous involvement (depending on the severity) can be performed with immunosuppressants, such as methotrexate, (the drug of choice for the patient in the report above). In the diffuse cutaneous form and when there is a risk of internal organ involvement, the use of mycophenolate or intravenous pulse therapy with cyclophosphamide is feasible.[4.6]

For Raynaud's phenomenon, the first line of treatment is calcium channel blockers, and phosphodiesterase 5 inhibitors, fluoxetine, losartan and venous prostanoids can also be used.[6]

Treatment of gastrointestinal manifestations can be done with proton pump inhibitors, H2 receptor antagonists, prokinetics, and antibiotics for cases of bacterial overgrowth.[6]

For joint manifestations, low doses of prednisone and/or methotrexate are good options.[4.6]

Pulmonary arterial hypertension (PAH) can be treated with vasodilators such as phosphodiesterase 5 inhibitors (sildenafil, tadalafil), endothelin 1 receptor antagonists (bosentan, ambrisentan), and prostanoids.[4.6]

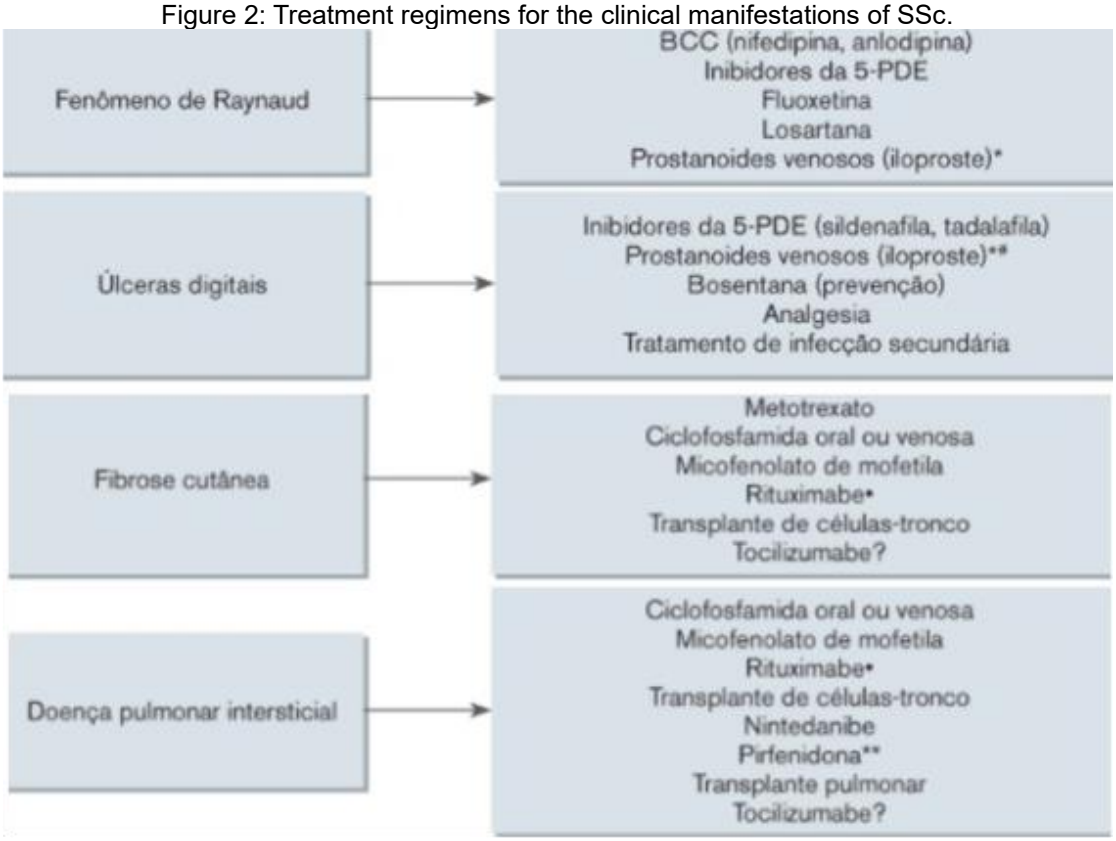
Interstitial lung diseases should be treated with monthly or oral intravenous cyclophosphamide, or with mycophenolate as induction treatment. The maintenance phase can be performed with mycophenolate or azathioprine. In refractory cases, rituximab is a possible option.[8]

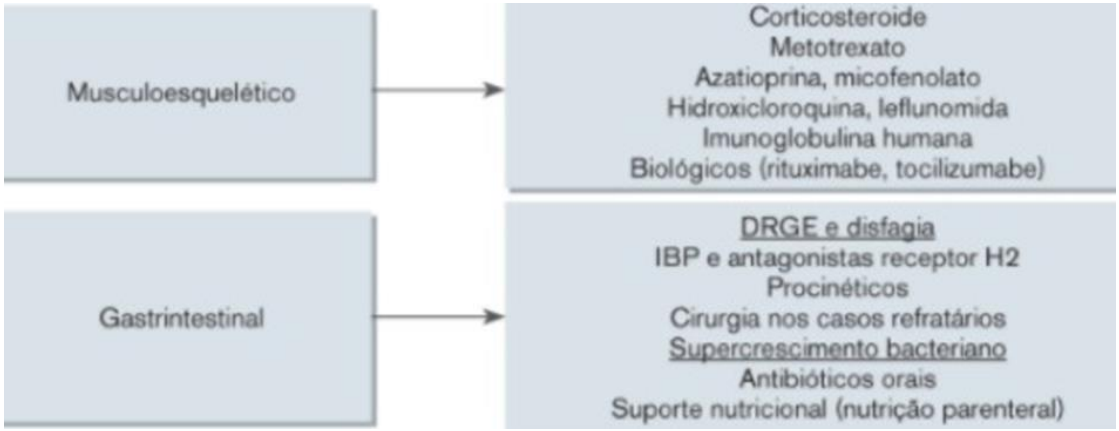
In symptomatic pericarditis, the use of non-steroidal anti-inflammatory drugs or low doses of corticosteroids are sufficient. In patients with large strokes, pericardiocentesis may be necessary.[4]

In scleroderma renal crisis, treatment can be done with high-dose ACE inhibitors (e.g., captopril). [4.6]

The table below summarizes the main treatment strategies according to the clinical manifestation presented by the patient.

Figure 2: Treatment regimens for the clinical manifestations of SSc.





Source: Freire, 2021

CONCLUSION

As seen in the course of this study, systemic sclerosis can affect the patient's quality of life, due to its wide and complex network of clinical manifestations, which makes the diagnosis challenging. We can conclude that systemic sclerosis is a pathology of great importance for medicine, and that there are still many clinical studies that seek new measures to bring more benefits and long-term survival.

REFERENCES

1. Varga, J. (2014). Esclerose sistêmica: (esclerodermia) e distúrbios relacionados. In A. S. Fauci et al. (Eds.), *Reumatologia de Harrison* (3ª ed., p. 264). São Paulo: Artmed.

2. Ministério da Saúde. (2013, 7 de fevereiro). Protocolo clínico e diretrizes terapêuticas: Esclerose sistêmica. Acesso em 26/05/2021, de <https://portalarquivos2.saude.gov.br/images/pdf/2014/abril/02/pcdt-esclerose-sistemica-livro-2013.pdf>.

3. Sampaio-Barros, P. D., et al. (2013). Recomendações sobre diagnóstico e tratamento da esclerose sistêmica. *Revista Brasileira de Reumatologia*, 53(3), 258-275. Acesso em 26/05/2021, de <https://www.scielo.br/j/rbr/a/T5ndk7DdLPFZThdYQwbvkNt/?format=pdf&lang=pt>.

4. Gonçalves, R. (2013). Esclerose sistêmica. Acesso em 26/05/2021, de <https://www.medicinanet.com.br/conteudos/revisoes/3995/esclerose_sistemica.htm>.

5. Zimmermann, A. F., & Pizzichini, M. M. M. (2013). Atualização na etiopatogênese da esclerose sistêmica. *Revista Brasileira de Reumatologia*, 53(6). Acesso em 01/06/2021, de <https://www.scielo.br/j/rbr/a/pDsN5ym4VYndGLYZMc8gjVy/?lang=pt>.

6. Dantas, A. T., et al. (2021). Esclerose sistêmica. In A. M. Katehasi et al. (Eds.), *Livro da Sociedade Brasileira de Reumatologia* (2ª ed., p. 131). São Paulo: Manole.

7. Zarur, E. B., et al. (2020). Esclerose sistêmica. In P. D. C. Ribeiro (Ed.), *Manual de reumatologia* (2ª ed.). Rio de Janeiro: Guanabara Koogan Ltda.

8. Zarur, E. B., et al. (2020). Esclerose sistêmica. In P. D. C. Ribeiro (Ed.), *Manual de reumatologia* (2ª ed.). Rio de Janeiro: Guanabara Koogan Ltda. [Figura 1].

9. Dantas, A. T., et al. (2021). Esclerose sistêmica. In A. M. Katehasi et al. (Eds.), *Livro da Sociedade Brasileira de Reumatologia* (2ª ed., p. 131). São Paulo: Manole. [Figura 2].

BREAST CANCER: NURSES' ROLE IN PAIN MANAGEMENT

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Stela Márcia Draib Gervasio[1], Rosana Maria Faria Vador[2], Leandra Ruzene Carlúcio[3] and Raquel Pereira Gomes Lima[4]

ABSTRACT

Introduction: Data from the World Health Organization (WHO) state that cancer (AC) was responsible for one in 6 deaths in the world, that is, 8.8 million deaths, of which 571 thousand were due to breast cancer. Pain is considered the fifth vital sign and because it is the most common symptom described by clients undergoing cancer treatment, regardless of the clinical situation in which each woman finds herself, it deserves real recognition and immediate care, as its constancy directly interferes with emotional conditions and their tasks, directly affecting their recovery. Thus, the present research aims to provide subsidies to help nurses in the management of pain in breast cancer patients, using alternative resources already applied by nursing for other interventions, now directed to the improvement of acute or chronic pain. The technical-scientific knowledge of this professional about the evaluation and performance of appropriate interventions for pain is essential to provide improvement in the quality of life of these clients, as well as their socialization during this period. Objectives To describe the role of nurses in pain management for women affected by breast cancer. Method: An integrative literature review was used, through national and international scientific articles published in the BVS, PUBMED, SCIELO, LILACS databases, as well as books, booklets/manuals of the Ministry of Health, between 2010 and 2018. Results: Twenty (20) articles, five (5) books and four (4) booklets/manuals of the Ministry of Health were selected to compose the review. Conclusion: Thus, this research demonstrates the degree of importance of this theme, proving that the prescription of alternative therapies by nurses is pertinent to treatment, as they can promote help in controlling and relieving pain in clients with breast cancer.

Keywords: Breast cancer. Pain. Alternative therapies. Nurse.

[1] Msc.
Taubaté Institute of Higher Education – ITES/Department of Nursing
E-mail: coord.enfermagem@ites.edu.br
[2] Msc.
Taubaté Institute of Higher Education – ITES/Department of Nursing
E-mail: rosanavador@gmail.com
[3] Msc.
Taubaté Institute of Higher Education – ITES/Department of Nursing
E-mail: leandraruzene@gmail.com
[4] Acadêm.
Taubaté Institute of Higher Education – ITES/Department of Nursing
Email: raqueldamiao@yahoo.com.br

INTRODUCTION

Cancer is still the leading cause of death worldwide, occurring mostly in low- and middle-income countries, reaching 70% of cases. Data from the World Health Organization (WHO) state that cancer was responsible for one in 6 deaths in the world, that is, 8.8 million deaths, of which 571 thousand were due to breast cancer. These data are so high that they even exceed deaths from complications related to HIV/IAIDS, tuberculosis and malaria combined, with the number of cases being up to two and a half times higher (WHO, 2017).

He is known for all the suffering that cancer brings to those involved and the physical pain it causes to the person affected by it. Pain is considered the fifth vital sign and because it is the most common symptom described by clients undergoing cancer treatment, regardless of the clinical situation in which each woman finds herself, it deserves real recognition and immediate care, as its constancy directly interferes with emotional conditions and their tasks, directly affecting their recovery (MATOS AMÉLIA, et al. 2017).

The vast majority of nurses distinguish pain through the individual's behavioral and emotional reactions, which end up altering their physiological factors such as blood pressure, breathing, tachycardia. From this perspective, one of the biggest problems in actually assessing pain, according to health professionals, is that when there are medications prescribed by the doctor to end the pain in high doses and even so the clients continue to report pain, many of them do not know how to measure this pain and end up taking changes in vital signs as a basis for this (BIASI et al, 2011).

Thus, the present research aims to provide subsidies to help nurses in the management of pain in breast cancer patients, using alternative resources already applied by nursing for other interventions, now directed to the improvement of acute or chronic pain. The technical-scientific knowledge of this professional about the evaluation and performance of appropriate interventions for pain is essential to provide improvement in the quality of life of these clients, as well as their socialization during this period.

METHOD

This is an integrative literature review, a descriptive study, with a qualitative-quantitative approach and exploratory character, using original articles, in Portuguese and English, available in full online, published in the last ten years. The databases used were: Latin American and Caribbean Literature on Health Sciences (LILACS), *Scientific Electronic*

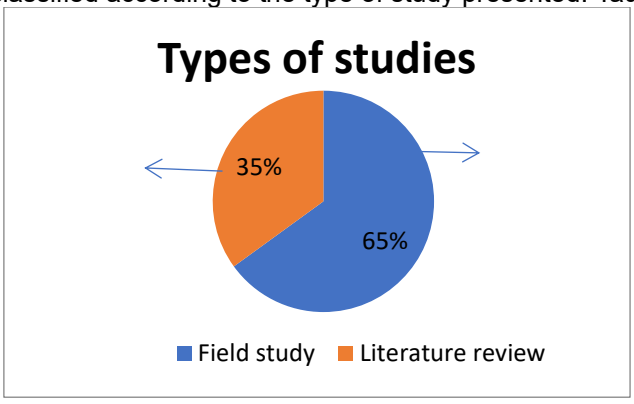
Labrary On-line (*SCIELO)* and Nation Center for Biotechnology Information (PubMed), books and booklets/manuals of the Ministry of Health. The search strategy was carried out from the crossings of the Health Sciences Descriptors (DECS): Breast cancer, pain, alternative therapies, nurse. The rights of the authors of the literature used in this study were respected, as determined by Law 9610 of February 19, 1998 (Brasil, 1998). Data collection took place from February to October 2018. The publication period used was between 2010 and 2018, and 20 articles were selected.

RESULTS

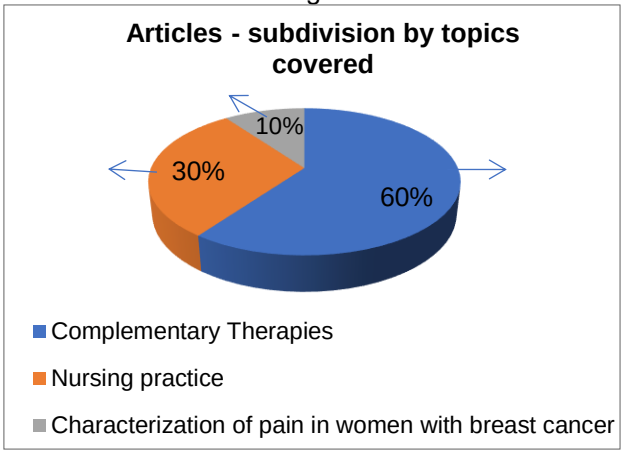
Table 1 – Distribution of articles, books and booklets selected according to year of publication. Taubaté, 2018. (n=29)

Year of publication	Absolute number of references searched	Percentage of references used
2010	3	10%
2011	3	10%
2012	4	11%
2013	8	32%
2014	5	16%
2015	3	5%
2016	1	5%
2017	2	11%
Total in percentage		100%
Total in absolute numbers		29

Graph 1 – Articles classified according to the type of study presented. Taubaté, 2018. (n=20).



Graph 2 - Distribution of articles according to titles covered. Taubaté, 2018. (n=20).



DISCUSSION

During the research, it was observed that the use of alternative therapies applied by nurses combined with conventional treatment has positive effects on the reduction of the intensity of cancer pain. The nurse's technical-scientific knowledge, its evaluation and the performance of appropriate interventions for pain are essential to provide improvement in the quality of life of clients with breast cancer.

The nurse can perform the comfort massage method for pain relief, as it promotes decreased anxiety and improves blood circulation. ABREU et al. (2012) state that relaxing massage causes a reduction in these factors, especially muscle tension, relieving pain, and muscle contraction contributes to increased pain, acting on nerve endings, especially in chronic pain.

The authors FLORENTINO et al. (2012) and SWELTZER *et al* (2009) state that thermal therapy, also used by nurses, is widely used for the relief of chronic pain. They state that heat promotes relief during muscle spasm and directly interferes in this cycle (pain-spasm-pain), increasing tissue extensibility and muscle relaxation, especially in cancer clients. GRANER et al. (2010), corroborate by explaining that this therapy can be performed with thermal bags, compresses or immersion of some part of the body in hot water, and can be performed 3 to 4 times a day, for 20 to 30 minutes.

FLORENTINO et al. (2012) point out that ice therapy has analgesic action related to muscle contracture, due to low blood flow. This method reduces edema and procrastinates the sending of nociceptive stimuli to the spinal cord. The application should be performed for 15 minutes, 2 to 3 times a day. The nurse can train his team to apply this technique because it is simple to use in any environment.

SWELTZER et al. (2009), report that heat and cold therapies are anti-inflammatory in the physiological function of vasoconstriction and vasodilation. It contains the primary

nociceptive afferent stimuli of the tissues, causing a decline in the activation of the peripheral and central nervous system, resulting in a reduction in pain.

According to GRANER et al. (2010), distraction helps to alleviate acute and chronic pain. It consists of the client concentrating attention on something other than pain, which can be a method responsible for other effective cognitive techniques, and can be applied by the nurse in the oncology outpatient clinic or in the oncology hospitalization unit, through an LED or LCD monitor, using programs aimed at physical and mental well-being, promoting relaxation and cognitive thoughts of hope and health.

BORGES & FERREIRA (2013) and GRANER et al. (2010) explain that the relaxation technique and guided imagery are excellent for reducing chronic pain. It consists of a combination of slow, rhythmic breathing with the mental image of relaxation and comfort. In the relaxation technique, the nurse instructs the client to close her eyes and breathe slowly, always advising her to inhale and exhale slowly, calming her thoughts, which will also cause her heart rate to decrease, promoting adequate blood circulation, implying better fluid drainage, causing a feeling of well-being as a whole.

In guided imagery, the nurse instructs the client to imagine that with each inhalation a healing energy will be produced in the region where the discomfort is being experienced, making it necessary for the nurse to direct the thought, explaining the steps of the technique and for the client to practice it 3 times a day.

In nursing, music therapy was used by the pioneer FLORENCE NIGHTINGALE (1859), with therapeutic intent. Later, music therapy was included as a Classification of Nursing Interventions (NIC) to assist in a change in behavior, feeling, among others. In addition to being a low-cost resource, acting to reduce pain, reduce anxiety, among other factors, it is a valuable instrument in the relief of acute and chronic pain, and can be implemented in any environment, as described by TAETS AND BARCELLOS (2010).

MATOS et al. (2017) allege that alternative therapies are already employed by nurses for pain control, such as transcutaneous electrical stimulation (TENS), acupuncture and homeopathy, as they claim. These techniques are associated with the existence of pain, muscle tension and anxiety, pain in patients brings a feeling of anguish and fear, thus causing muscle tension, consequently pain.

SCHULZ et al. (2012) state that transcutaneous electrical stimulation (TENS) is another method that promotes the improvement of acute pain by providing physiological relaxation, activation of pain inhibitory mechanisms, acting to block the pain impulse and releasing endorphins and enkephalins.

Acupuncture is a technique used to relieve chronic pain, in which it stimulates nerve endings in the skin and tissue, reducing spasms through the insertion of fine needles applied to the skin manually with analgesic and anti-inflammatory action GRANER et al. (2010).

NEUBERN (2013) comments that hypnosis is an effective component for pain relief and potent to reduce the amount of analgesic agents of extreme need in patients with acute and chronic pain. The effectiveness of hypnosis depends on how each individual's hypnotic concentration will be.

COFEN, in Resolution No. 0500/2015, provides that therapies such as transcutaneous electrical stimulation (TENS), acupuncture and hypnosis can be exercised by the nursing professional as long as he or she has specialization and/or professional qualification.

The Ordinance of the Ministry of Health No. 971 of May 3, 2006, on the National Policy of Integrative and Complementary Practices in the Unified Health System, authorizes them, using procedures for care in the public network. As stated in Resolution No. 0500/2015 of the Federal Nursing Council, which recognizes Alternative Therapies as a specialty and/or qualification of the Nursing professional, it ensures that the nurse prescribes these techniques to contribute to the care provided to the client (MS, 2006; COFEN, 2015).

These therapies are also highlighted in Opinion No. 028/2010 of the Regional Nursing Council – SP, which defines that it is the nurse's responsibility to apply complementary therapies in any environment and free from damage from malpractice, negligence and imprudence (COREN – SP, 2010).

Nurses who have knowledge about alternative therapies for pain control and relief can and should prescribe them in the places where they perform treatment and/or follow-up of these women with breast AC, whether during hospitalization for any reason, or for the performance of the chemotherapy cycle or simply routine examination for evaluation and general follow-up of the woman.

CONCLUSION

The alternative means used by the nurse are heat and cold, massage, music therapy, distraction, relaxation techniques, transcutaneous electrical stimulation (TENS), acupuncture and hypnosis. It is inferred that these practices should be prescribed according to the individual need and the moment of each woman, in each chemotherapy cycle, in each routine nursing consultation or when necessary. This research demonstrates the

degree of importance of this theme, proving that the prescription of alternative therapies by nurses is pertinent to treatment, as it can promote help in the control and relief of pain in clients with breast cancer.

REFERENCES

1. Abreu, et al. (2012). Os efeitos da massoterapia sobre o estresse físico e psicológico. *Revista Científica da Faculdade de Educação e Meio Ambiente*, 3(1), 101. Disponível em <http://www.faema.edu.br/revistas/index.php/Revista-FAEMA/article/view/119>.

2. Biasi, et al. (2011). Manejo da dor no paciente oncológico pela equipe de enfermagem. *Perspectiva, Erechim*, 35(129), 157-166. Disponível em <http://www.uricer.edu.br/site/pdfs/perspectiva/129_163.pdf>.

3. Borges, F. T. (2013). Relaxamento: estratégia de intervenção no stress. *Revista Portuguesa de Enfermagem de Saúde Mental*. Disponível em <http://www.scielo.mec.pt/scielo.php?script=sci_arttext&pid=S1647-21602013000200006>.

4. Brasil. Ministério da Saúde, Instituto Nacional de Câncer José Alencar Gomes da Silva. (2017). *Estimativa 2018: Incidência de câncer no Brasil*. Rio de Janeiro: Ministério da Saúde.

5. Brasil. Ministério da Saúde. (2006). *Portaria nº 971 de 03 de maio de 2006. Aprova a Política Nacional de Práticas Integrativas e Complementares (PNPIC) no Sistema Único de Saúde*. Brasília: Ministério da Saúde.

6. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. (2013). *Controle dos cânceres do colo do útero e da mama* (2ª ed.). Brasília: Ministério da Saúde.

7. Brasil. Organização Mundial Da Saúde. (2018). *Estimativa da incidência do câncer, mortalidade e prevalência no mundo*. Disponível em <https://www.paho.org/bra.../index.php?option=com_content&view=article&id=5588:folha-informativa-cancer&Itemid=839>.

8. Conselho Federal de Enfermagem (COFEN). (2015). *Resolução 500 de 8 de dezembro de 2015*. Rio de Janeiro: COFEN.

9. Conselho Regional de Enfermagem de São Paulo (COREN-SP). (2010). *Parecer COREN-SP CAT Nº 025/2010. Assunto: Musicoterapia*. São Paulo: COREN-SP.

10. Conselho Federal de Enfermagem do Estado de São Paulo (COREN-SP). (2014). *Parecer nº 028/2010. Revisão e atualização*. Rio de Janeiro: COFEN.

11. Florentino, D., et al. (2012). A fisioterapia no alívio da dor: uma visão reabilitadora em cuidados paliativos. *Revista do Hospital Universitário Pedro Ernesto*, 18(1), 107-111. Disponível em <http://revista.hupe.uerj.br/detalhe_artigo.asp?id=326>.

12. Graner, K. M., et al. (2010). Dor em oncologia: intervenções complementares e alternativas ao tratamento medicamentoso. *Temas Psicologia*, 18(2), 345-355. Disponível em <http://pepsic.bvsalud.org/scielo.php?script=sci_arttext&pid=S1413-389X2010000200009>.

13. Matos, A., et al. (2017). Medidas não farmacológicas na pessoa com dor: Resultados sensíveis da intervenção dos enfermeiros. *Revista Ibero-Americana de Saúde e

Envelhecimento*, 3(3). Disponível em <http://www.revistas.uevora.pt/index.php/saude_envelhecimento/article/view/242>.

14. Neubern, M. S. (2013). Hipnose, dor crônica e técnicas de ancoragem: A terapia de dentro para fora. *Psicologia: Teoria e Pesquisa*, 29(3), 297-304. Disponível em <http://www.scielo.br/scielo.php?pid=S0102-37722013000300007&script=sci_abstract&tlng=pt>.

NEGLECT IN THE MENTAL AND PHYSICAL HEALTH CARE OF HEALTH PROFESSIONALS

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Mirela Ambrósio Leal, Fernanda de Freitas Medeiros de Souza, Vivaldo Palma Lima Filho, Samuel Batista Monte Alto do Vale Lordão, Ana Flávia Souto Fonseca Sarni and Dener de Freitas Ribeiro

ABSTRACT

The health area is composed of a multiprofessional team, and each sector of activity has an extreme impact on the quality of life of each patient, considering that their demands are also multidisciplinary. However, even with the stratification of care and division of functions among the responsible team, there is still a significant overload of health professionals, especially in the hospital setting. This overload is reflected in factors such as professional exhaustion or burnout syndrome, which is one of the pillars of neglect regarding physical and mental self-care among health professionals. Likewise, lack of time, poor pay, lack of professional appreciation, poor working conditions, and emotional overload are other examples of factors that contribute to this scenario. With this in mind, this study aims to review the main conditions associated with the self-neglect of health professionals, with regard to physical and mental health, bringing together factors common to all areas of activity and with emphasis on nursing and medical services.

Keywords: Mental health. Health professionals. Negligence.

INTRODUCTION

There are several factors that impact self-care with mental and physical health among health professionals. Among them, it is possible to mention both external factors, and therefore modifiable, as well as intrinsic factors inherent to the various areas of health activity. In the context of the Unified Health System (SUS), professionals still face other challenges, such as the lack of equipment, supplies, medicines and even human labor for the demands presented. All this conditions the professional to greater emotional and psychological exhaustion.

In addition to the context of the Covid-19 pandemic, which was a time of intense physical and mental exhaustion for professionals in all areas of health, it is important to mention both the factors intrinsic to the profession, such as greater exposure to situations of grief and death, the need for psychological and emotional resilience, for example, and the modifiable factors, such as lack of time, poor remuneration, low professional recognition, overload of functions and lack of resources in the SUS, as these are factors that precede the pandemic, coexisted with it and remained after its resolution.

METHODOLOGY

The present work is a literature review, which was removed from the SciELO (Scientific Electronic Library Online) and PubMed platforms. The research was carried out in July 2023, meeting the inclusion criteria, which were articles from the years 2003 to 2023, in Portuguese, Spanish and English, online and full text texts, theses, master's dissertations, book chapters, monographs, literature in journals and scientific journals were included in the bibliographic review. As strategies for better evaluation of the texts, the following health descriptors (DeCS) were used: "Mental Health", "Physical Health" and "Health Professionals" and "Self-Neglect".

DISCUSSION

Currently, the physical and emotional overload during the care of patients hospitalized in the hospital environment is often neglected by health professionals (SANTOS, 2023). Lack of care for oneself can occur when the professional gets involved in the care of others in a way that is distant from himself, as if this care could be carried out with neutrality. This refers to the discourse about health professionals as disease-free, compared to "ascetic priests" who in their professional practice use their instinct, their art, their skills, and even a kind of happiness of their own to fulfill all their tasks and be whole, immune to diseases (SILVA, 2020).

The health team is frequently exposed to various factors that compromise their physical and mental health, such as dealing with pain, suffering and death, as well as the system of continuous shifts or work in uninterrupted shifts and provision of services 24 hours a day, seven days a week, adding to the transition between shifts for shift change. The negative impact on physical and mental health is also due to the lack of attention and time for issues related to the performance of professionals as individuals inserted in a social environment (SANTOS, 2023).

Dealing with lives that are almost always in fragile situations, making decisions that involve vital risks, performing clinical or surgical interventions on sick individuals - all this makes the health professional more likely to feel physically and psychologically worn out throughout their professional life. To a large extent, the doctor's action involves not only the patient, but also the patient's family nucleus, which makes the professional responsible and involved beyond the technique of medicine, going beyond a mere consumer-producer relationship (MACHADO, 1997).

Although the characteristics of each profession are maintained, several aspects of professional activity in health are shared by physicians, nurses, social workers, occupational therapists, psychologists, physiotherapists, speech therapists; with regard to occupational health, for example, the psychic suffering inherent to work in the hospital environment is common to all these professionals (NOGUEIRA, 2003).

A common condition among health professionals is burnout or burnout syndrome, which is defined as a pathological syndrome resulting from prolonged occupational stress. The three main characteristics of this condition are: emotional exhaustion, depersonalization, and a feeling of professional ineffectiveness. It is postulated that the dimensions of the burnout syndrome appear sequentially in time. Thus, emotional exhaustion develops first, and then depersonalization arises in an attempt to cope with exhaustion and, finally, the ability to resist work demands decreases, resulting in a reduction in feelings of personal fulfillment (BROWN; GOSKE; JOHNSON, 2009).

Regarding physical health, the results of a study on the level of physical activity of health professionals (ACIOLI, 2013) revealed that physicians and nurses were the professionals with the lowest proportion of active subjects, even presenting values below the national average of 36%17 (Jatkinson et al.,18), found that physicians, even taking walks during their workday, were unable to meet a substantial proportion of the daily needs, making it necessary to complement the practice of physical activity. On the other hand, nursing technicians and physiotherapists presented higher values than doctors, nurses and even in relation to the national proportion. A possible explanation for the higher proportion of

active individuals among these professionals may be related to the influence of the activities developed in their work routines (ACIOLI, 2013). In their work routines, technicians are responsible for moving patients, taking care of personal hygiene, administering drugs and transporting different equipment. All these activities require greater energy expenditure, as they require these professionals to travel greater distances within the hospital environment, whether walking, going up and down stairs, as well as performing vigorous activities that require physical strength, such as transferring patients and bathing in bed. A similar explanation can be thought of for physiotherapists who use the mobilization of patients in their routines, such as transfer to chairs, armchairs, orthostatism, in addition to walking (ACIOLI, 2013).

When related to the psychophysical symptoms of health professionals, some authors have highlighted with greater emphasis musculoskeletal disorders, being mainly related to complaints of back pain (FERREIRA, 2008), chronic foot problems, with an incidence of 12.6% (RIOS, 2010) and depression, with an incidence of 7.7%, in addition to stress and mental exhaustion, which is due to the demands and workloads imposed, leading to a musculoskeletal imbalance and emotional exhaustion reported by these professionals (SANTOS, 2023)

NEGLIGENCE IN NURSING PROFESSIONALS' SELF-CARE

In the historical development of nursing, care for people has been pointed out as an epistemological object of the profession. The nurse is the professional who takes care of people from birth to the moment of death. However, it is questioned whether this professional also takes care of himself. Several studies have pointed to stress, work overload and other problems that denote a certain lack of care with themselves among nurses. Associated with these factors are the great pressure in the work environment, high ethical responsibility, and low salaries (SILVA, 2020).

Self-care is essential and comprises individual habits, customs, beliefs, and values. Self-neglect, observed as the main limit to such care, may occur because the nurse's education aims at caring for others, not directing attention to care for themselves. Associated with these factors, fragmentation, inadequate communication between team members, and the lack of attribution of meaning to the work are determinants for its disqualification (SILVA, 2020).

Often, although there is a perception of the need to take care of oneself, professionals are unable to put it into practice. Everyday occupations consume the time that nurses could dedicate to themselves, so that caring for oneself is in the background and is

sometimes forgotten. The neglect of self-care seems to result from the lack of time to eat properly and take care of oneself physically and aesthetically and from the need to give up time for oneself for work. Many professionals have more than one employment relationship, which reduces free time and impairs self-care. Lack of time, which can be interpreted as the absence of priority for oneself, has a great possibility of causing stress and other psychic disorders. In addition, the absence of adequate rest, added to the professional's exposure to adverse conditions in the labor market, can cause chronic pain, agitation, insomnia, anxiety, and, consequently, self-medication (SIVA, 2020).

In addition to these, other limiting factors in self-care were described by nurses: inadequate working hours, excessive bureaucracy, low pay, submission, impotence, competitiveness, and incompatibility between chores, family, and leisure (SILVA, 2020).

NEGLIGENCE IN THE SELF-CARE OF MEDICAL PROFESSIONALS

The impairment of the quality of life of physicians and, consequently, of their professional practice can interfere in an impactful way in society, especially through possible medical errors that are often irreparable (GRACINO, 2016).

Competitiveness and the need to know and be exposed to different situations, functions and workplaces are much more affected by doctors whose employment position is not yet consolidated. Professionals with less than ten years in the market, for example, are more subject to multi-employment (even accepting underemployment, below-average salaries, etc.) and to working more intensely on duty, and their clientele in the office is still scarce (MACHADO, 1997). All the factors mentioned above have an important impact on the quality of life and well-being of health professionals, and submission to them is an example of self-neglect in mental health care.

The main reasons alleged for burnout were: overwork, long working hours, multi-employment (27%); low pay (17%); poor working conditions (16%); area of expertise/specialty (9%); excess of responsibility, life-and-death relationship with patients (12%) (MACHADO, 1997).

Among the risk factors for psychological illness among physicians most addressed in the studies, the high demand for both physical and emotional work, family conflicts due to the profession, financial difficulties and dissatisfaction with the health system stand out (BROWN; GOSKE; JOHNSON, 2009).

The percentage of physicians affected with symptoms of depression is high in both hemispheres of the planet, with younger physicians being at greater risk, which was confirmed in the study by Dyrbye et al. (2014), in which symptoms of depression and

suicidal ideation were more prevalent during college than in residency and early career (MAGNAVITA AND FILENI, 2014).

On the other hand, protective factors were observed, such as dedication to the academic practice of teaching and research, technical improvement and dedication of time to leisure and physical activities. It was also possible to observe that the beginning of the medical career, especially internship and residency, is the most exhausting and demanding of the mental and physical health of physicians (GRACINO, 2016).

IMPACTS GENERATED BY THE COVID-19 PANDEMIC

The pandemic caused by Covid-19 negatively affected the mental and physical health of health professionals by increasing work-related stressors, especially those who worked on the front line of care, as they dealt daily with the fear of becoming infected and infecting others, as well as with the lack of personal protective equipment and work overload. In a recently published study, psychological impacts such as anxiety, perceived stress, and depression were observed since the beginning of the Covid-19 epidemic, which gradually increased during the course of the disease. Analogous to the general population, the psychological impacts generated by epidemics and pandemics are intense. However, in health professionals, these impacts are amplified for several reasons: in addition to presenting a higher risk of infection by the virus, they are exposed to the possibility that there will be a lack of personal protective equipment, mechanical ventilators, hospital supplies, in addition to having to decide, sometimes, which patients will be entitled to certain assistive technologies (DANTAS, 2021). This has been an extremely relevant aspect in the mental health determinants of professionals since 2020.

FINAL CONSIDERATIONS

In addition, the mental health of all professionals should always be valued, even so, there is a very intense degree of negligence on the part of contractors and administrators. When we approach the health aspect, we understand the extensive demand on the part of patients and staff, so projects that project and intensify the care for the mental and physical health of health professionals should always be presented.

REFERENCES

1. Nogueira-Martins, L. A. (2003). Saúde mental dos profissionais de saúde. *Revista Brasileira de Medicina do Trabalho*, *1*(1), 59–71. Disponível em: https://www.rbmt.org.br/details/281/pt-BR/saude-mental-dos-profissionais-de-saude

2. Borges, J. P. A., Dos Santos, L. A., & De Assis Simões, A. L. (2020). Indicadores de qualidade na assistência à saúde da criança na atenção primária à saúde: Uma revisão integrativa. *Brazilian Journal of Health Review*, *3*(3), 7101–7116.

3. De Melo Ferreira, J. P., et al. (2023). Atitudes frente à morte e luto em profissionais de saúde na linha de frente do cuidado a COVID-19: Uma revisão integrativa. *Brazilian Journal of Health Review*, *6*(4), 14252–14264.

4. Machado, M. H. (1997). *Os médicos no Brasil: um retrato da realidade*. Rio de Janeiro: FIOCRUZ.

5. Silva Júnior, E. J. da, Balsanelli, A. P., & Neves, V. R. (2020). Care of the self in the daily living of nurses: An integrative review. *Revista Brasileira de Enfermagem*, *73*(2).

6. Gracino, M. E., et al. (2016). A saúde física e mental do profissional médico: uma revisão sistemática. *Saúde em Debate*, *40*(110), 244–263. https://doi.org/10.1590/0103-1104201611019

7. Brown, S. D., Goske, M. J., & Johnson, C. M. (2009). Beyond substance abuse: Stress, burnout, and depression as causes of physician impairment and disruptive behavior. *Journal of the American College of Radiology*, *6*(7), 479–485.

8. Magnavita, N., & Fileni, A. (2013). Association of work-related stress with depression and anxiety in radiologists. *Radiologia Medica*, *119*(5), 359–366.

9. Santos, V., Gomes Feitosa, A., Barreto, L., Guedes, A., Bastos, N., & Sales, B. (n.d.). Qualidade de vida dos profissionais de saúde em ambiente hospitalar [Internet]. [citado em 13 de julho de 2023]. Disponível em: https://www5.bahiana.edu.br/index.php/fisioterapia/article/download/312/283

10. Ferreira, N., & Oliveira, J. (2008). O nível de qualidade de vida dos fisioterapeutas do complexo de saúde do Campus da Unicamp [Dissertação de mestrado]. Campinas, SP: Universidade Estadual de Campinas.

11. Dantas, E. S. O. (2021). Saúde mental dos profissionais de saúde no Brasil no contexto da pandemia por COVID-19. *Interface (Botucatu)*, *25*, e200203. https://doi.org/10.1590/Interface.200203

12. Santos, W. J. dos, Silva, E. T. A. F. da, Altino, J. A., Vieira, C. B. L., Meira, M. do A., & Monte, C. D. (2022). Saúde física e mental de profissionais de unidades de saúde da família na pandemia do COVID-19. *Revista Portuguesa de Enfermagem de Saúde Mental*, *(27)*, 111–122.

13. Acioli Neto, A., Araújo, R., Pitangui, A., Menezes, L., França, E., Costa, E., et al. (2013). Qualidade de vida e nível de atividade física de profissionais de saúde de unidades de terapia intensiva. *Revista Brasileira de Atividade Física & Saúde*, *18*(06).

VACCINATION OF PATIENTS IN A NEIGHBORHOOD OF FORTALEZA: A SURVEY STUDY

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Ana Beatriz Ramalho Leite Silva[1], Maria Beatriz Bezerra Pereira[2], Nicole Lauren Ramos Nobre[3], Theo Marcílio Pompeu[4] and Jocileide Sales Campos[5]

ABSTRACT

The history of vaccination begins in the eighteenth century, when the first vaccine was developed in the context of smallpox, by Edward Jenner, who demonstrated that by inoculating a contaminated person's secretion into a healthy one, he acquired immunity to the disease, and through these experiments, the first vaccine emerged. . In Brazil, in the twentieth century, Rio de Janeiro faced several epidemics, such as smallpox, plague and yellow fever. As a result, the physician Oswaldo Cruz, in 1904, to combat them, implemented several sanitary measures, among them, the mandatory nature of vaccination. Such an attitude unleashed enormous popular discontent, which became known as the "Vaccine Revolt", in which the population held several protests in the streets, as well as direct combat with armed force, which generated numerous deaths. However, even with several movements against it, it is undeniable that vaccination was one of the most successful public health interventions for the eradication of several diseases. Thus, the objective of this study is to analyze the vaccination coverage of a region of Fortaleza, the knowledge and popular beliefs about this practice, to investigate the main barriers that hinder vaccination, to assess whether the public measures implemented are sufficient to meet the vaccination goal.

Keywords: Vaccination. Vaccine Revolt. Covid-19. Vaccination Calendar.

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Federal University of Ceará

INTRODUCTION

The history of vaccination begins in the eighteenth century, when the first vaccine was developed in the context of smallpox, by Edward Jenner, who demonstrated that by inoculating a contaminated person's secretion into a healthy person, he acquired immunity to the disease, and through these experiments, the first vaccine emerged (KAYSER, 2023; OLIVEIRA *et al*, 2023); PROTKIN, 2023). In this context, this experiment worked as a precursor to the creation of several other vaccines, which contribute to the reduction of the prevalence and morbidity and mortality of numerous diseases worldwide (KAYSER, 2023; OLIVEIRA *et al*, 2023).

However, the topic of "vaccination" has always been controversial, and proof of this are the various anti-vaccine movements that have emerged during all these years since its creation, the first of which was in 1953, in England, with the creation of the first anti-vaccination league in London (OLIVEIRA *et al*, 2023).

In Brazil, in the twentieth century, Rio de Janeiro faced several epidemics, such as smallpox, plague, and yellow fever (PORTO, 2023). As a result, physician Oswaldo Cruz, in 1904, in order to combat them, implemented several sanitary measures, including mandatory vaccination ((CRESCÊNDIO, 2023; SATO 2023; PORTO, 2023). This attitude triggered enormous popular discontent, which became known as the "Vaccine Revolt", in which the population held several protests in the streets, as well as direct combat with armed force, which generated numerous deaths (CRESCÊNDIO, 2023; SATO, 2023; PORTO, 2023)

However, even with several movements against it, it is undeniable that vaccination was one of the most successful public health interventions for the eradication of several diseases (SATO, 2023). An example of this is the number of deaths that was reduced in traditional vaccine-preventable diseases, such as measles, neonatal tetanus, and pertussis, in which there was a reduction from 705,487 deaths in 2000 to 165,770 in 2015 (RESTREPO-MENDEZ *et al*, 2023).

In addition, the World Health Organization (WHO) estimates that the vaccines currently available prevent 2 to 3 million deaths per year globally (KAYSER, 2023). In this context, some programs were created to encourage mass vaccination, including the Expanded Immunization Program (PAI), created by the WHO in 1947, which expanded access to vaccination, which reflected in an increase in vaccination coverage against Diphtheria-Tetanus and Pertussis (DTP) (SATO, 2023). Brazil's National Immunization Program (PNI), in turn, promotes the vaccination of more than 15 antigens free of charge (SATO, 2023).

Regarding vaccination coverage in children, in 1990, it was 95% (SATO, 2023). However, since 2016, there has been a significant drop in this number, as well as an increase in infant mortality (SATO, 2023). Statistics also show that, in the states of Ceará and Pernambuco, 1,310 cases of measles were registered between 2013 and 2015, in addition to the resurgence of this epidemic in 2018 in the states of Roraima and Amazonas, with 1,500 new cases, which draws attention to a possible decrease in vaccination coverage in Brazil and in the world (SATO, 2023). This scenario is due to several factors, including the weakening of the Unified Health System (SUS) with regard to public policies for engaging the population, social and cultural divergences, and misinformation and fake news on the internet (SATO 2023).

With regard to misinformation and false information, it is believed that a large part of the current anti-vaccine movements are due to this (SATO 2023). With this, vaccine hesitancy also originates, defined when there is refusal or delay in the vaccination process, even though they are available in the health system (SATO 2023)

. In the Coronavirus (COVID-19) pandemic, for example, this was widely observed, largely due to the speed of production of new vaccines, amid the fear of the unknown of the disease, as well as the serious adverse effects that emerged through vaccines, including anaphylaxis and thrombocytopenia syndrome (KAYSER, 2023).

Finally, the present study aims to analyze the vaccination coverage of a region of Fortaleza, the knowledge and popular beliefs about this practice, to investigate the main barriers that hinder vaccination, in order to evaluate whether the public measures implemented are sufficient to meet the vaccination goal.

METHODOLOGY

After being published on Plataforma Brasil, then approved by the Ethics Committee of the Christus University Center (Unichristus) and by the Municipal Health Department of Fortaleza, on behalf of the Coordination of Studies, Research and Special Projects (COEPP), the present study was initiated in a basic health unit in the city of Fortaleza.

Initially, questionnaires were applied to patients at UBS Pio XII, using a type of non-probabilistic convenience sample, which aim to investigate the relationship that patients currently have with vaccination. In addition, through these questionnaires, it is intended to assess whether, in that region, the actions of the public authorities are sufficient in publicizing immunization programs, and also to understand whether in the context of the COVID-19 pandemic, there was any resistance from patients to the booster doses of the new vaccine, as well as whether it interfered with the rest of the vaccines. All of this served

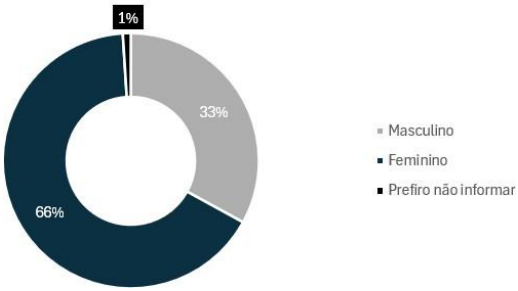
as a source of data for the elaboration of the scientific research in question. For this, the Epi info application, version 7.2.5, was used and the significant value of the sample was calculated, being N=93.

RESULTS

PROFILE OF THE STUDY PARTICIPANTS

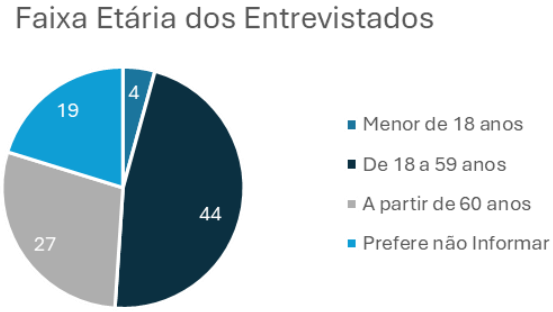
People in the waiting room of the Pius XXII Basic Health Unit were interviewed, who were initially categorized as gender (Figure 1), 66% female (n=62), 33% male (n=31) and 1% chose not to inform their gender (n=1). In addition, the participants were classified according to age group, and the following were found: 4 people under 18 years of age, 44 people between 18 and 59 years of age, 27 people aged 60 years or older, and 19 people preferred not to inform their age (Figure 2).

Figure 1 - Sex of the interviewees



Source: developed by the author.

Figure 2 - Age group of the interviewees

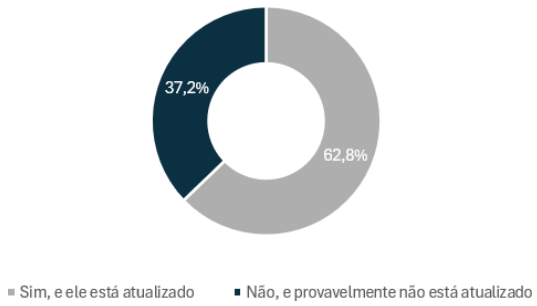


Source: developed by the author.

FACTORS ABOUT THE VACCINATION SCHEDULE:

The participants were asked about their knowledge about the status of their vaccination schedule. In this aspect, most of the interviewees stated that they have knowledge and that it is up to date (62.8%), while 37.2% reported not having knowledge about the status and/or that it is probably not up to date (Figure 3).

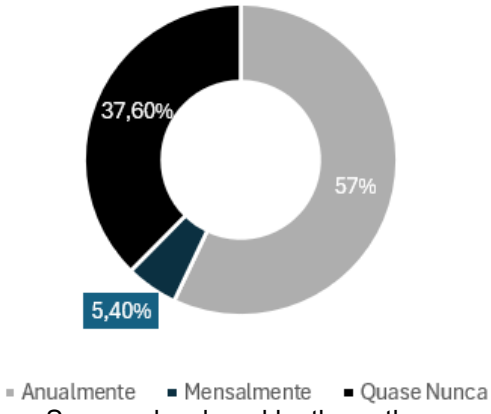
Figure 3- Status of the vaccination schedule
Status do calendário vacinal



Source: developed by the author.

In addition, the present study investigated the frequency with which the population updates their vaccines. This response was categorized as: annually (57%); almost never (37.6%) and monthly (5.4%) (Figure 4).

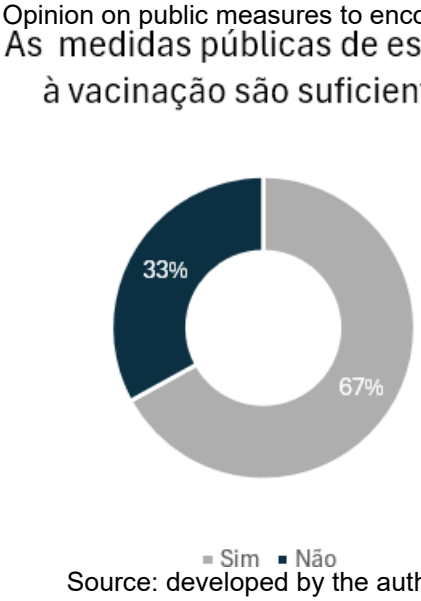
Figure 4- Frequency of updating the vaccination schedule
Frequência de atualização das vacinas



Source: developed by the author.

In addition, the participants' perception of what prevents more frequent vaccination to keep the vaccination schedule up to date was questioned. Among the answers obtained are: lack of information and encouragement by health professionals about the vaccines they need to take, lack of interest, lack of time to go to the Basic Health Unit, lack of a specific vaccination schedule for the elderly population, distrust about efficacy, fear of possible adverse reactions, etc. Another point investigated was the perception of public measures to encourage vaccination in the neighborhood, whether they are sufficient or not. In this regard, 67% of the answers "are sufficient" and 33% of "insufficient" answers were obtained (Figure 5).

Figure 5- Opinion on public measures to encourage vaccination

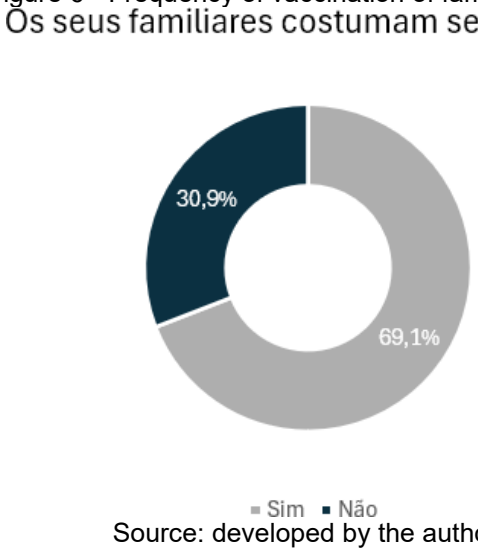


Source: developed by the author.

Still on this aspect, he was asked about what could be improved, among the answers are: more campaigns in Basic Health Units, in schools and on television, in addition to encouragement by health professionals in routine consultations to clarify the importance of vaccination and stimulate the population.

Also on this aspect, it was asked if their family members usually get vaccinated frequently, most of the interviewees (69.1%) answered yes, while 30.9% answered no (Figure 6).

Figure 6 - Frequency of vaccination of family members



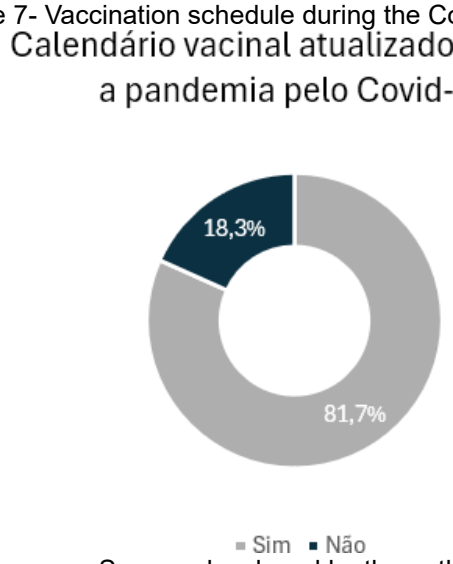
Source: developed by the author.

VACCINATION IN THE CONTEXT OF THE COVID-19 PANDEMIC

Another aspect addressed in this study was about the Covid-19 Pandemic X Vaccination. In this context, it was asked whether the participants kept the vaccination schedule up to date during the pandemic. The majority (81.7%) answered that they kept it,

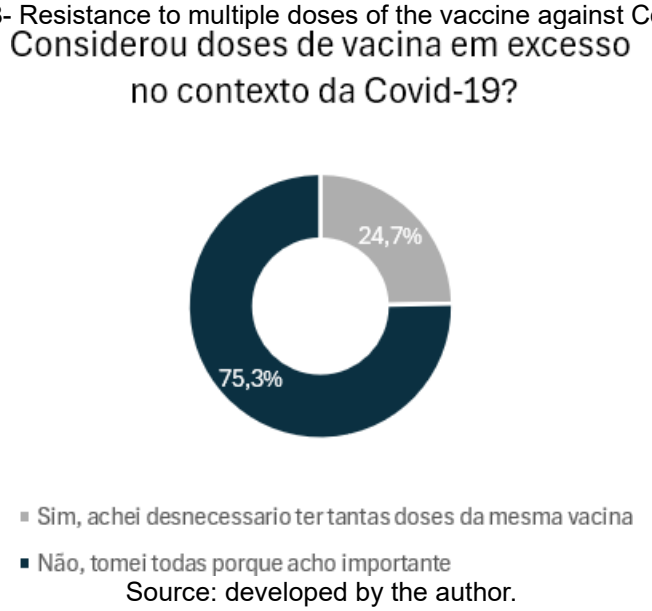
while 18.3% did not (Figure 7). In addition, another question asked was about the resistance in relation to taking multiple doses of the vaccine against Covid-19, which resulted in 75.5% believing that all doses are important, while 24.7% believe that so many doses of vaccine for the same disease are unnecessary (Figure 8).

Figure 7- Vaccination schedule during the Covid-19 pandemic



Source: developed by the author.

Figure 8- Resistance to multiple doses of the vaccine against Covid-19

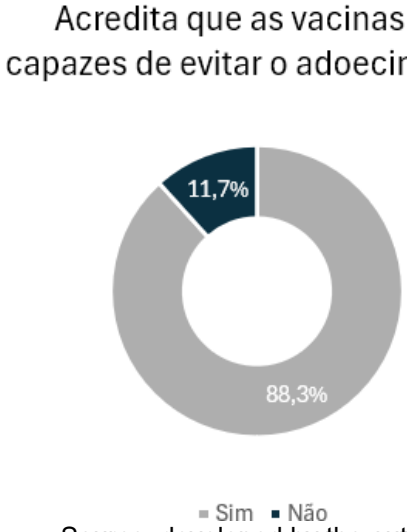


Source: developed by the author.

VACCINE X ILLNESS

In addition, it was asked if the participants believe that vaccines are capable of preventing illness. Regarding this question, most of the interviewees (88.3%) answered yes, while 11.7% answered no (Figure 9).

Figure 9- Belief about the effectiveness of vaccination

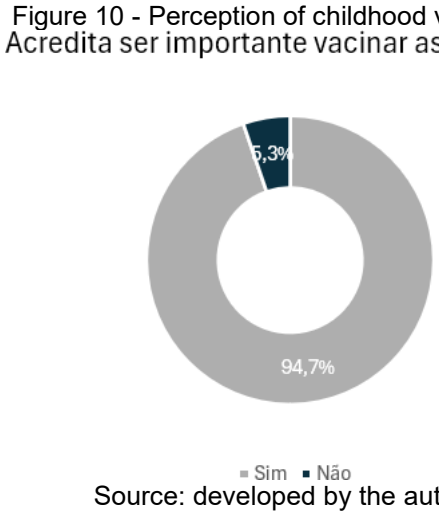


Source: developed by the author.

CHILDHOOD VACCINATION

In addition, this study sought to identify the population's perception of childhood vaccination. For this, the importance of vaccinating children was asked, this question obtained 94.7% of positive answers and only 5.3% negative (Figure 10).

Figure 10 - Perception of childhood vaccination

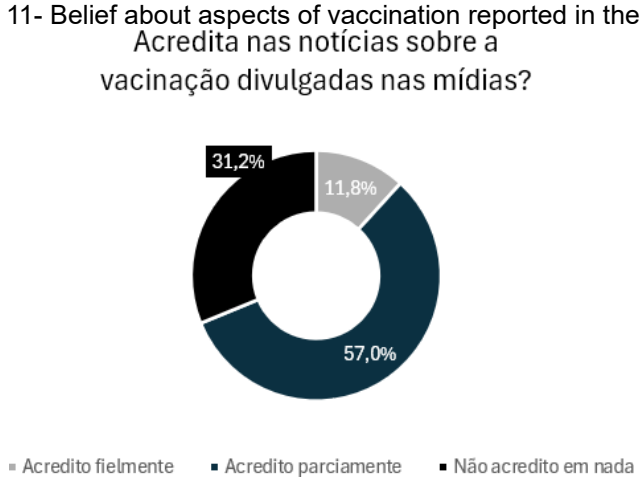


Source: developed by the author.

VACCINE X SOCIAL MEDIA:

People's beliefs about the aspects disclosed on the internet about vaccines were investigated, which was categorized into 3 responses (Figure 11): I believe faithfully (11.8%), I partially believe (57%) and I don't believe in anything (31.2%).

Figure 11- Belief about aspects of vaccination reported in the media

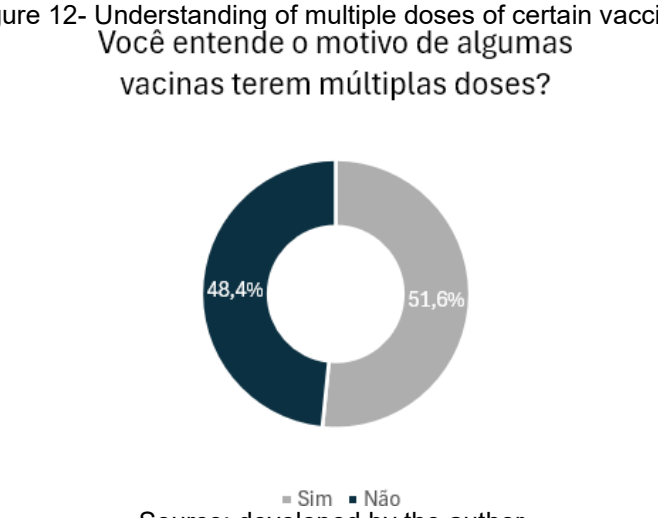


Source: developed by the author.

VACCINES WITH MULTIPLE DOSES

Another point asked to the participants was whether they understand why some vaccines have multiple doses. In this aspect, more than half of the participants (51.6%) did not understand and 48.4% answered that they understand (Figure 12).

Figure 12- Understanding of multiple doses of certain vaccines

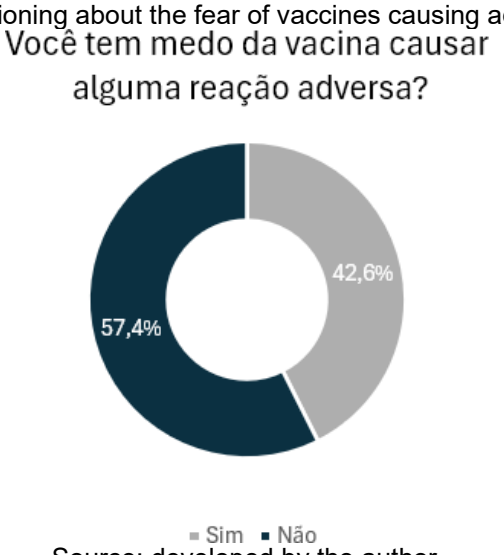


Source: developed by the author.

VACCINES X ADVERSE REACTIONS

Finally, the interviewees were asked about the existence of fear of the vaccine causing any adverse reaction. Regarding this aspect, the following result was obtained: 57.4% answered that they are not afraid and 42.6% answered that they are afraid of possible adverse reactions (Figure 13).

Figure 13- Questioning about the fear of vaccines causing adverse reactions



Source: developed by the author.

DISCUSSION

In this context, in addition to many individuals in the region of São João do Tauape having effective prior knowledge about vaccination, many of them have important and essential opinions and positions for transmitting information and deconstructing barriers that may prevent many people from making such a decision of great significance for the health and life of any citizen.

In view of this research and the results evidenced, the essentiality that vaccines have in protecting health and preventing vaccine-preventable diseases, especially during childhood, is indisputably known. Through them, sequelae such as physical disabilities and also thousands of deaths are avoided. Vaccination is included as one of the best public health intervention measures, present worldwide, and undoubtedly represents one of the great advances in medical technology in recent decades. (CARVALHO, 2015)

The study showed that a large part of the population of the neighborhood studied (62.8%) is aware of their vaccination schedule, as well as keeps it up to date. However, a significant portion of the population (33%) still believes that there is a lack of incentives for vaccination, and opined that they could have more information, dissemination and campaigns. Regarding the purpose of vaccination, as in the present study, most parents are aware of the importance of vaccination and vaccinating their children, as well as the ability of the vaccine to prevent diseases.

Vaccination is considered an action of social responsibility that not only protects those who receive the vaccine, but also those who cannot be vaccinated for health reasons, being essential to preserve public health, epidemic control, in addition to promoting the promotion of public health, this act is essential for, mainly, the prevention of various

infectious diseases, aiding herd immunity, and thus considerably reducing the spread of diseases in entire communities. (KRAUSE, 2023)

For Nascimento (2023), it is highlighted that the right to vaccination is among the list of rights linked to health, aiming at its performance in the prevention of illnesses and deaths. Therefore, vaccines are intended to protect human beings: they "teach" the immune system to fight viruses and bacteria that challenge public health. Yellow fever, polio, flu, measles, rubella, rotavirus, pertussis, meningitis, tuberculosis and hepatitis are targets of the Brazilian vaccination calendar, with free immunization offered by the Unified Health System (SUS). (BIRTH, 2023)

For Vilanova (2020), vaccines offer lifelong protection, as vaccines have as their main target to generate immunity for the individual, through the stimulation of the adaptive immune system that, with B lymphocytes, generate specific antibodies or through cellular mechanisms, mediated by other leukocyte cells. This is due to the fact that vaccines have killed or weakened versions of viruses and bacteria and once antibodies are produced in responses to the vaccine, they become a permanent part of your body's immune system (VILANOVA, 2020).

In the following work: "How to interpret the benefits of Covid vaccines", by the author Nadanovsky (2021), he stated that with the arrival of vaccines, there was great tranquility around the world, as they were of fundamental importance to stop the pandemic in a short time, since the pandemic came due to the fact that the Covid virus was unknown and no one had contact with it, but with mass vaccination, there was contact with the virus through vaccination, which caused immunity for vaccinated individuals (NADANOVSKY, 2021).

In this context, Lourenço et al. (2020), explain that there are many types of vaccines, but they all have the same objective, to generate specific immunity through antibodies and cellular mechanisms. But it is important to note that they have different immunization times, so it is necessary to reinforce these vaccines to maintain protection throughout their personal life (LOURENÇO, 2023).

In our study, even in the context of the pandemic, 81.7% were able to keep their vaccine card up to date, while 75.3% took all doses because they thought it was important, 24.7% did not take all of them because they thought it was unnecessary to have several doses of the same vaccine. Regarding the reason why some vaccines have multiple doses, 51.6% of patients understand such dose amounts, while 48.4% do not.

The various occasions of vaccine hesitancy are evidenced as a collective health problem. Especially when it comes to Covid-19 hesitancy among health professionals, due to the responsibility they should assume in relation to the promotion of vaccination among

the population. Regarding the factors that interfere in the vaccination decision-making process of health professionals, some similarities could be observed between some studies, with regard to the greater trend of vaccine acceptance of male health professionals, with older ages, higher education rates, and married (CARDOSO, 2023).

In the aspect of public policies, the logistics of information and disclosures that are more present about the benefits of vaccines still need to be reviewed and improved in a systematic way, in order to allow a vaccination policy with greater transparency, which includes all phases of supply and dissemination of what is necessary and essential to transmit to society, always establishing strategic actions aimed at the regions (AVORN, 2020).

Finally, it is known that in the context of emergency situations, vaccines are considered vital means, such as in the face of outbreaks, epidemics and pandemics, making it necessary to fortify investment in research, development and distribution of vaccination for the future of society, and should be valued, accessible and widely adopted to ensure a healthier and safer world for future generations (LEIGH, 2022).

FINAL CONSIDERATIONS

Based on the questionnaires applied and the results obtained, it is concluded that vaccination is part of a very broad means of knowledge, attitudes and dissemination. Currently, the majority of the population keeps their vaccination schedule up to date and has a certain knowledge about this subject, however, it is worth emphasizing the importance of fortifying information about the objectives of vaccines, about which ones need more than one dose, in addition to establishing conversations regarding the adverse effects that a large percentage of individuals have questioning those present in the vaccination context.

REFERENCES

1. Avorn, J., & Kesselheim, A. (2020). Regulatory decision-making on COVID-19 vaccines during a public health emergency. *JAMA*, 324(13), 1284-1285.

2. Cardoso, J. B., et al. (2023). Decisão de profissionais de saúde sobre sua vacinação anti-Covid-19: revisão integrativa. *Saúde em Debate*, 47, 677-692.

3. Carvalho, I. V. R. L. de, et al. (2015). Conhecimento das mães a respeito das vacinas administradas no primeiro ano de vida. *Revista Brasileira de Ciências da Saúde*, 205-210.

4. Césarea, N., et al. (2020). Longitudinal profiling of the vaccination coverage in Brazil reveals a recent change in the patterns hallmarked by differential reduction across regions. *International Journal of Infectious Diseases*, 98, 275-280. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7326384/pdf/main.pdf. Acesso em 30 mai. 2023.

5. Crescêncio, C. L. (2010). Revolta da vacina: higiene e saúde como instrumentos políticos. *Biblos*, 22(2), 57-73. Disponível em https://periodicos.furg.br/biblos/article/view/962/471. Acesso em 30 mai. 2023.

6. Curiel, R. P., & Ramírez, H. G. (2021). Vaccination strategies against COVID-19 and the diffusion of anti-vaccination views. *Scientific Reports*, 11(1), 6626. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7988012/pdf/41598_2021_Article_85555.pdf. Acesso em 30 mai. 2023.

7. Iriart, J. A. B. (2017). Individual autonomy vs. collective protection: Non-vaccination of children among higher income/educational level segments as a challenge to public health. *Cadernos de Saúde Pública*, 33(2), e00012717. Disponível em https://www.scielo.br/j/csp/a/pGZxXzB99VDsSNHcTDHF3pL/?format=pdf&lang=en. Acesso em 29 mai. 2023.

8. Kayser, V., & Ramzan, I. (2021). Vaccines and vaccination: History and emerging issues. *Human Vaccines & Immunotherapeutics*, 17(12), 5255-5268. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8903967/pdf/KHVI_17_1977057.pdf. Acesso em 29 mai. 2023.

9. Krause, J. C., et al. (2023). A importância das vacinas na prevenção de doenças infecciosas. In *Fórum Rondoniense de Pesquisa*.

10. Leigh, J. P., et al. (2022). Factors affecting COVID-19 vaccine hesitancy among healthcare providers in 23 countries. *Vaccine*, 40(31), 4081-4089.

11. Lourenço, I., et al. (2020). Você sabe como funciona uma vacina? Entenda os desafios da vacina contra o coronavírus. *Coronavírus Secretaria de Estado de Saúde de Minas Gerais*. Disponível em https://coronavirus.saude.mg.gov.br/blog/146-voce-sabecomo-funciona-uma-vacina. Acesso em 28 set. 2023.

12. Maciel, E., et al. (2022). The SARS-CoV-2 vaccination campaign in Brazil and the invisibility of science evidences. *Ciência & Saúde Coletiva*, 27(3), 951-956. Disponível em https://www.scielo.br/j/csc/a/YFbPSKJvkTj4V3pXd8b7yvJ/?format=pdf&lang=en. Acesso em 30 mai. 2023.

13. Moura, A. D. A., et al. (2018). Vaccination strategies and results for tackling the measles outbreak in Ceará State, Brazil, 2013-2015. *Epidemiologia e Serviços de Saúde*, 27(1), e201634310. Disponível em https://www.scielo.br/j/ress/a/7nR8MdMkqYBnVSt6CrkQLfg/?format=pdf&lang=en. Acesso em 29 mai. 2023.

14. Moura, C., et al. (2022). The impact of COVID-19 on routine pediatric vaccination delivery in Brazil. *Vaccine*, 40(15), 2292-2298. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8885307/pdf/main.pdf. Acesso em 30 mai. 2023.

15. Nadanovsky, P., et al. (2021). Como interpretar os benefícios das vacinas contra a Covid-19?.

16. Nascimento, J. M., & Borgomoni, A. P. (2023). Responsabilidade do Estado na vacinação. *Unisanta Law and Social Science*, 11(2), 92-102.

17. Oliveira, I. S., et al. (2022). Anti-vaccination movements in the world and in Brazil. *Revista da Sociedade Brasileira de Medicina Tropical*, 55, e0592-2021. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9131779/pdf/1678-9849-rsbmt-55-e0592-2021.pdf. Acesso em 29 mai. 2023.

18. Plotkin, S. (2014). History of vaccination. *Proceedings of the National Academy of Sciences of the United States of America*, 111(34), 12283-12287. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151719/pdf/pnas.201400472.pdf. Acesso em 29 mai. 2023.

19. Porto, M. Y. (2003). Uma Revolta Popular contra a vacinação. *Ciência e Cultura*, 55(1), 53-54. Disponível em http://cienciaecultura.bvs.br/pdf/cic/v55n1/14861.pdf. Acesso em 30 mai. 2023.

20. Pullan, S., & Dey, M. (2021). Vaccine hesitancy and anti-vaccination in the time of COVID-19: A Google Trends analysis. *Vaccine*, 39, 1877-1881. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7936546/pdf/main.pdf. Acesso em 30 mai. 2023.

21. Ransing, R., et al. (2021). COVID-19 anti-vaccine movement and mental health: Challenges and the way forward. *Asian Journal of Psychiatry*, 58, 102614. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7901495/pdf/main.pdf. Acesso em 30 mai. 2023.

22. Restrepo-Mendez, M. C., et al. (2016). Missed opportunities in full immunization coverage: Findings from low- and lower-middle-income countries. *Global Health Action*, 9(30963). Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4856841/pdf/GHA-9-30963.pdf. Acesso em 29 mai. 2023.

23. Rincón, H. E. H., et al. (2022). Resistencia de la población hacia la vacunación en época de epidemias: a propósito de la COVID-19. *Revista Panamericana de Salud Pública*, 46, e148. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9553013/pdf/rpsp-46-e148.pdf. Acesso em 30 mai. 2023.

24. Sato, A. P. S. (2018). What is the importance of vaccine hesitancy in the drop of vaccination coverage in Brazil? *Revista de Saúde Pública*, 52, 96. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6284490/pdf/0034-8910-rsp-S1518-52-87872018052001199.pdf. Acesso em 29 mai. 2023.

25. Silveira, M. M., Conrad, N. L., & Leite, F. P. L. (2021). Effect of COVID-19 on vaccination coverage in Brazil. *Journal of Medical Microbiology*, 70(001466). Disponível em https://www.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.001466#tab2. Acesso em 29 mai. 2023.

26. Succ, R. C. D. M. (2018). Vaccine refusal - what we need to know. *Jornal de Pediatria*, 94, 574-581. Disponível em https://www.sciencedirect.com/science/article/pii/S0021755717310045?via%3Dihub. Acesso em 29 mai. 2023.

27. Vilanova, M. (2020). Vacinas e imunidade. *Revista de Ciência Elementar*, 8(2).

28. Westhoff, M. A., et al. (2023). How to respond to misinformation from the anti-vaccine movement. *INQUIRY*, 60, 1-9. Disponível em https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9940232/pdf/10.1177_00469580231155723.pdf. Acesso em 29 mai. 2023.

THE PRESENCE OF CLEFT PALATE: PHYSICAL AND SOCIAL CONSEQUENCES

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Matheus Santos Silva, João de Queiroz Netto, Mariely Tonet, Antônio Vinicius Pavan, Felipe de Oliveira Nunes and Dener de Freitas Ribeiro

ABSTRACT

Introduction: The presence of cleft palate has several consequences for the integral development of the individual who is born with this anomaly, and in turn they vary from the impact on physical and social integrity. Methods: The theoretical framework used the SciELO and PubMed databases to search for studies from 2001 to 2023, in English and Portuguese. Discussion: The consequences of cleft palate are not widely disseminated, so it is insufficiently addressed, the impacts on phonation, breathing and mental health are serious and impact mortality rates. Cheiloplasty is one of the surgeries of choice and the presence of more procedures depends on the extent of the anomaly. Even so, early diagnosis and preparation of the family and the team that will assist the patient are of paramount importance to minimize such impacts. Conclusion: It is concluded that the presence of cleft palate is an enormous challenge for the patient and their companions. The insecurity and physical and social challenges demonstrate the importance of the surgical procedure.

Keywords: Cleft palate. Paediatrics. Physical consequences.

INTRODUCTION

Embryology is responsible for explaining the structural formation of the human being, unveiling the formation of cells, tissues, organs, explaining division, cavitary formation and the organs themselves. During the third week of gestation, the germ layers, ectoderm, mesoderm and endoderm, are formed. The endoderm layer originates the respiratory and gastrointestinal tract. In the fourth week of gestation, the division of the digestive tract occurs and at this stage the processes that explain the changes that form the cleft palate or cleft lip will begin (MOORE et al., 2008). Cleft palate or cleft lip is the result of a failure in the embryological process, characterized by the lack or failure of intertissue fusion that makes up from the structures of the mouth to the oropharynx, in some cases. In addition, this congenital malformation has been increasingly common worldwide, but its etiology is not yet fully elucidated (SHIBUKAWA, 2019). Cleft palate has a low mortality rate, however the morbidity rate is notorious, considering that the presence of the anomaly requires nutritional, auditory, and dental support and is expensive. In addition, the condition requires psychological support, since the acceptance and challenges that involve social development affect not only the person with the malformation, but also the support network. In this way, demonstrating the importance of studies that highlight and raise awareness in society, in addition to boosting work in this area, with the aim of reducing the mortality involved (ATUKORALA, 2020).

METHODOLOGY

The literature review presented has a theoretical framework taken from the SciELO and PubMed data platforms. The research period was from November 2023, the inclusion criteria were articles from the years 2001 to 2023, in Portuguese and English, books, online texts and full texts. The following health descriptors (DeCS) were used: "Cleft palate", "Multidisciplinary team" and "Consequences".

DISCUSSION

During the fourth week of gestation, the digestive tract occurs in three layers, middle cephalic and caudal. From this age changes will last throughout the individual's life, such as the cleft palate, in this case lateral to the formation of the oral cavity, the brachial arches will give rise to the head and neck. The 1st brachial arch corresponds to the lower third of the face. Concomitantly, the central nervous system is developed and the frontonasal process develops and gives rise to the nasal fossae and processes. The junction of the primitive maxilla with the nasal processes was the primary palate, the cheek and the lateral upper lip.

These changes last an average of 10 weeks and the formation of the crack occurs at the failure at the junction of these structures. (MOORE et al., 2008).

The etiology is not yet fully clarified, however it is noticeable that genetic and environmental factors are involved, among which the most significant are smoking and alcohol (PINHEIRO, 2017). In addition, risk factors include advanced maternal age, male gender, and low birth weight. (RIBEIRO, E.; MOREIRA, 2004).

The cleft lip can present several conformities, being complete, incomplete, unilateral or bilateral and also symmetrical or asymmetrical. Early diagnosis can help in the prognosis, preparation of the multidisciplinary team and the family. Imaging tests have become fundamental for prenatal counseling. The evaluation takes place through morphological ultrasound, which is done in the first trimester of pregnancy and aims to visualize malformations. In the case of clefts, the incidence of the retronasal triangle is an important milestone for the evaluation of the palate (BUNDUKI et al., 2001).

Cheiloplasty is the surgery of choice for the synthesis of the cleft palate, for it to be successful it is necessary to have minimal tissue resection, anatomical preservation and reconstruction in the three planes, mucosal, muscular and cutaneous. (CAPELOZZA et al., 2002). Surgical management aims at language, speech, hearing, airway patency, psychosocial and aesthetic development (CAMPBELL, 2010 et al., 2002). In addition, ultrasonography obtains images that allow the observation of muscles in movement and at rest, and also allow them to be observed in different planes, so pre and postoperative planning will be more effective (POWER, et al., 2010).

The surgical procedure is not classified as an emergency, which allows many risks to be minimized. Avoiding the operation in children weighing less than 4500 grams, hemoglobin, white series and coagulogram with alterations. However, even with ideal conditions, the main complications are: hypoxemia, respiratory obstruction, hypovolemia, and edema. Most complications are related to anesthesia (BIAZON; OF CÁSSIA; PENICHE, 2008).

In order for the surgery to be performed according to the predilections mentioned above, the ideal team will be multidisciplinary, including a plastic surgeon, oral and maxillofacial surgeon, speech therapists, dentists, pediatricians, social workers and otorhinolaryngologists (FURR MC, et al., 2010). The protocol used includes lip and palate closure at first, followed by bone grafting, orthognathic surgery and secondary rhinoplasty to correct possible residual deformities. Rehabilitation and social insertion depend on the patient's adherence and the experience of the multidisciplinary team (SHAW WC, et al., 2001).

The presence of the cleft can affect everything from the functional aspect to the aesthetic aspect of the individual, in most cases, the individual has a hypernasal voice, problems chewing, breathing, in addition to aesthetics, suffering bullying and social stigma. These issues are directly related to the response to treatment, as well as its adherence and prevention of evasion. Psychological support is also a strong ally, both for the patient and for the companions who are responsible for going to the appointments throughout the patients' follow-up. Considering that patients with cleft palate have a higher risk of hospitalization for psychiatric disorders and consequently a high mortality rate (Guimarães et al, 2014).

CONCLUSION

In turn, it is concluded that the presence of cleft palate is an enormous challenge for the patient and their companions. The insecurity and physical and social challenges demonstrate the importance of the surgical procedure. In addition, the success of the procedure depends directly on the therapeutic planning offered, most of the time by early diagnosis through ultrasound, which allows multidimensional observation of the extent and involvement of the cleft. Even if the images do not have the capacity to accurately reflect in some planes, the identification of the cleft helps not only in the surgery, but also in the preparation of the family nucleus and the multidisciplinary team. The team is fundamental for the development of the individual, considering that the various professionals will promote comprehensive care for the patient, preventing, in most cases, the mortality of this pathology from growing, since the risks for psychiatric disorders, difficulties in breathing, swallowing and phonation are present and seriously impact the quality of life of patients with this anomaly. Demonstrating the importance of studies that cover the various aspects of the life of individuals with cleft palate, from their early diagnosis to their development as a human being inserted and active in society.

REFERENCES

1. Moore, K. L., et al. (2008). *Embriologia clínica*. [s.l.]: Rio De Janeiro: Elsevier.

2. Shibukawa, B. M. C., et al. (2019). Factors associated with the presence of cleft lip and/or cleft palate in Brazilian newborns. *Revista Brasileira de Saúde Materno Infantil*, 19(4), 947–956.

3. Atukorala, A. D. S., & Ratnayake, R. K. (2020). Cellular and molecular mechanisms in the development of a cleft lip and/or cleft palate: Insights from zebrafish (Danio rerio). *The Anatomical Record*, November 2.

4. Pinheiro, K., et al. (2017). *Fissuras labiopalatinas: Revisão de literatura*. Universidade Brasil - Campus Fernandópolis.

5. Ribeiro, E., & Moreira, A. S. C. G. (2004). *Atualização sobre o tratamento multidisciplinar das fissuras labiais e palatinas*. Faculdade de Medicina do Juazeiro do Norte.

6. Bunduki, V., et al. (2001). Diagnóstico pré-natal de fenda labial e palatina: Experiência de 40 casos. *Revista Brasileira de Ginecologia e Obstetrícia*, 23, 561–566.

7. Capelozza, L., & Silva Filho, O. G. (2002). Abordagem interdisciplinar no tratamento das fissuras labiopalatinas. In J. M. Mélega (Ed.), *Cirurgia plástica: Fundamentos e arte II: Cirurgia reparadora de cabeça e pescoço* (pp. 59–88). Rio de Janeiro: Guanabara Koogan.

8. Campbell, A., Costello, B. J., & Ruiz, R. L. (2010). Cleft lip and palate surgery: An update of clinical outcomes for primary repair. *Oral Maxillofacial Surgery Clinics of North America*, 22(1), 43–58.

9. Power, S. M., Matic, D. B., Zhong, T., Murad Husein, M., Lao, A., & Spouge, A. R. (2010). Definition of the lateral bulge deformity after primary cleft lip repair using real-time high-resolution ultrasound. *Journal of Craniofacial Surgery*, 21(5), 1493–1499.

10. Furr, M. C., Larkin, E., Blakeley, R., Albert, T. W., Tsugawa, L., & Weber, S. M. (2011). Extending multidisciplinary management of cleft palate to the developing world. *Journal of Oral and Maxillofacial Surgery*, 69(1), 237–241.

11. Shaw, W. C., Semb, G., Nelson, P., Brattström, V., Mølsted, K., Prahl-Andersen, B., et al. (2001). The Eurocleft project 1996–2000: Overview. *Journal of Craniomaxillofacial Surgery*, 29(3), 131–140.

12. Guimarães, R., et al. (2014). Qualidade de vida em pacientes submetidos à cirurgia ortognática: Saúde bucal e autoestima. *Revista Psicologia: Ciência e Profissão*, 34(1), 242–251.

13. Biazon, J., De Cássia, A., & Peniche, G. (2008). Estudo retrospectivo das complicações pós-operatórias em cirurgia primária de lábio e palato. *Revista da Escola de Enfermagem da USP*, 42(3), 519–544.

14. Souza, L. C. de M., et al. (2022). Fissuras labiopalatinas: Do diagnóstico ao tratamento. Revisão de literatura. *Research, Society and Development*, 11(17), e249111739067.

15. Costa, R. R. da, Takeshita, W. M., & Farah, G. J. (2013). Levantamento epidemiológico de fissuras labiopalatais no município de Maringá e região. *Revista da Associação Paulista de Cirurgiões Dentistas*, 67(1), 40–44.

16. Fernandes, T. F. S., Mesquita, S. T., & Feniman, M. R. (2015). As repercussões sociais em indivíduos com distúrbios da comunicação associados às fissuras labiopalatinas com e sem perda auditiva. *Audiology - Communication Research*, 20(1), 40–47.

CAREFUL-EDUCATIONAL TECHNOLOGIES IN CHILD HEALTH: A TREND IN THESES AND DISSERTATIONS OF BRAZILIAN NURSES

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Cíntia Vanuza Monteiro Bugs[1], Aline Cammarano Ribeiro[2], Amanda Suélen Monteiro[3], Jociele Anchieta do Nascimento[4] and Sara Picolini[5]

ABSTRACT

Objective: to know the trend of theses and dissertations about the careful-educational technologies used in Child Health by Brazilian nurses. Method: This is a narrative review study. The search was guided by the review question: What is the trend of the theses and dissertations that were developed by Brazilian nurses about the Careful-educational Technologies used in Child Health? The data search took place in June 2024 in the Theses and Dissertations Bank of the Coordination for the Improvement of Higher Education Personnel (CAPES) and in the Digital Library of Theses and Dissertations (BDTD), based on different search strategies for each source, involving the descriptors: nursing, "educational technology" and "child health" and their alternative terms. The number of searches resulted in 315 studies. 12 studies were excluded because they could not be applied in the context of Primary Health Care actions, and 267 that did not answer or were not related to the review question. 8 duplicate studies were counted only once. Thus, the corpus of the research was composed of 28 productions. Among these, there are 24 dissertations and four theses. Results: The Careful-Educational Technologies used in Child Health focused on the elaboration of instruments, followed by booklets, websites, booklets, educational videos, applications, serial album, ebook, toy making and realistic simulation scenarios of situations that require attention to the child. It can be observed that there is still a predominance of technologies produced with printed educational materials, but in recent years it has been observed the construction of materials for use in online and download form, ratifying the current technological scenario in which we are inserted. Final considerations: It is considered that such technologies enable quick and easy access, and can optimize the health care and education actions of nursing professionals involved in child care. It is suggested that new studies be developed that address the theme, in favor of the constant improvement of Child Health Nursing conducts, and that existing technologies be implemented.

Keywords: Nursing. Educational Technology. Child Health.

[1] Doctoral student in Nursing, Federal University of Santa Maria (UFSM)
[2] Doctor in Nursing, Federal University of Santa Maria (UFSM)
[3] Nurse, Resident in Nursing in Urgency and Trauma at the Franciscan University
[4] Master's student in Nursing, Federal University of Santa Maria (UFSM)
[5] Undergraduate student in Nursing Federal University of Santa Maria (UFSM)

INTRODUCTION

Children's health represents a priority field in the scope of health care for populations, as assisting children implies meeting the essential needs for their development (GAÍVA; ALVES; MONTESCHIO, 2019). In this perspective, nurses are considered protagonists in child care, as they carry out actions to monitor healthy child development and promote comprehensive care, based on health education for family members or their caregivers (SANTOS et al., 2021).

Over the years, nurses have intensified the use of technologies, as they can help their actions with positive results, presenting themselves in varied formats with resources that can be playful, attractive and that include the co-participation of the means used. This scenario contemplates one of the great possibilities of professional performance in nursing, of low cost and great effectiveness in the health and well-being of the assisted population (MUNIZ; BIKE; SOUZA, 2023).

The use of technologies is an important tool to guide the conduction of nursing knowledge. Technologies are understood as products or processes that allow the involvement of professionals in the provision of effective care to the user and in the development of the health education process, contributing to the provision of relevant information to the target audience (NIETSCHE; TEIXEIRA; MEDEIROS, 2014).

In this context, the concept of Care-Educational Technologies (TBI) emerges, which aim to give meaning to a set of scientific and daily knowledge of Nursing professionals, involving the process of caring/educating and educating/caring for oneself and the other, based on the principles of human praxis (SALBEGO, 2016).

In this way, TCE presents itself as an innovative possibility to conceive and justify technological products and processes developed, validated and/or used, from a perspective that merely transcends its conception as educational or assistance technologies in isolation, that is, without the interrelationship between caring and educating. Thus, TBI occurs when human beings manifest levels of consciousness during their professional praxis (SALBEGO et al., 2018). In this study, the term TBI will be addressed due to the breadth and integration of functions that the concept presents. Thus, the objective is **to know the trend of theses and dissertations about the careful-educational technologies used in Child Health by Brazilian nurses.**

METHOD

This is a narrative review study which comprises the characterization of the productions on the content addressed, identifying trends in relation to the theme. It seeks to

describe and broadly discuss the state of knowledge on a given subject, contributing to the elaboration of concepts in the health area, which can contribute to improvements in care actions (BRUM et al., 2016).

For this purpose, the review question was defined: What is the trend of the theses and dissertations that were developed by Brazilian nurses about the Careful-educational Technologies used in Child Health? The bibliographic survey was carried out in May 2024. The search strategies were based on the combination of Health Sciences Descriptors (DeCs) and keywords and their variations in numerous tests in the Catalog of Theses and Dissertations of the Portal of the Coordination for the Improvement of Higher Education Personnel (CAPES) and the Digital Library of Theses and Dissertations (BDTD), and the searches that guide this research were defined. through the result of the largest number of studies that deal with the theme in question, as presented in Chart 1.

Chart 1 – Search strategies used in the Narrative Review

Databases	Search Strategies
CAPES Thesis and Dissertation Catalog	nursing OR nurse OR nurse OR "educational technology" OR "health technology" OR "software application" OR "audio-visual resources" OR "mobile applications" OR "mobile devices" OR website OR videos OR "educational booklet" OR booklet OR "serial album" OR banner OR "construction and validation" AND "child health" OR "child health" OR "child care" OR "child care" OR childcare
Digital Library of Theses and Dissertations (BDTD)	(nursing OR nurse OR nurses OR nurse OR nurses) AND ("careful-educational technology" OR "educational technology" OR "health technology" OR "software application" OR "audio-visual resources" OR "mobile applications" OR "mobile devices" OR "health education" OR validation OR "content validation") AND ("child health" OR "child health" OR "child care" OR "child care" OR childcare)

Fonte: BUGS, C. V. M., 2024.

For the selection of studies, the following inclusion criteria were adopted: theses and dissertations prepared by Brazilian nurses that answered the review question, and that the technology can be applied in Child Health in the context of Primary Health Care actions. No time frame was used. As this was a study that involved only scientific texts, there was no need for approval by a Research Ethics Committee.

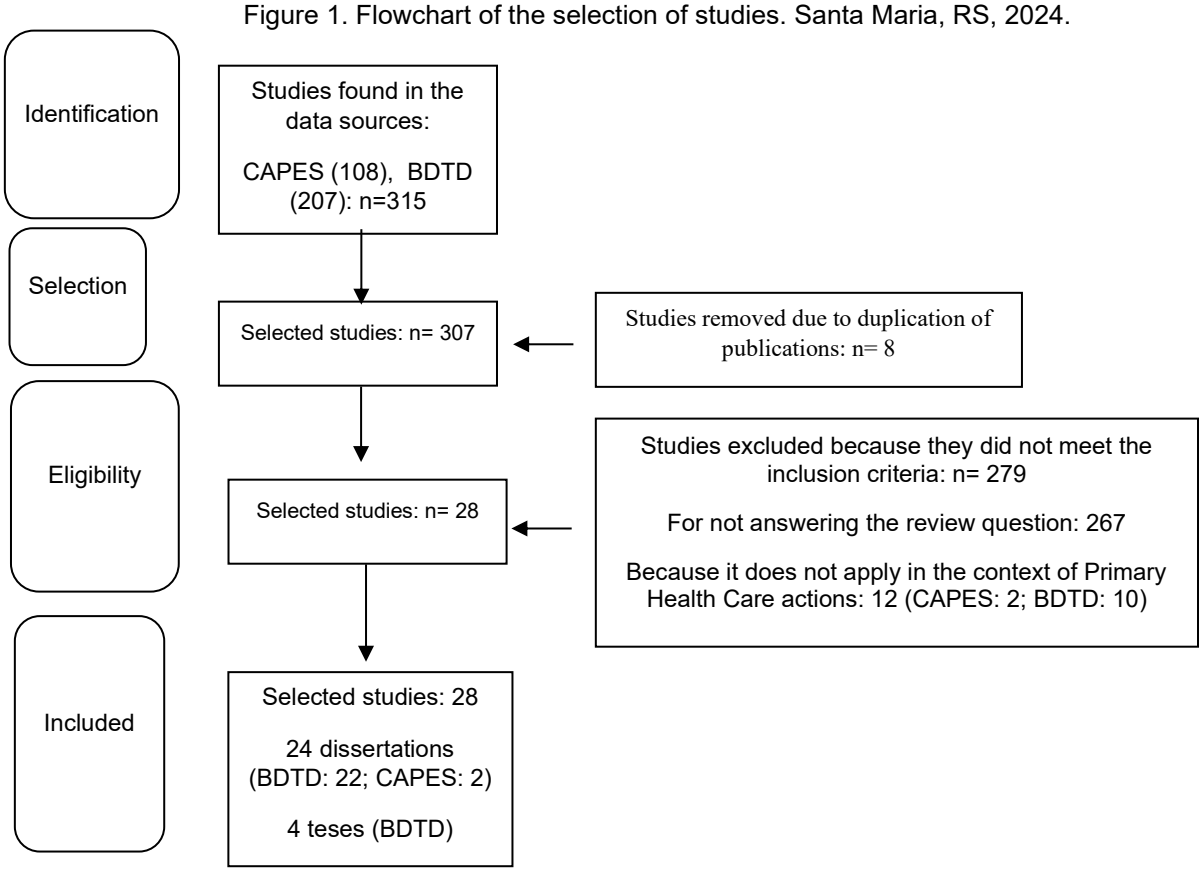
Subsequently, based on a careful reading of the titles, abstracts and keywords, a database was organized in the Microsoft Excel® program to extract information from the studies. Afterwards, the pre-selected studies were read in full in order to extract the following variables: title, author, year of publication, graduate program and institution,

objectives, method used and main results, these data are separated into two synoptic tables presented in the results. In this way, it was sought to understand the synthesis of knowledge for the construction of the review. In addition, the ethical aspects and definitions presented by the authors were respected, which were duly cited and referenced.

RESULTS

The search began with 315 studies. Eight studies were duplicates and counted only once, resulting in 307 studies. Of these, 12 were excluded because they could not be applied in the context of Primary Health Care actions, and 267 because they did not answer the review question. Thus, 28 studies were selected that made up the corpus of the research. The flowchart for the selection of studies is presented below (Figure 1).

Figure 1. Flowchart of the selection of studies. Santa Maria, RS, 2024.



Source: Survey data, 2024.

To describe the selected productions, a synoptic table was prepared (Chart 2) containing the following information: type of study (thesis or dissertation) and data source; name of the author; year of realization; graduate program and home institution. The studies were coded by the letter "D" in the dissertation case and the letter "T" in the thesis, followed by ordered cardinal numbers.

Table 2. Synoptic table. Selected productions on the theme Caring-educational technologies in Child Health.

Type/Source	Title	Author	Year	Graduate Program	Institution
D1 BDTD	Construction and validation of an instrument for systematizing nursing care for children with allergy to cow's milk protein	Sabrina Ferreira da Silva	2021	Professional Master's Degree in Technology and Innovation in Nursing	University of Fortaleza – UNIFOR
D2 BDTD	Technology for early screening of autism in nursing consultations in primary care	Cintia Soares Cruz de Castro	2021	Professional Master of Science in Nursing Technology and Innovation	University of Fortaleza – UNIFOR
D3 BDTD	Development of technology to support nursing consultation in childcare	Fernanda Rocha Honório de Abreu	2019	Professional Master of Science in Nursing Technology and Innovation	University of Fortaleza – UNIFOR
D4 BDTD	Construction and validation of a website on premature care	Ana Paula de Souza Tenório	2016	Postgraduate Degree in Child and Adolescent Health at the Health Sciences Center	Federal University of Pernambuco
D5 BDTD	Immunization of children with autism spectrum disorder: educational material for nursing staff	Aurora Tontini de Araujo	2024	Graduate Program in Teaching Master's Level/ PPGEN	State University of Western Paraná/UNIOESTE – Foz do Iguaçu Campus
D6 BDTD	Construction and validation of a playful educational booklet to carry out the preoperative nursing visit	Marcela Cristina Machado Zanqueta Vasques	2020	Graduate Program Botucatu School of Medicine	São Paulo State University "Júlio de Mesquita Filho"
D7 BDTD	Technology for Guidance of Family/Caregiver of Children Undergoing Surgical Procedures	Renata Rodrigues da Luz	2022	Graduate Program in Health Care Practice, Health Sciences Sector	Federal University of Paraná
D8 BDTD	First home visit to the newborn: production of assistive technology	Ginaina Catia de Prá Oliveira	2019	Graduate Program in Professional Nursing, Health Sciences Sector	Federal University of Paraná
D9 BDTD	Elaboration and validation of videos on first aid: production based on the demand for knowledge of teachers and early childhood education staff	Priscila da Silva Miranda	2022	Academic Program in Health Care Sciences at the Aurora Afonso Costa School of Nursing	Fluminense Federal University
D10 BDTD	Elaboration of a booklet for caregivers of pediatric tracheostomized patients in the Western Brazilian Amazon: a methodological study	Iunaira Cavalcante Pereira	2023	Professional Master's Degree in Clinical Nursing/MPEA	Aurora de Afonso Costa School of Nursing - Fluminense Federal University/UFF
D11 BDTD	Ebook as an educational technology in teaching the safe care of children with cow's milk protein allergy and other allergies in the school environment	Débora Cristina Mendonça de Andrade	2020	Professional Master's Program in Health Education at the Aurora de Afonso Costa School of Nursing	Fluminense Federal University/UFF
D12 BDTD	Construction and validation of a maternal self-efficacy scale in infant feeding	Viviane Maria Pereira de Carvalho Magalhães	2018	Graduate Nursing Degree, Health Sciences Center	Federal University of Pernambuco
D13 BDTD	Construction and validation of content and semantics of the scale of perception of	Lígia Simões Ferreira	2020	Graduate Program in Nursing	Federal University of Mato Grosso do Sul

	family self-efficacy in the home care of children on peritoneal dialysis				
D14 BDTD	Construction and validation of a toy and history for the care of children submitted to cardiac catheterization in a therapeutic toy session	Rosalia Daniela Medeiros da Silva	2015	Graduate Nursing Degree, Health Sciences Center	Federal University of Pernambuco
D15 BDTD	Cross-cultural adaptation of *the Self-efficacy in Infant Care Scale* for Brazil and content validation of the Brazilian version	Talita Helena Monteiro de Moura	2015	Graduate Nursing Degree, Health Sciences Center	Federal University of Pernambuco
D16 BDTD	Development and validation of an instrument for the assessment of newborns in the first week of comprehensive health	Luana Amaral Alpirez	2014	Associate Master's Program in Nursing UFAM-UEPA	Federal University of Amazonas
D17 BDTD	Upper airway infections: construction and validation of educational technology with early childhood educators	Anne Grace Andrade da Cunha	2014	Graduate Program in Nursing	Federal University of Amazonas, in Broad Association with the University of the State of Pará
D18 BDTD	Clinical simulation in the preparation of family members of Children with tracheostomy in the process of discharge Hospital	Fernanda Priscila Mello Almeida da Silva	2022	Masters Nursing Professional Healthcare	Universidade Federal Fluminense/UFF - RJ
D19 BDTD	Educational technology for learning Lactation Physiology: creation and validation of visual content	Polyana de Lima Ribeiro	2019	Graduate Program in Nursing	Federal University of Santa Maria (UFSM) - RS
D20 BDTD	Mobile application on the first nursing consultation with the newborn in primary care: construction and validation	Beatriz Molina Carvalho	2021	Programama Post-Graduation in Public Health Nursing	University of São Paulo at Ribeirão Preto College of Nursing
D21 BDTD	Renal Ped: prototype of *a serious game* for children on peritoneal dialysis	Nathália Lázaro Rocha	2022	Programama Post-Graduation in Public Health Nursing	University of São Paulo at Ribeirão Preto College of Nursing
D22 BDTD	Prevention of child overweight in Primary Care: construction and validation of a serial album	Mirna Ferré Fontão Más	2015	Professional Master's Degree Graduate Program in Primary Health Care and SUS	University of São Paulo School of Nursing
D23 CAPES	Construction and validation of a child care manual in Home mechanical ventilation for nurses of Primary Health Care	Francisca Emanuelle Sales Eugênio Bezerra	2019	Master's Degree Course Child and Child Health Professional Adolescent	Health Sciences Center of the State University of Ceará
D24 CAPES	Construction and validation of an educational booklet for the management and Driving a child with neurological sequelae caused for cancer	Samira de Morais Sousa	2020	Master's Degree Course Professional in Health Management Program Postgraduate Program in Collective Health at Health Sciences Center	University State of Ceará
T1 BDTD	Child Health Handbook in the context of Primary Care:	Camila Padilha Barbosa	2018	Graduate Program	Federal University of Pernambuco

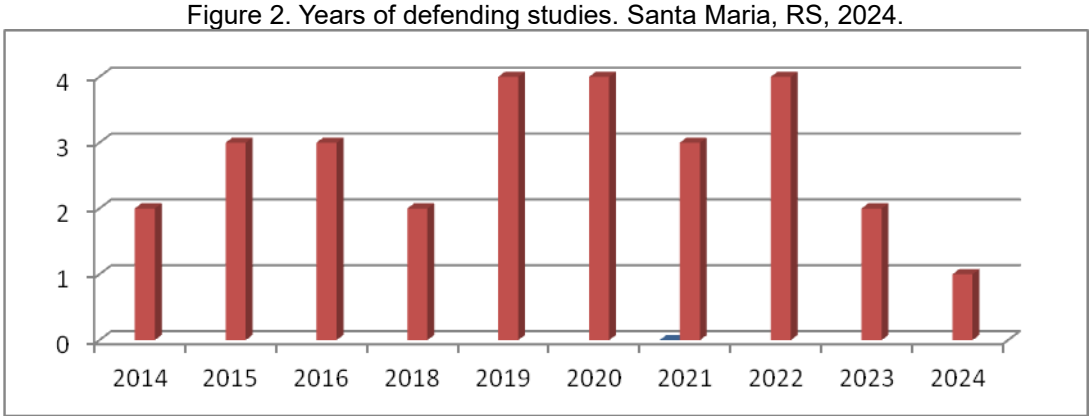
	Development and evaluation of educational software			in Child and Adolescent Health Center of Health Sciences	
T2 BDTD	Promotion of the functional development of children born prematurely: organization of theoretical and operational bases and construction of a family support guide	Rayla Amaral Lemos	2016	Graduate Program in Nursing	University of São Paulo School of Nursing
T3 BDTD	Validation of educational booklets for family members of children/adolescents with leukemia for home care	Cicero Ivan Alcantara Costa	2023	Graduate Program in Nursing	State University of Rio de Janeiro
T4 BDTD	*Prototype software* for monitoring child growth and development based on the International Classification of Nursing Practices (ICNP)	Cilene Nunes Dantas	2016	Health Sciences Center Graduate Nursing Program	Federal University of Rio Grande do Norte

Source: Survey Data, 2024.

PROFILE OF STUDIES RELATED TO THE THEME OF CAREFUL-EDUCATIONAL TECHNOLOGIES IN CHILD HEALTH

Among the 28 studies analyzed, 24 (85.71%) are master's dissertations and four (14.29%) are doctoral theses. The corpus of this research was composed of works defended between the years 2014 and 2024, with emphasis on the years 2019, 2020 and 2022 with four (14.28%) studies each (Figure 2). Thus, it is observed that the study of this theme can be considered growing and current, considering that the number of productions has advanced in recent years.

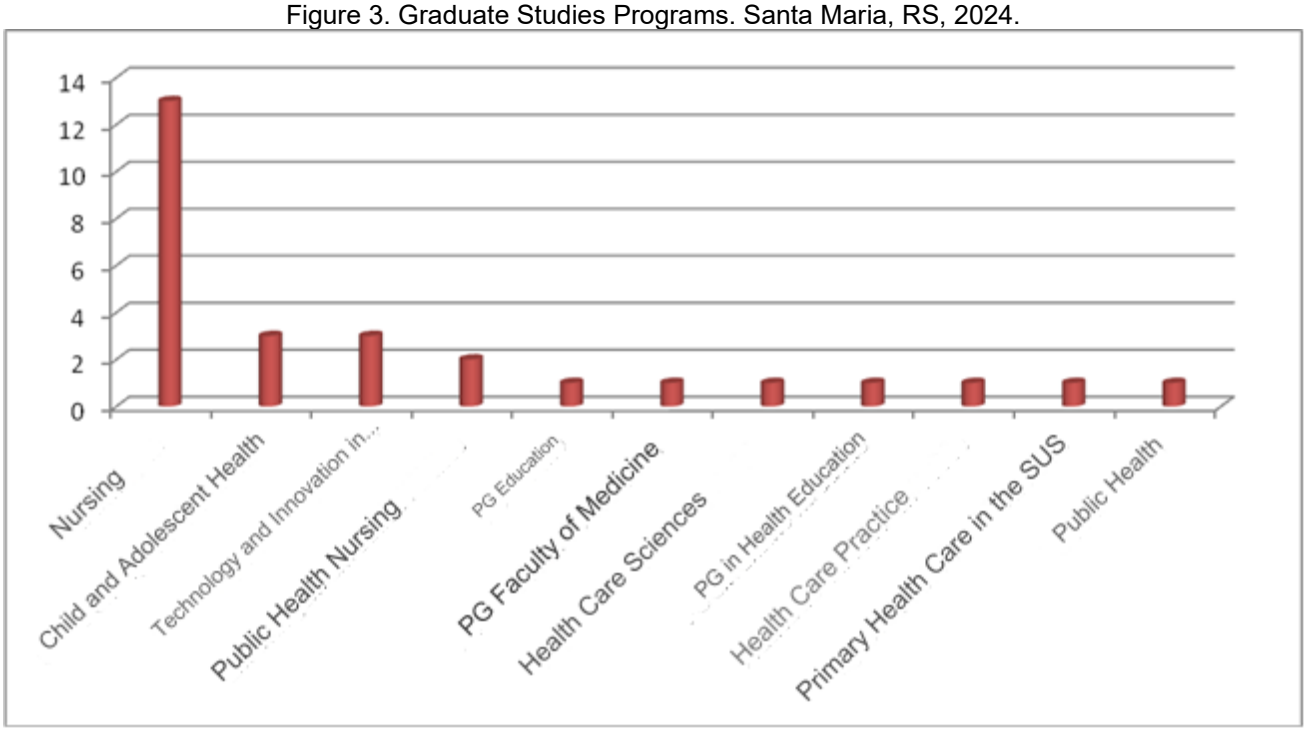
Figure 2. Years of defending studies. Santa Maria, RS, 2024.



Source: Survey data, 2024.

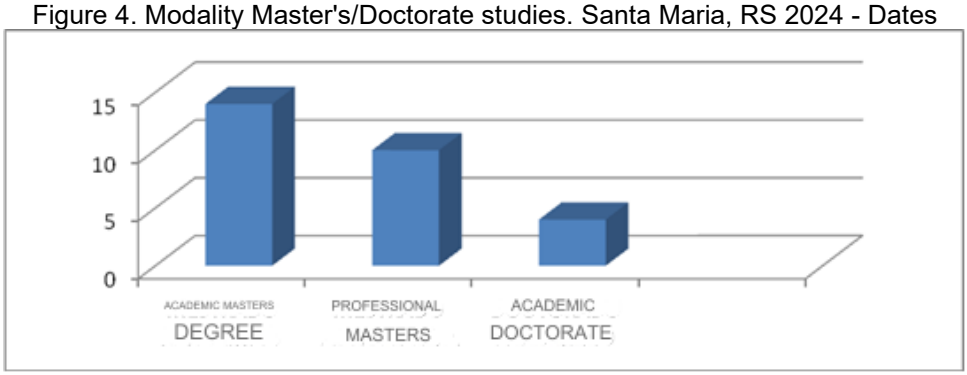
The theses and dissertations are from the most diverse graduate programs, however, most of the studies, specifically 13 of them (46.42%) correspond to Nursing Programs (Figure 3). Also noteworthy is the predominance of studies in the Academic Master's modality with 14 (50%), followed by 10 (35.71%) Professional Master's studies and, finally, four (14.28%) Academic Doctorate studies (Figure 4).

Figure 3. Graduate Studies Programs. Santa Maria, RS, 2024.



Source: Survey data, 2024.

Figure 4. Modality Master's/Doctorate studies. Santa Maria, RS 2024 - Dates



Source: Survey data, 2024.

Regarding the Brazilian geographic region of the universities of the selected research, the predominance was in the northeast region with 11 (39.28%) studies, followed by the southeast region with 10 (35.71%) studies. The southern region included the elaboration of four (14.28%) studies; the North region with two (7.14%) studies and, finally, the Central-West region with one (3.57%) study.

Chart 3 presents the details of the dissertations and theses that made up the corpus of the study.

Table 3. Dissertations and theses according to objective, method and main results. Santa Maria, RS, 2024.

Studies	Objectives	Methodology	Main results
D1 BDTD	**General:** To build and validate an instrument for the Systematization of Nursing Care for children with Milk Protein Allergy (CMPA) attended in the Childcare consultation in Primary Care. **Specific:** - Identify the Nursing Diagnoses in children with Cow's Milk Protein Allergy; -Validate the elaborate technology for content and appearance with expert judges.	Methodological Study. The study was developed in five phases: 1) Integrative literature review; 2) Search in medical records and definition of the most prevalent diagnoses; 3) Construction of the 1st version of the Technology with emphasis on the Systematization of Nursing Care for children with CMPA; 4) Validation of appearance and content by expert judges; 5) Redesign of the technology and elaboration of the 2nd version. The instrument was validated by 16 expert judges.	The construction process resulted in the elaboration of the first version of the technology, which was entitled "Nursing care plan for children with suspected or diagnosed CMPA". This version was built in the Word program, totaling six pages. It consists of a header, for recording pertinent information such as: Name; Date of birth; Address; sex; Age; Weight; Stature. It was found necessary to create a data identification of the child's guardian and investigation of allergies in the family. After information about the nursing history, investigation of psychosocial and psychospiritual needs, notes about the performance of the physical examination. It has a first column with the number of the Nursing Diagnosis (ND); a second column with the defining characteristics of the ND; a third column with the nursing diagnosis statement and the related factors or risk factors; and a fourth column with nursing interventions and nursing actions. The technology was considered valid, as the total Agreement Index (CI) of the instrument was 92.2%.
D2 BDTD	**General:** To design and validate a technology to support the Nursing Consultation for children with Autism Spectrum Disorder for early screening. **Specific:** - Encourage the use of the Systematization of Nursing Care in Childcare in the early screening of Autism Spectrum Disorder; - List the main characteristics of Autism Spectrum Disorder; -Validate the technology with specialists in the area of Child Health.	Methodological and Descriptive Study. The study was developed in three stages: 1) Integrative literature review 2) Construction of the content of the technology 3) Validation of the content and appearance of the technology Question investigated in the Integrative Review: What are the characteristics of child development for early screening of Autism Spectrum Disorder (ASD)? Validation carried out by 15 Experts.	The structured form brings content that proposes the early screening of ASD and the Systematization of Nursing Care (NCS) to children in PHC. The instrument was divided into three parts: the first is composed of the Nursing History, the second is the Cognitive Development Assessment and the third is the NCS. The sum of all Content Validity Indexes (CVIs) was 0.90, which evidenced the effectiveness of the technology. The instrument as a way to facilitate the screening of childhood Autism.

D3 BDTD	Develop a software to support nursing consultation in childcare.	Methodological Study. For the development of the scientific content of the software, a Narrative Review was carried out in the main publications of the Brazilian Ministry of Health, books, websites, protocols, publications in journals, involving the main nursing actions in the face of the Childcare consultation in Primary Health Care and the use of NCS. To idealize the software, meetings were held with professionals from the Technology and Innovation sector. After consolidating the literature and defining theoretical components, the development of screens and the software programming process began.	The technology developed was named Childcare in Focus. It is presented with registration screens, terms of use, welcome, in addition to initial screens and spaces for anamnesis, physical examination, child growth and development, feeding, hygiene, immunization, sleep and rest, accident prevention, Supplementation and Complementary Exams, Care Plan (Nursing Diagnoses, intervention and evaluation), ending with a final report and time spent to carry out the consultation. The technology has health education strategies and possible guidelines that the nurse can be evaluating in the consultation and, if necessary, send to the parents/guardian's cell phones in the consultation by text message. It offers tips and guidance on the professional's conduct, care plan with nursing diagnoses and in case of possible doubts with nursing management and care. The study was not validated.
D4 BDTD	Build a website about care for premature infants for family guidance and perform website content validation.	Methodological Study. It was carried out in two phases, starting with the process of building the website on care for premature infants to guide the family and later with the validation of the website's content by nurses. Website construction and development stages: 1st Stage: Definition Website objectives: to provide guidance on the care that family members should have with premature infants. Target audience: parents and family members of the premature baby. Content: theoretical basis through the educational booklet "Care for the premature baby: guidelines for the family"; Manuals and Notebooks of Care of the Ministry of Health; Universal Declaration of Rights for Premature Infants and scientific articles. 2nd Stage: Architecture Organization of information: grouping of information, identification and separation into main subjects. Step 3: Design Selection of the type and size of the font used, revision of texts, color	The construction of the website lasted an average of fifteen months and had a total of fifteen pages. All pages of the website followed the same standardization in relation to colors, the site's logo, the menu, the text, the size and the color of the font as its layout. The use of a website to guide parents and family members about the care provided to premature infants is a facilitator for the performance of health education activities by nurses, as well as a means of communication that is easily accessible by the premature infant's relatives, especially by cell phone, which is globalized and fast, offering up-to-date, reliable information and providing the sharing of such information.

		control, insertion of images and audio indication for accessibility. Design carried out by a web design professional. 4th Stage: Implementation Hosting of the website content on an institutional server of UFPE at the URL: http://www.ideias.ufpe.br/prematuro Finalization and integration of all pages. Verification of all links and analysis of the interface and the test of the navigation of the website carried out by the author. 34 nurses evaluated the technology.	
D5 BDTD	**General:** Develop educational material to strengthen care practices in the immunization process of autistic children. **Specific:** - To analyze the experiences and strategies used by the nursing team with regard to the immunization program and health of autistic children. - To portray the perceptions of nursing professionals about the immunization process in children with Autism Spectrum Disorder. - Describe the process of development of the educational booklet in the face of the immunization process and health of the autistic child.	Applied Research. Study Scenario: The city of Foz do Iguaçu, is located in the extreme west of the state of Paraná. Study population: 36 nursing professionals who care for children diagnosed with Autism Spectrum Disorder (ASD) in the vaccination rooms of the Basic Health Units (UBS). The study followed two stages: Step I: Elicitation of requirements. Stage II: Elaboration of Educational Technology. Stage I: contemplated the subsidies used for the structuring of the Educational Technology, based on a search in the literature. Stage II: Elaboration of Educational Technology The technology was built using the Canva Pro® tool, containing information/evidence about autism and the childhood immunization process. This evidence is presented in various formats, all of an informative nature, containing: texts, figures, images, as well as guidelines for nursing professionals, seeking the use of clear, objective and easy-to-understand language.	An educational booklet was built that can be used as an informative technological resource to help and encourage the promotion of the health of autistic children in health units. The curricular organization phase relied on pertinent information found in the social representations of nursing professionals, such as: What is autism?; What are the support levels for ASD?; The use of visual cues to assist in the immunization process of autistic people at the UBS, among other important issues, such as the description of some characteristics presented by autistic people. The research contributes as an innovation of care in the process of immunization of children with ASD for nursing professionals and multiprofessional teams, as they will be able to use the content and the booklet in daily practice with the patient and family, strengthening the professional/autistic/family bond.
D6 BDTD	Construct and validate a playful educational material to guide children aged 7 to 12 years and their families during the preoperative nursing visit.	This is a methodological study with non-probabilistic sampling. Steps: -Systematization of the scientific content having as theoretical reference the conceptual model of the Systematization of Perioperative Nursing Care (SAEP) proposed by Castellanos and Jouclas. In addition, an integrative literature review was carried out and the researchers' expertise in the theme was considered; -Creation of illustrations by the Center for Distance Education and Health Information Technologies;	- A printed educational material was prepared and validated, developed in Portuguese, has 21 pages and is available free of charge in printed format, it is an instrument proposed as a guide for nurses to transmit health education to children who will be admitted to the operating room. -The educational material developed in this research aims to offer nurses a playful tool to guide children and their families about the perioperative period, with a

		-A playful educational material, such as a comic book, was developed to address the perioperative period, including the surgical team, the operating room and routines, equipment and the main procedures performed in the surgical anesthetic act. -Validation of educational material by judges. Inclusion Criteria: Nurses and physicians (surgeons and anesthesiologists) with experience in teaching, research, or assisting in children's surgery (surgery, anesthesiology, or pediatrics). - Improvement and revision of illustrations by a company specialized in design. -Validation of educational material by parents and children who have undergone surgery. Inclusion Criteria: Parents who have accompanied a child aged 7 to 12 years (belong to the school age group), and school-age children aged 7 to 12 years who have had elective surgery for the first time and are discharged from the hospital. -19 judges participated in the content validation: 14 nurses and 05 physicians, 07 doctors, 04 with postdoctoral degrees and 03 associate professors. 22 mothers participated in face validation.	view to minimizing the difficulties faced, especially in the preoperative period and in the admission to the operating room. -The educational material can favor the familiarization of both children and their guardians with the hospital and surgical context and minimize the possible difficulties experienced during hospitalization. -The educational material is an instrument proposed as a guide so that nurses can transmit health education to children who will be admitted to the operating room.
D7 BDTD	**General:** Develop audiovisual technology for pre- and postoperative guidance for family members/caregivers of children undergoing surgical procedures. **Specific:** To evaluate the technology developed with a group of health professionals involved in the care of children undergoing surgery and the target audience, family members/caregivers of children who underwent surgery.	Applied methodological research of technological production, developed in three phases and eight stages. The first phase - pre-production that included stage 1, called exploratory, defined the objective of the technology to be developed, the type of technology (2D animation videos), the elaboration of the script for the production of the videos, based on the scientific literature. The second phase - production, included stage 2, referring to the validation of the content of the script by a group of judges (nurses, surgeons and anesthesiologists); Stage 3, in which the Storyboard was elaborated; Step 4, corresponding to the selection of images and animation; Stage 5, in which the recording of the narrations took place; Step 6, the videos are edited. In the third phase - post-production, stages 7 and 8 were included, in which the evaluations of the videos were carried out by the group of judges and the target audience. The videos were evaluated by 23 health professionals (GROUP I)	The content for the construction of the script of the videos, that is, the main pre and postoperative care of pediatric surgeries, as mentioned, was based on the literature review and the Guidelines for Practice in Surgical Nursing and Processing of Health Products. Four videos were edited, with an average duration of two minutes and 34 seconds, the longest of which was three minutes and 22 segundos.com the contents about: Understanding the operating room; Surgery and Anesthesia; Care for the child before surgery; Care of the child after surgery. The technology developed has the potential to contribute to the health education process, guiding the family/caregiver of children undergoing surgical procedures, in relation to the pre- and postoperative care of pediatric surgeries, according to the evaluators.

		involved with pediatric surgical procedures, who also participated in the validation of the script content in the video production phase. GROUP II was composed of seven family members/caregivers of children undergoing elective surgical procedures, who participated in the evaluation of the satisfaction of the videos.	
D8 BDTD	**General:** Develop an assistive technology to support the first Home Visit to the newborn and family. **Specific:** - To identify the difficulties and facilities of nurses and Community Health Agents regarding the realization of the first Home Visit to the newborn, in the municipality of Pitanga, Paraná; - To build with health professionals an assistance technology applicable to the home visit of the newborn and family; - Validate the assistive technology applicable to the home visit of the newborn and family; - Train Community Health Agents to apply assistance technology.	Methodological Research, with a mixed approach, guided by the Methodology of Problematization with the Arco de Maguerez, composed of five stages: 1 - Observation of reality and definition of a problem; 2 - Key points; 3 – Theorizing; 4 - Hypotheses of solution; 5 - Application to reality. 11 nurses, 2 physicians and 81 Community Health Agents working in Primary Health Care in Pitanga-PR participated in the research. After defining the content of the technology through workshops, it was validated by the Content Validation Index, with the concomitant use of the Likert scale, to issue the evaluators' judgment.	The Assistive Technology was an instrument to guide the first home visit to the newborn and family. It was built based on scientific literature and meetings between health professionals to reflect on the literature and the context, validated and registered for use in the Municipality, later the CHWs were trained for use, as a proposal to qualify the performance of the first HV to the NB in Pitanga-PR. Thinking about the continuation of care and also about the qualification of care, it was agreed with the CHWs that after filling out the Technology, they should be sent to the nurse of the reference team to be attached to the child's medical record.
D9 BDTD	-Identify the experience of early childhood education teachers and staff in providing first aid care to children; - Describe the care provided by teachers and employees in the face of accidents in the school context; - List the contents considered necessary by teachers and staff for the preparation of an educational video on first aid to children in the school environment; - Develop an educational video on first aid care for children in the school environment; -Validate educational video on first aid to children in the school	Methodological research for the elaboration and validation of educational technology in video format. The study was carried out at the Application College of a Federal University, located in the state of Rio de Janeiro. The development of the research was carried out in 6 stages: 1st Stage - Search for themes: field research with teachers and employees, so that the themes and content for the composition of the educational video could be recognized and listed. 2nd Stage-Theoretical Study: Theoretical foundation of the educational video. This stage was intended to explore the existing literature in manuals, scientific articles, guidelines and expert guidance on child first aid care. 3rd Stage - Elaboration of the Educational Video: In this stage, the information obtained in the interviews	The educational videos prepared can be used in the educational processes developed for teachers and employees, as well as be made available for consultation when they need to update their knowledge or clarify doubts. In order to ensure essential care in child health problems in the school context. During the preparation of the videos, essential care was highlighted, as well as actions that are harmful to the child and that can cause worsening of their condition. After this stage, the videos were validated with expert judges in the study area, all of whom achieved high levels of agreement: choking (98%), falling (99%) and seizure (98%).

	environment with expert judges and target audience.	and literature contributed to subsidize the content of the educational video. 4th Stage – Validation of the educational video with the expert judges: The validation stage provided a detailed evaluation of the content that makes up the instrument. 5th Stage – Adequacy of the educational video: suggestions for video adjustments. 6th Stage: Validation of the Video with the target audience: the other professionals of the school (teachers and employees) who did not participate in the interview were invited. Participants in the field research: 13 professionals who make up the school team, belonging to the educational segment called Early Childhood Education. Expert judges: 17 professionals, including 13 nurses, 2 pediatricians, 2 social communicators. Validation with the target audience: 15 professionals working in early childhood education, of which 2 are librarians, 2 are student mediators, 2 teachers, 1 janitor, 1 educational agent, 1 cook, 1 doorkeeper, 1 general services assistant, 1 psychologist, 1 social worker, 1 administration assistant.	The contributions of this study comprise the sphere of teaching, practical and social, as for teaching, technology can be used with the public for which it is intended.
D10 BDTD	**General:** To develop an Educational Material with transitional care, aimed at the patient and his family/caregiver, for the management of tracheostomy at home in pediatric patients at hospital discharge. **Specific:** - Identify and map what are the transition care in the postoperative tracheostomy user, through the Scope Review; - Identify the care and difficulties with tracheostomized patients; - Describe the sociodemographic profile of the interviewed population; - Validate the booklet as an educational technology.	Methodological Study. The interview stage and Evaluation of the Target Audience with the family members were carried out in a Children's Hospital. Booklet developed in 4 phases: (1) Definition of the content: two stages: Scoping Review and the second stage, interview with the family members/caregivers of pediatric tracheostomized patients. (2) Elaboration of the Primer's Prototype: The structure of the prototype was organized in columns with: The categories of the interviewees' statements, along with the phenomena of interest of the scoping review and, finally, a column describing all the care with the tracheostomy raised both in the Scoping Review and in the Interview. (3) Production of the booklet for the family: The contents addressed in this phase were clear and objective about tracheostomy care, from the basic care that is directed to the care of the family described in the interviews, to those identified in the scoping review. (4) Evaluation of the booklet by experts: 12 expert judges.	This educational technology provides guidance to family members and caregivers regarding the main daily care provided to children with tracheostomy, improves the understanding of these caregivers about the care to be performed and helps them in the dialogue with health professionals in home actions. The topics were defined: Initial Information, which is related to Family Support and Caregivers, General Care, Aspiration, Advanced Care, Final Considerations, Important Contacts and References.

D11 BDTD	**General:** Develop educational technologies, with emphasis on the production of an E-book as a pedagogical tool to support distance learning for the safe care of children with cow's milk protein allergy and other allergies, for the professional training of nurses and education professionals. **Specific:** - To analyze existing national and international publications on the management of safe care for children allergic to cow's milk protein at risk of anaphylaxis in the out-of-hospital environment; - To identify the knowledge of nursing students about the management of safe care for children with CMPA at risk of anaphylaxis; - Present the elaboration and application of a workshop for the teaching of nursing students, with the construction of an Action Plan for the management of the safe care of children with CMPA; - Structure a distance learning course for the teaching of all professionals who work in schools; - Produce and validate an E-book as didactic material to support the course in the distance modality; - Propose an Intervention Plan for Safe Care1 in the professional training of nurses and education professionals.	Applied research, of an interventional nature, with the development of educational technologies based on the Design Thinking method, that is, centered on the human being. Descriptive and exploratory character, with a qualitative approach. The first stage of data collection consisted of an integrative review. The second stage of data collection, in order to identify the knowledge of nursing students about the management of safe care for children with cow's milk protein allergy (CMPA) in a pedagogical workshop. The workshop was structured based on the Problematization Methodology, in which a Pre and Post-test was applied, using a semi-structured questionnaire, composed of closed questions. An Action Plan was also prepared by the participants addressing the issue related to the safety of children allergic to milk protein in the school environment. From this workshop and a previous review, an E-book was structured as didactic material for the distance learning course, which is intended to be applied later to this study. The E-book was validated by expert judges.	The technology developed was an E-book or digital book with 126 pages, to support the student of the distance course. To support the course, which lasts 40 hours, the E-book entitled "Safe Care of Children with Food Allergies in the School Environment" was created, in PDF format. This material is intended for all professionals who work in public and private schools in the country, upon proof of Acting in schools/daycare centers. The objective of the course is to equip all professionals who deal directly or directly with the indirectly with children so that they can act in a preventive way to risks related to food allergies, in addition to optimizing the emergency response in an allergic reaction/anaphylaxis. The aim is to create a social impact in schools, bringing who knows, paradigm shifts.
D12 BDTD	**General:** To validate a scale constructed to assess maternal self-efficacy in infant feeding. **Specific:**	This is a methodological study in which Pasquali's theoretical principles were adopted for the elaboration of the scale. The first stage consisted of the identification and definition of the construct "promotion of infant feeding", based on a review. The content	The Maternal Self-Efficacy in Infant Feeding scale addresses practices recommended by the WHO to promote infant feeding. The items were elaborated with the purpose of achieving a simple,

	- Develop items and theoretical dimensions of the maternal self-efficacy scale in infant feeding. - Verify the content and semantic validity of this scale.	analysis was carried out by 22 judges, professionals with experience in the theme of infant feeding. The collection period was from October 2017 to January 2018, using an electronic form, containing a synopsis of the theory of self-efficacy, professional qualification, instructions for filling out the scale, and the instrument to be validated. A semantic analysis was carried out with 30 judges, mothers with children registered in a Basic Health Unit, belonging to the Sanitary District IV, in January 2018, through an interview conducted at home. The form applied contained information related to the characterization of the sample and the instrument to be evaluated.	clear and objective language with a view to being accessible to the smallest stratum of the target population. Among several self-efficacy scales that refer to child care, none addresses maternal practices in infant feeding in a peculiar way. The differential of the scale is that it is anchored in the Theory of Self-Efficacy, which is known to be able to identify mothers with low confidence and with a higher risk of developing inadequate infant feeding practices, as evidenced by its results. It contemplates aspects not only of food practice, but of responsive eating, a topic that needs to be further explored in Brazil. The final version of the scale was composed of 30 items and two domains (feeding practice and maternal behavior). The instrument will allow nurses and health professionals to assess maternal confidence and identify their difficulties in managing infant feeding. This will provide the direction of educational actions in the childcare service.
D13 BDTD	**General:** Perform content and semantic validations of an instrument to measure the family's perception of self-efficacy for the care of children on peritoneal dialysis at home. **Specific:** - Build an instrument to measure the self-efficacy of the family of children on peritoneal dialysis at home based on the difficulties and challenges faced by the family; - Perform content validation with experts on the subject; - Perform semantic validation with the target population.	This methodological study adopted the model proposed by Pasquali to guide the construction and validation of the instrument. Bandura's Self-Efficacy Theory was the theoretical framework that grounded the construction of the scale. The theoretical procedures center was conducted in three stages: (a) definition of the construct through literature review and field study; (b) content validation; (c) semantic validation. The study was carried out at the pediatric nephrology outpatient clinic of a university hospital	The proposition of the scale items was supported by the analytical synthesis of the categories identified in the scoping review and in the field study with families of children on peritoneal dialysis at home. From the content validation carried out by five specialists in the field of the concept, using the Delphi technique, a Content Validity Index of 0.84 was obtained after three rounds and a total Kappa of 0.70, demonstrating good agreement among the professionals. Five families of children on dialysis at home participated in the semantic validation; After two rounds, 100% agreement was verified, with reports of good comprehensibility of the items. The scale constructed contains 26 items that explore the perception of the collective

			effectiveness of the family in this context of care. The measurement instrument constructed is a tool to identify the perception of the family's collective effectiveness, that is, the care behaviors that it feels capable of performing to meet the demands of the child and the family at home in the face of difficulties.
D14 BDTD	**General:** Validate a toy and story as an educational technology for the preparation of children who will be submitted to cardiac catheterization in a therapeutic toy session. **Specific:** - Build the toy and story for the preparation of children who will undergo cardiac catheterization. - Validate the content of the toy and story for the preparation of children who will undergo cardiac catheterization.	Methodological study, developed in two stages: - Construction of the toy and story that occurred through understanding the care provided to the child submitted to cardiac catheterization and interview with team professionals. - Validation of the content of the educational technology carried out by 23 judges (storytellers, early childhood educators, nurses, doctors, psychologists, psychopedagogues and occupational therapists).	The toy constructed in this study consists of nine rag dolls, a prototype of the angiograph and the anesthesia machine, and objects for hospital use. The elaborate story addresses in a playful way the physical structure of the Hemodynamics room and all the stages that comprise the pre, trans and post-cardiac catheterization. The toy and story validated in this study, when used in a therapeutic toy session, may constitute a dialogue between health, education and art, capable of enabling interaction between the health professional, the child and family members.
D15 BDTD	**General:** Adapt the *Self-efficacy in Infant Care Scale (SICS)* to the cultural reality of Brazil. **Specific:** -Translate the *Self-efficacy in Infant Care Scale (SICS)* into Portuguese in the Brazilian context. -To verify the validity of the content of the *Self-efficacy in Infant Care Scale (SICS),* Brazilian version, to detect the self-efficacy of mothers in child care.	First Integrative Literature Review Article was carried out, entitled: "Home care for the promotion of child health in Brazil: an integrative review". Second article: "Cross-Cultural Adaptation and Content Validation of the *Self-efficacy in Infant Care Scale* for Brazil". This is a methodological, quantitative study. Cross-cultural adaptation process that followed the following steps: initial translation, synthesis of translations, back-translation, committee of judges and pre-test of the final version. Content validation was performed through the analysis of eight experts and semantic analysis by 30 mothers of children aged 0 to 12 months, followed up in childcare in Sanitary District V of the city of Recife, PE.	The adapted scale consists of 43 items distributed in four domains: promotion of development; general health care; safety and diet. After translation, adaptation and content validation, SICS proved to be adequate to the Brazilian cultural reality. The application of the scale to the mothers in the pre-test and appearance validation allowed the content of the items to be brought closer to regional expressions and made them more understandable. In child nursing care, a large volume of information is common, so it is expected that the SICS contributes to the optimization of the time of the childcare consultation, through the selection of information from the caregiver's trust and that it subsidizes the planning of educational actions aimed at the difficulties in care. The use of this scale will be useful to select the information to be discussed in the childcare consultation.

D16 BDTD	**General:** To develop an instrument for the evaluation of the newborn in the First Week of Integral Health. **Specific:** **-**Validate the content of the instrument for the evaluation of the newborn in the First Week of Integral Health.	This is a descriptive study with a quantitative approach, methodological development, the type of content validation of an instrument for the evaluation of newborns with a view to being able to use it in the consultation carried out during the First Week of Integral Health (PSSI). The development of the study occurred in two stages: - development of an instrument for the evaluation of newborns in the PSSI; - content validation of the instrument for newborn assessment in the PSSI. The instrument was developed based on the actions recommended in the line of child health care ministries. To validate the content of the instrument, the Delphi technique was used . The study was carried out in interdependent stages: - elaboration of an instrument for the evaluation of the newborn in the PSSI; - analysis of the instrument's content by 10 expert judges, who evaluated the general appearance of the instrument, the ease of understanding, the feasibility for care practice, the items covered and the relevance of the topics; - correction and incorporation of changes in the instrument according to the analysis of the judges; - Validation of the instrument's content.	The instrument consists of the following items: Block A - Identification of the mother, father, child and health professional who is providing care, obstetric history of the postpartum woman, general information about prenatal care, labor and birth. Block B - checklist containing possible danger signs for the newborn, space for other observations, indication of the conduct if danger signs are identified in the newborn. Block C – check-list containing information on the actions recommended in the PSSI, such as neonatal, ophthalmological, hearing and cardiology screenings, vaccination status, guidance on breastfeeding, care and hygiene of the newborn and the mother. Block D – evaluation of the mother's general condition, checklist with risk situations for the mother-baby pair.
D17 BDTD	**General:** To build and validate an educational booklet with daycare educators on prevention/care in upper airway infections in childhood. **Specific:** **-** Identify the contents that are relevant for the construction of an educational booklet for daycare educators on prevention/care of upper airway infections in childhood; - Analyze and discuss the content and appearance aspects that are highlighted by the committees participating in the validation process; - Identify if the topics addressed present a clear and simple way for the understanding of early childhood	Technology validation research, with methodological development, focusing on the elaboration and validation of instruments, and emphasis on the qualitative-quantitative approach. For the development of this study, it was decided to follow three phases: - Construction of the educational booklet through an integrative review, which guided the definition of the contents to compose the booklet and, subsequently, the layout of the first version was carried out. - The second phase occurred with the process of validating the content of the booklet by the expert judges and preparing the second version. Expert Judges - The third phase was followed by the appearance validation process, a step that was up to the target audience. Regarding the quantitative analysis, the material was validated from the point of view of content and appearance, since it presented an excellent level of agreement between the expert judges (90.91%) and the representatives of the target audience (99.15%).	The Booklet in its final version has 26 pages, consisting of: cover; Back; catalogue sheet; Technical; summary; presentation; seven topics, referring to the content covered; references used and; verse. The information contained in the booklet was organized in a way that portrayed the path of care needed to be carried out by early childhood educators in the daycare center, offering them contextualization about upper airway infection, a brief explanation of the children's respiratory system, forms of transmission, prevention, care and risk factors. A material rich in drawings was chosen, with the objective of facilitating the assimilation of the contents addressed by all early childhood educators, including any professional who assists in the care of children throughout the daycare center.

	educators of children in daycare; -Evaluate whether the educational booklet is a statistically valid tool to be used in the daycare center by the target audience.	In the qualitative analysis, thematic analysis was adopted, consisting of three thematic categories: readability of the texts; adjustments in the layout; and general evaluation.	
D18 BDTD	-Build simulation scenarios from Deliberate Practices in Rapid Cycles aimed at family members of children dependent on technological care with tracheostomy in the process of hospital discharge; - Validate the simulation scenarios from the Deliberate Practices in Rapid Cycles with expert judges in the area of child health and simulation Clinic.	Methodological research for the elaboration of clinical simulation scenarios based on Deliberate Practice in Rapid Cycles and validation of these scenarios by expert judges in the area of child health and clinical simulation for the preparation of family members of children dependent on technological care with tracheostomy in the process of hospital discharge. Carried out in five stages: - Theme search: integrative review - Theoretical study: search in the national and international scientific literature, in books, guidelines, consensuses. -Construction of the scenarios: the scenarios were built in such a way that the participants can feel as close as possible to the real situation. -Validation of clinical simulation scenarios in the Deliberate Practice in Rapid Cycles modality by the expert judges: 12 participants, 9 were from the area of child health care and 3 professionals from the area of interest of clinical simulation. -Adequacy of the clinical simulation scenarios in the Deliberate Practice in Rapid Cycles modality after validation with the expert judges: the suggestions and/or comments for adjustments to the constructed scenarios were grouped according to each domain evaluated (objective, structure and presentation, relevance) and categorized based on similarities and specifications of the suggested modifications.	Generated product: Construction of clinical simulation scenarios in the modality of Deliberate Practice in Rapid Cycles for the preparation of family members in the management of procedural care of technology-dependent children with tracheostomy in the process of hospital discharge. The themes found in the integrative review and the theoretical study carried out were of great value, as it was possible to reveal some of the vulnerabilities existing in the care practices of CSHCN at home, highlighting the need for better instrumentalization and guidance of family members regarding the management of tracheostomy. It was also observed that there was a lack of recommendations, clinical guidelines, and well-defined care protocols for carrying out this management safely. In an overall evaluation of the scenarios, all three scenarios were considered valid because they achieved an agreement rate higher than 70%. The participation of the expert judges was essential, as it made it possible to evaluate the scenarios with complementary perspectives. Preparing these families during the transition of care for these children from the hospital to home is very important for the execution of procedural care with excellence, ensuring the quality of this transition in a safe way and nursing care for the health of this clientele.
D19 BDTD	Create the visual content of an educational technology for learning the physiology of lactation and validate the content with expert judges.	Methodological study conducted by the conceptual model of Translating Knowledge into Action to develop a tool/product with knowledge. The creation took place from March to October 2018.	The product was developed from the animation technique to favor learning from the representation of organs, hormones and nerve impulses, main elements of lactation physiology attributed to an

		The script for animation was developed from the identification of the imagery content of lactation physiology and the sealing of key images through a search in textbooks and manuals developed by the Ministry of Health, in the National Digital Library of Brazil, Virtual Health Library and SCIELO books. The validation took place from October to November 2018, when about 100 professionals with expertise in breastfeeding or maternal and child health and with experience in teaching, research or care were invited. These professionals were accessed by the International Network in Defense of the Right to Breastfeed, *the International Board of Lactation Consultant Examiners,* the International Network of Child Health Nursing, and the Network for the Study of Educational Technologies, and through the snowball technique, a sample was composed of 27 expert judges who answered a *Likert-type* questionnaire on an online platform.	implious content, difficult to understand. In addition, the technology articulates a part recorded on video to locate the target of the content to be learned. In the validation, the technology obtained an index and Overall Content Validity of 0.84. The visual educational technology for learning lactation physiology is validated in content. This technological support tool can be inserted as an auxiliary resource in health education actions, and may have positive repercussions for the practice of breastfeeding.
D20 BDTD	**General:** Develop and validate a mobile application about the first nursing appointment to the newborn **Specific:** -Develop and validate the content of a mobile application on the nurse's first consultation with the newborn in primary care. -Build a mobile application about the nurse's first consultation with the newborn in primary care and validate the navigability and interface of this mobile application.	Methodological research, with a quantitative approach, used the theoretical framework proposed by Perrenoud (2000) and the methodological framework of Filatro's Instructional Design (2007). The App was created from Android Studio version 4.0.1, with the Integrated Development Environment and Intellij IDEA. The development of the content was based on the results of the Integrative Review. It also considered official materials from the Brazilian Ministry of Health about the care of newborns (NB). *Baby Date* was built with 59 screens and between March and June 2021, 15 judges allocated to three groups (G1, G2, G3) with five judges in each, validated the content. The judges pointed out the need for changes, and the App totaled 67 screens. After the content went through a review of the appropriate use of the Portuguese language. The validation of navigability and interface took place between August and September 2021, with five judges: three nurses and two technology professionals. Both had 100% agreement.	The validated version of the App has 67 screens. The *Baby Date* mobile application corroborates the creation of digital materials that are advancing in the nursing universe. The content of this device was initially created to support nursing students in learning how to care for newborns and their families during the baby's first consultation after discharge from the maternity ward. However, it is understood that it can also contribute to the actions of primary care nurses. This App sought to point out the direction of care through topics considered essential to be addressed in the childcare consultation. Baby *Date* can be considered as a reliable material and conducive to be used to offer qualified assistance to the NB.
D21 BDTD	**General:** Develop a serious *game* type for children with Chronic Kidney Disease and their families	Methodological Research, with a theoretical framework of meaningful learning by David P. Ausubel and a methodological framework by Jeannie Novak.	The *serious game* has five lessons. The beginning has the choice and assembly of an avatar.

	focused on care in renal replacement treatment in the Peritoneal Dialysis modality. **Specific:** - Identify the main difficulties of children and their caregivers in continuing the treatment of children with Chronic Kidney Disease at home; - Identify the most frequent doubts of children with Chronic Kidney Disease and their caregivers in relation to the disease and its management at home; -Develop a prototype of a serious game about care related to Peritoneal Dialysis for children with Chronic Kidney Disease.	The study complied with the concept stages and the *Game Design Documnet.* In the first stage, a qualitative study was carried out with semi-structured interviews with children with Chronic Kidney Disease undergoing treatment with Peritonel Dialysis and with their main caregivers. The analysis was carried out through Inductive Thematic Analysis. The themes added to specific literature for the care of children in Peritoneal Dialysis and documents and regulations of the Brazilian Ministry of Health, and guidelines for the use of the device in Peritoneal Dialysis, grounded the content of the serious *game prototype*. The *Game Design Document* was prepared by the researcher and a graphic designer.	Lesson 1: Peritoneal Dialysis catheter care. Lesson 2: Feeding children with Chronic Kidney Disease. Lesson 3: Hand hygiene. Lesson 4: Peritoneal dialysis at home. Lesson 5: Infection prevention. The prototype has images to color, pictures that demonstrate healthy eating, interaction with the player for hand hygiene, sequence to be indicated for Peritoneal Dialysis and a quiz on peritonitis. The offer of this device favored the teaching-learning process of children with Chronic Kidney Disease undergoing Dialysis treatment. Its use is indicated not only for children and their caregivers, but also for health professionals in the hospital or primary care setting, who can use it as a training tool for home care.
D22 BDTD	**General:** To construct and validate a serial album for the prevention of child overweight in primary care. **Specific:** -Characterize the knowledge and demands of mothers and health professionals about the themes to be addressed in the serial album. - Organize the contents and themes for the construction of the serial album. - Submit the serial album to the judges' evaluation.	This is a descriptive study that focuses on the development and validation of an instrument for educational intervention. Developed in the municipality of Itupeva – São Paulo/SP. It was developed in three stages: 1) Listening workshop with mothers and primary care health professionals. 2) Construction of the serial album. 3) Validation of the serial album. Three workshops were held. Two with 10 mothers and one with 14 primary care professionals. The workshops were recorded, transcribed and submitted to content analysis. The themes extracted from the workshops, technical documents from the Ministry of Health and figures available in the web image bank were used in the construction of the serial album. The Serial Album was validated by eight judges, professionals linked to the municipality's Health and Education Board.	The construction of the Serial Album was based on the themes extracted from the workshops held with mothers and health professionals. The material was organized according to the themes "Recognition of overweight/obesity"; "Consequences for the child's health"; "Strategies for prevention and promotion of child health". The Serial Album was made up of 27 leaflets with front and back. The construction and validation of the Serial Album, based on critical education, involves the participants, facilitates the use of this technology by health professionals in the educational process in primary care, and favors the understanding and incorporation of important steps for the prevention of child overweight.
D23 CAPES	To construct a manual of care for children on home mechanical ventilation for nurses in Primary Health Care and the validation of its content and appearance.	Methodological research, of a descriptive nature, carried out from October 2018 to July 2019. For the theoretical foundation, an integrative review was carried out on the theme.	The study proposed the development of a "Manual for child care on home mechanical ventilation for nurses in Primary Health Care". After careful evaluation by professionals who are experts

		Then, the manual was prepared with the help of a graphic designer, who prepared the illustrations under the guidance of the researcher. To this end, criteria were used that describe aspects related to language, illustrations and layout/design. After the construction of the manual, the content and appearance were evaluated by 22 specialists. These were health professionals, mostly nurses, inserted in teaching and/or care in Pediatrics and Primary Health Care, recruited through a search on the Lattes Platform and snowball sampling. Each participant answered the printed technology assessment instrument. The data were organized in Microsoft Word documents and Microsoft Excel spreadsheets, presented in charts and tables. In the data analysis, the Content Validity Index was used.	in the field, this educational technology was validated for its content and appearance. Validation was performed by 22 specialists and satisfactory CVI was obtained. The following aspects were included in the manual: definition of invasive mechanical ventilation; Indications; organization of the household; and care that requires invasive treatment because these children belong to a diverse group of patients with complex health care needs. Manual contains graphic design and digital illustration, with attractive figures, easy to understand and consistent with the cultural context of the target audience. We sought to combine content that is relevant in terms of information, but objective and with language accessible to nursing professionals who work in Primary Health Care.
D24 CAPES	**General:** To build and validate an educational booklet for caregivers of children with neurological sequelae caused by cancer. **Specific:** a) To identify the main difficulties in caregivers' knowledge about the care of children with neurological sequelae caused by cancer; b) To prepare an educational booklet on the care of children with neurological sequelae to be carried out by the caregiver; c) Validate the appearance and content of the booklet with the expert judges.	Methodological study carried out from January 2018 to December 2020, in a tertiary hospital in the municipality of Fortaleza-CE. The study consists of an integrative review; and validation of the booklet with expert judges using the Content Validation Index (CVI). To evaluate the reliability of the proposed items, where a CVI greater than or equal to 0.75 was considered. In the semi-structured interview with the mothers/caregivers, it was possible to detect the main points pertinent to the practical experience of the target audience. The interviews were transcribed and the most frequent doubts resulted in the classification of three categories. The booklet was validated by 6 judges as to content and appearance.	The booklet is a valid, practical, and easy-to-understand educational material for caregivers and health professionals. This educational booklet was developed in order to promote guidance and training for mothers of children with neurological sequelae caused by Central Nervous System cancer and had its content and appearance validated by expert judges. The team of judges participating in this validation process was composed of higher education professionals with extensive experience in the health area, preferably working in pediatrics or oncology, and with practical knowledge in the production of educational material. The material is indispensable for the multiplication of information based on scientific evidence, thus enabling the promotion of children's health.
T1 BDTD	To develop and evaluate an educational software on the Child Health Handbook (CSC) aimed at the continuing	Study of technological production with the development of educational software and quali-quanti approach. The methodological path was divided into three stages:	The corpus produced was organized into five thematic categories for continuing education: monitoring of children with Down Syndrome;

	education of childcare professionals in primary care.	1) To identify the needs of primary care professionals for continuing education on the CHR, an exploratory study with a qualitative approach. Seventeen primary care physicians and nurses in Recife responded to a semi-structured interview. For the analysis of the interviews, the content analysis technique according to Bardin was used, with the aid of the Atlas ti software. 2) To develop an educational software on CHR for the continuing education of childcare workers in the context of primary care based on the pedagogical assumptions of meaningful learning, with subsidies from the information collected in the diagnosis stage. 3) To evaluate the SSC educational software in the context of primary care from the perspective of child health specialists. In this stage, four nurses and four physicians performed a pedagogical evaluation of the educational software. To this end, a questionnaire adapted from Behar (1993) was used, with concepts arranged on a Likert-type scale. The data were analyzed using the Content Validation Index (CVI) and the Percentage of Agreement among the specialists with cut-off points of 80% and 90%, respectively.	children's rights; guidance on oral, eye, hearing health, among others. The educational software Child Health Handbook in the Context of Primary Care was evaluated by the experts with a General CVI of 95% and a General Percentage of Agreement equal to 92.6%. The conceptual and work process needs for the use of the CHR by primary care professionals as justifications for its underutilization indicated the need for continuing education for nurses and childcare physicians in primary care. With this proposal, the educational software developed was considered by the experts as suitable for continuing education because it had achieved its goal as a teaching-learning tool.
T2 BDTD	**General:** To systematize the theoretical and operational bases of care for children born prematurely and to compose health education material to promote their functional development at home. **Specific:** -Seek evidence and fundamental information about functional development and its implications for home care; - Build educational material on the care and promotion of the functional development of children born prematurely; -Validate the content and appearance of the educational material in a participatory process with	This is a methodological study, with a mixed, exploratory and analytical approach. An integrative review was conducted. This content guided the construction of an educational material to support and guide families. The educational material was submitted to caregivers and professional-judges for validation, through participatory strategies. The judges, selected from the Lattes Platform, answered a web-questionnaire, or participated in a focus group. Family caregivers, invited to a preterm follow-up service, participated in focus groups. The qualitative data were submitted to Thematic Content Analysis and the quantitative data to descriptive analysis. 80% was defined as the level of agreement.	A total of 53 professionals participated in the study, 45 from the health area and nine from the communication and education area, and 16 caregivers. The educational material entitled "Sofia's Story: Battles and Achievements of the Family in the Care and Development of the Premature Child" was widely accepted, validated by health professionals and family caregivers, who reported interest in applying it in their practice and sharing it with other families. The families considered the language of the material clear and accessible, and its content realistic in relation to their experiences, reflecting their experience and main issues in fellatio the theme addressed. The educational material produced has the potential to support families in promoting

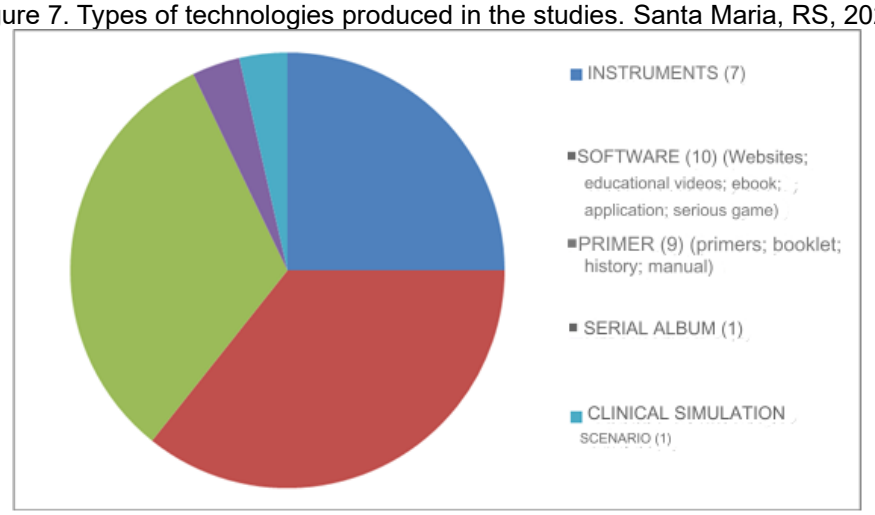
	family members and professional-judges.		the development of children born prematurely.
T3 BDTD	**General:** Validate educational booklets for family members of children/adolescents with leukemia for home care. **Specific:** -Evaluate the adequacy of content and images of the educational booklets for family members of children/adolescents with leukemia for home care with expert judges and the target audience. -Validate with expert judges the content and images of the educational booklets for family members of children/adolescents with leukemia for home care. -Validate with the target audience the content and images of the educational booklets for family members of children/adolescents with leukemia for home care.	This is a study of content and appearance validation by expert judges and the target audience of the booklet entitled "Educational booklet for family members of children/adolescents with leukemia for home care". The booklet was built in the Master's Degree (2017-2019) and divided into four volumes: "Care in the feeding of children/adolescents with leukemia at home", "Care with the central venous catheter at home", "Care for children/adolescents with low immunity at home", "Application of bone marrow stimulator medication at home". The participants were divided into four groups, and each group evaluated a volume of the booklet. Data collection took place through a questionnaire on *Google Forms*, first with the expert judges, from November 2021 to April 2022, then with the target audience from February to October 2022. Validation with expert judges occurred in two evaluations. In the first group, the groups were composed of 10 (3 nurses, 5 nutritionists and 2 physicians), 11 (9 nurses and 2 physicians), 12 (10 nurses and 2 physicians) and 12 (9 nurses and 3 physicians). In the second evaluation, 10 (5 nurses, 3 nutritionists and 2 physicians), 11 (9 nurses and 2 physicians), 10 (8 nurses and 2 physicians), 11 (9 nurses and 2 physicians). With the target audience, it occurred in only one evaluation, where the groups had 13, 12, 12 and 12 family members.	After the modifications considered necessary by the expert judges, the four volumes had an overall agreement rate of 99%, 98%, 99% and 96%. The target audience approved the volumes with an overall agreement rate of 99% each, with no suggestions for changes. The validation of this booklet is important, as it contemplates a series of doubts of family members in the continuity of care at home. In this way, the booklet makes it suitable for distribution and use in health units, with the aim of supporting family members in the home care provided to children and adolescents. In addition, it will allow health professionals to intervene in advance with family members with guidelines to promote a safer hospital discharge.
T4 BDTD	**General:** To develop a *Software* (Prototype) for Nursing Consultation (SC) applied to the monitoring of child growth and development (HC) in Primary Health Care (PHC). **Specific:** - Build and validate a Nursing History (HE) instrument for the first consultation and for the subsequent consultation applied to the follow-up of the infant HC, based on the Theory of Basic Human Needs (TNHB) and the International	Methodological study for the elaboration of the instrument for the nursing consultation, which consisted of five phases: - Literature review; - Structuring of instruments for validating the content of the nursing consultation for the follow-up of the children's DC; - Selection of judges to participate in the study; - Validation of the content of the Nursing History: Delphi Technique; - Development of the Telenursing environment (prototype software) for the monitoring of the children's DC. Data analysis was performed using simple descriptive statistics, using absolute and relative frequencies, mean, standard deviation, binomial test, and content validity index.	Results were presented in three manuscripts: 1) Nursing consultation for monitoring child growth and development in Primary Health Care: an integrative review. 2) Validation of nursing history instrument to monitor child growth and development. 3) Prototype software for monitoring child growth and development in Primary Health Care. The first article is related to the findings for the characterization of the child's consultation, which revealed gaps in the monitoring of child growth and development due to limitations related to the theoretical and/or practical

	Classification of Nursing Practices (ICNP).		knowledge of nurses in Primary Health Care. The second article reveals the content validation of the instruments for the first consultation and subsequent consultation applied to the child. It refers to the use of the Delphi 1 stage, in which eight judges evaluated the nursing history instruments, from the Delphi 2 and 3 stages, six. The nursing history was considered valid in its content. Article 3 is related to the *software*, developed on a *web* platform and presents the previously established requirements that are related to the system, resulting in activities that are accessible to the users (administrator and nurse user) registered in the system. The nursing history instruments and software developed and validated can guide the practice of PHC nurses, provide opportunities for more effective communication and the empowerment and autonomy of nurses.

Source: Survey Data, 2024.

Figure 7 presents the visualization in a summarized way about the types of technologies that were produced in the studies of the dissertations and theses of the barrels, thus outlining the production trend. It can be seen that the instruments of the most distinct spheres of child care prioritize studies, followed by booklets, websites, booklets, educational videos, applications, serial albums, ebooks, toy making and realistic simulation scenarios of situations that require attention to the child.

Figure 7. Types of technologies produced in the studies. Santa Maria, RS, 2024.



Source: Survey Data, 2024.

In recent years, there has been an ascendancy in the production of materials built for use in online and download form, ratifying the current technological scenario in which we are inserted. From the year 2021 onwards, there is a decrease in the production of technologies, but it is believed that these may still be unavailable publicly. Such technologies enable quick and easy access, and can optimize the actions of care, guidance and health education of nursing professionals involved in the care of children.

DISCUSSION

The predominance of studies was based on methodological research, more precisely 23 studies that make up this review. Methodological studies aim to develop instruments, allowing the researcher to use models with mixed methods (quanti-quali), or only one of them. Such studies address the development, validation and evaluation of research tools and methods (POLIT; BECK, 2018).

To compose the content of the technologies, the studies evidenced the previous performance of Integrative Literature Review D1, D2, D6, D11, D12, D14, D15, D17, D18, D20, D23, D24, T1, T2. Integrative literature review is a specific method that summarizes the past of empirical or theoretical literature to provide a more comprehensive understanding of a given phenomenon (BOTELHO; CUNHA & MACEDO, 2011). It allows the combination of several methodologies (experimental and non-experimental studies) and has the potential to play an important role in Evidence-Based Practice (EBP) in Nursing (SOUZA; SILVA; & CARVALHO, 2010; WHITTEMORE & KNAFL, 2005).

The Narrative Literature ReviewD3, D5, D7, D9, D16, D19, D20, D21, D22 was used by some studies to assist in the elaboration of the content of the technologies produced by them. In this sense, narrative review articles are broad publications appropriate to describe

and discuss the development or state of the art of a given subject, from a theoretical or conceptual point of view. These are texts that constitute the analysis of the scientific literature in the interpretation and critical analysis of the author. Despite the fact that its strength of scientific evidence is considered low due to the impossibility of reproducing its methodology, narrative reviews can contribute to the debate of certain themes, raising questions and collaborating in the acquisition and updating of knowledge in a short period of time (ROTHER, 2007).

Two studiesD10, D13 used the *Scoping Review* to map the scenario about the intended technologies and also to support the conceptual content that would contemplate such constructions. Thus, the *scoping review* technique is being widely used in the area of health sciences with the purpose of synthesizing and disseminating the results of studies on a subject (LEVAC; COLQUHOUN; O'BRIEN, 2010; JBI, 2015). The objective of a scoping analysis is to map, through a rigorous and transparent method, the state of the art in a thematic area, intending to provide a descriptive view of the reviewed studies, without critically evaluating them or summarizing evidence from different investigations, as occurs in a systematic review (ARKSEY; O'MALLEY, 2005).

Most of the studies, specifically 24 of themD1, D2, D4, D6, D8, D9, D10, D11, D12, D13, D14, D15, D16, D17, D18, D19, D20, D22, D23, D24, T1, T2, T3, T4, performed the validation of the technologies with expert judges in the proposed themes. Thus, for the validation of a technology, it is important to have an evaluation by experts on the subject, who can suggest, add, correct or even modify the items they deem necessary (ALEXANDRE; COLUCI, 2011).

The instruments constructed in the studies outlined numerous situations of care for children and their families. Two studiesD1 and D2 developed Nursing Care Systematization (NCS) forms for care in one of them, for children with Cow's Milk Protein Allergy (CMPA) and the other, for early screening of Autism in children in the nursing consultation.

In this context, Cow's Milk Protein Allergy (CMPA) is defined as an immunologically adverse reaction to the antigens present in cow's milk. Its signs and symptoms generally present in the first 12 months of life, after weaning or after its first exposure (SAARINEN et al., 1999). Some studies show a prevalence of 2 to 5% among infants under 1 year of age diagnosed with CMPA, but the rates of underdiagnosis are still high, reaching 15%. This food allergy is the most frequent in children under the age of 3 years and, in the last century, its prevalence has doubled (ERRAZURIZ et al., 2016). Thus, studyD1 has the potential to be used as a resource for the improvement of NCS for children and, thus, can also support the development of holistic, singular and qualified nursing care.

The instrument, which was developed as a way to facilitate the screening of childhood autism, has the potential to provide not only the child, but also the nurse with information so that he or she becomes more active with regard to autism and innovative in the child's cognitive development. The role of nurses in the early detection of signs and symptoms is relevant to contribute to the early identification of AutismD2. To elucidate, Autism is understood as a psychosocial disorder, and a genetic condition of the individual, whose impairments are mainly related to an excluding sociocultural environment, which affects the areas responsible for social interaction, communication and restrictive behavior (ZAVALETA RAMÍREZ et al., 2014).

It is understood that the professionals who are part of the health teams need practices that can stimulate discussion and enhance care for Autism in Primary Health Care (PHC), especially the nurse who is part of the direct monitoring of children in Childcare. However, they must be able to assess possible changes in the child's growth and development, by age group, paying attention to developmental milestones by age, in order to make an early diagnosis of possible changes (LIMA et al., 2021).

Two other instrumentsD8, D16 were constructed in dissertations to meet the needs of the newborn (NB). One of themD8 aimed to develop an Assistance Technology to guide the performance of the first home visit (HV) to the newborn and his family entitled: First home visit to the newborn and family. The product presented itself as an important tool that will allow professionals to detect maladjustments early, and to carry out care and surveillance of warning signs, with guidance for referrals of newborns at risk.

From this perspective, the first approach through HV in the first week of life, preferably up to the fifth day of life, is recommended both at the federal and state levels, due to the recognition of risks in this period, as well as the objective of promoting health and preventing future problems (BRASIL, 2011), being indispensable for the provision of care to the baby safely at home (SANTOS et al., 2014).

A master's thesisD16 developed an instrument to assess newborns in the First Week of Integral Health (PSSI), in order to organize the care process of health promotion and disease prevention actions in Primary Health Care (PHC) in the first week of life of newborns. Thus, PSSI emerged as a strategy for the care of the mother and the newborn, considering that this period is of great vulnerability in the lives of the woman and the child. In this strategy, care is proposed to be provided to the mother-child binomial, aiming at health promotion and disease prevention, through the encouragement of exclusive breastfeeding, the prevention of anemia, malnutrition and diarrheal diseases. Vaccination of vaccine-preventable diseases is encouraged and childcare and postpartum appointments

are scheduled. It is also possible to promote the early detection of health problems in the child by performing the heel prick test, the ear test, the eye test, and the evaluation of risk factors for the mother and the newborn. This set of conducts is guided by the Ministry of Health in order to guarantee comprehensive child health care (BRASIL, 2004).

Two studiesD12, D13 performed the construction of Self-Efficacy Scales, the firstD12 refers to the assessment of maternal self-efficacy in infant feeding. Self-efficacy is a predictor of health behaviors, which enables nurses to identify the difficulties perceived by mothers in this process and to direct educational actions. This scale can help nurses to assess and also help mothers at the time of childcare, through actions aimed at minimizing their needs and anxieties related to breastfeeding. Thus, mothers should feel able and prepared to feed their children in a healthy way in order to promote the well-being and proper growth and development of the child. The belief in one's ability to successfully perform a behavior capable of producing results can be defined as self-efficacy (BANDURA, 1994).

The studyD13 proposed the construction of a family self-efficacy scale for the care of children on peritoneal dialysis (PD) at home. This scale allows the nurse to identify the weaknesses of family members in the care of these children, allowing this professional to develop actions to assist in this home care process through joint conducts and ideas with the families, according to the context and reality in which they are inserted.

In this environment, for home PD to be performed, the involvement of the family is indispensable, which, in turn, needs guidance until it becomes able to care for the child and perform the procedures at home (LOMBA et al., 2014). PD is a daily process, for an indefinite period of time, in which the family needs to be supported to participate in the child's care. The nurse needs to introduce the family to the care of the child, enabling him to assume the execution of dialysis procedures at home, for the management of the treatment and also to perceive signs and symptoms of complications with the therapy and with the child (AMARAL, 2016; WIGHTMAN et al., 2019).

The dissertationD15 aimed to adapt the *Self-efficacy in Infant Care Scale* (SICS) to the cultural reality of Brazil. This scale is shaped like a self-administered questionnaire to assess the mothers' self-efficacy in child care. The use of scales to identify the mother's confidence in the childcare monitoring is capable of providing exchanges of experiences and overcoming anguish and difficulties (VASCONCELOS; FLEET; MARTINS; MACHADO, 2012). Among the strategies aimed at overcoming problems, there is health education, which is a social practice and should be centered on the problematization of the context and based on the analysis of reality. Educational actions planned according to the health needs

of the population should be aimed at improving the determinants of health (ALVES; AERTS, 2011).

Some studies have developed *D3, T1, T4 software* for the execution of child health conducts. In this follow-up, the following were also elaborated: *D4 website*, E-book [D11], mobile applicationD20, *serious gameD21* and educational videosD7, D9, D19. The *software* can support the Childcare Nursing ConsultationD3; educational *software* on the Child Health Handbook (CHR) for the continuing education of childcare professionals within the scope of PHC1 and a prototype software for applied nursing consultation for actions and monitoring of child growth and developmentT4.

In view of the importance of the use of NCS in childcare consultations with children and its direct influence on the nurse's work process and the quality of the care offered, the importance of using Information Technology (IT) emerges as a support for the improvement of clinical health records and support for the development of the computerized nursing process (DOMINGOS et al., 2017). With each passing day, there are profound and constant changes, with technological innovation growing and accelerating, making available to professionals and users, the most diverse types, such as educational technologies, managerial technologies and assistive technology (BARRA et al., 2017).

It is also worth mentioning that Health Technology represents a set of systematized knowledge (scientific and empirical), in a constant process of innovation, which is applied by nursing professionals in their work process, to achieve a specific objective. The characteristic of nursing technology is peculiar, because when caring for human beings, it is not possible to generalize conducts, but rather to adapt and standardize them to the most diverse situations, in order to offer unique and appropriate care to the individual (ROJAS et al., 2016).

In the form of *a websiteD4*, a study on care for premature infants was developed to guide the family. The studyD11 built an *E-book* as a pedagogical tool to support distance learning for the safe care of children with cow's milk protein allergy and other allergies, focused on the professional training of nurses and education professionals. The D20 mobile application was developed for the first nursing consultation for the NB in PHC. The *serious game D21* was created for the care of children with Chronic Kidney Disease undergoing treatment with Peritoneal Dialysis, it can be used by the child and also for training family members and health professionals.

The educational videos developed as technologies to aid health actions were intended to: pre- and postoperative guidance for family members/caregivers of children undergoing surgical proceduresD7; first aid care for children in the school environmentD9

and learning lactation physiologyD19. These videos fostered health education through audiovisual technology, in order to produce knowledge in an accessible, playful and easy-to-understand way, which can be shared in the context of PHC, so that access to safe and early information can minimize anguish and doubts of families and children.

Thus, educational technologies, whether face-to-face or in the distance learning modality, such as in virtual learning environments, need to be used in order to focus on the student and their active and collaborative learning, facilitate the teacher's mediation attitude and the development of the relationship of partnership and collaboration between teacher-student, student-student and between groups (MASETTO, 2010). Video-type educational technologies can be strategies for health education. They are favorable to the teaching-learning process, contributing to the understanding and comprehension of care, since it induces motivation, curiosity and stimulates the participation of the caregiver (CAKMAK et al., 2018).

Nurses play a crucial role in the education process of children and their families, with the objective of providing quality care and promoting safety in care. In this process, nurses can make use of means that aim to communicate and understand the participants, and technologies are mentioned as one of the resources for this performance (LIMA, 2018). The use of intelligent technologies and the standardization/protocolization of practices are initiatives that can contribute to the promotion of pediatric patient safety, with direct repercussions on health care (WEGNER et al., 2017).

The educational booklets were produced by nine studiesD5, D6, D10, D14, D17, D23, D24, T2, T3 that covered the themes: educational material to strengthen care practices in the immunization process of autistic childrenD5; playful educational material to guide children aged 7 to 12 years and their families during the preoperative nursing visitD6; educational material with transitional care, aimed at patients and their families/caregivers, for the management of tracheostomy in pediatric patients at hospital dischargeD10; toy and story for the preparation of children who will undergo cardiac catheterization in a therapeutic play sessionD14; educational booklet with daycare educators on prevention/care in upper respiratory tract infections in childhoodD17; manual for child care on home mechanical ventilation for nurses in PHC23; educational booklet for caregivers of children with neurological sequelae caused by cancerD24; educational material in health to promote the care of premature childrenT2; educational booklets for family members of children and adolescents with leukemia for home care conductsT3.

The booklets are characterized as educational material due to easy visualization (illustrations) and appropriate language according to the target audience, given the ease of

access to information. Based on health education, the booklet is shown to be a relevant resource in the didactic-pedagogical process, that is, it is an effective and low-cost Educational Technology that boosts health education activities (JORGE, PEDROSA, 2020). Understanding the importance of these tools in the care environment and in society favors a clear, objective, and complete understanding, since individuals have knowledge linked to cultural values (WEISSHEIMER et al., 2021).

Only one study evidenced the construction of a serial albumD22 about the prevention of child overweight in primary care, and one study aimed to build clinical simulation scenariosD18 based on Deliberate Practices in Rapid Cycles aimed at family members of children dependent on technological care with tracheostomy in the process of hospital discharge.

Visual resources are important points of support in a presentation for both the spectator and the presenter, as they allow the organization of the material presented verbally by the presenter and follow the proposed sequence, in addition to illustrating important points for the understanding of the subject (SCHMIDT; PAZIN-FILHO, 2007). Thus, the serial album allows the presentation of a subject in a gradual and organized way, avoiding dispersion or confusion and facilitating the fixation of essential points (CAIRES, 2007). In relation to the text, it should be objective, use simple language, as well as serve as a script to assist the speaker regarding the subject to be addressed, subsidizing the speech (FREITAS, 2009).

Among the most varied educational strategies for preparing for home discharge, the simulation technique, widely used by health professionals and academics in the context of teaching, can be promising in the transition process of technology-dependent children from the hospital to home, since the care to be performed in the home environment requires previous training (HUNT et al., 2014). Simulation is defined as a pedagogical method that uses one or more educational techniques or equipment in a simulation experience with the aim of promoting, improving or validating a participant's progression (MEAKIM et al., 2013).

The clinical simulation methodology can be divided into three moments: preparation phase (pre-briefing and briefing), scenario (or act of simulating) and debriefing, phase in which participants share their feelings and possible improvements to important points that happened during the scenario. With the end of the simulation, the participants do not practice the scenario again after receiving the feedback and the debriefing time ends up reducing the space for practice, being many times longer than the time allocated for the development of the scenario, important limitations for the validation of learning (SAWYER et al., 2016).

To conclude, it can be inferred that thinking about care from the perspective of the use of technology allows reflection on the inherent capacity of human beings to seek innovations capable of improving quality of life, well-being and personal satisfaction (ROCHA et al., 2008). Thus, in the context listed by this review, health education can contribute to transforming reality so that health professionals support families in child health promotion care practices, considering the characteristics of each culture, through actions based on the individual needs of each child. (FALKENBERG; MENDES; MARTIN; SOUZA, 2014).

FINAL CONSIDERATIONS

The performance of nurses in the care of children in the context of PHC unveils a wide range of possibilities, as well as reflects the complexity of the conducts developed by these professionals. Thus, the use of technologies meets amplified attention, as they contribute to the performance of actions based on up-to-date innovations, which can result in functionality and effectiveness for both professionals and family members who play the role of caregivers of these children.

In recent years, more precisely from 2021 onwards, there has been a decrease in these studies, although it is understood that they may not yet be publicly available for research. From this perspective, it is considered that the trend of Brazilian theses and dissertations produced by nurses is moving towards the construction of digital technologies. But this development is happening gradually, according to the specificities and needs of the target audience, paying attention to the context in which they are inactive and their possibilities of using technologies.

It is important that new technologies continue to be developed, with a specific look at children and their numerous and distinct particularities, fostering health education for their families, in favor of care that respects and is really aimed at minimizing care maladjustments for sick children or those with chronic health conditions, and also for health promotion and disease prevention for those who need routine care.

REFERENCES

1. Abreu, F. R. H. (2019). *Desenvolvimento de tecnologia de apoio a consulta de enfermagem na puericultura* (Dissertação de Mestrado Profissional). Universidade de Fortaleza, Fortaleza.

2. Alexandre, N. M. C., & Coluci, M. Z. O. (2011). Validade de conteúdo nos processos de construção e adaptação de instrumentos de medidas. *Ciência & Saúde Coletiva, 16*(7), 3061-3068. https://doi.org/10.1590/S1413-81232011000800006

3. Almeida, S. L. P., et al. (2023). Guia para Sistematização da Assistência e Processo de Enfermagem: tecnologia educacional para a prática profissional. *Revista Brasileira de Enfermagem, 76*(4). Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10103638/pdf/0034-7167-reben-76-s4-e20210975.pdf

4. Alpirez, L. A. (2014). *Desenvolvimento e validação de um instrumento de avaliação do recém-nascido na primeira semana de saúde integral* (Dissertação de Mestrado). Universidade Federal do Amazonas.

5. Alves, G. G., & Aerts, D. (2011). As práticas educativas em saúde e a estratégia saúde da família. *Ciência & Saúde Coletiva, 16*(1), 319-325. http://www.scielo.br/scielo.php?pid=S1413-81232011000100034&script=sci_arttext

6. Amaral, T. B. (2016). As consequências sociais relacionadas ao aumento de pacientes com Doença Renal Crônica em Terapia Renal Substitutiva. *Caderno de Saúde e Desenvolvimento, 9*(5), 85-95.

7. Andrade, D. C. M. (2020). *Ebook como tecnologia educacional no ensino do cuidado seguro da criança com alergia à proteína do leite de vaca e demais alergias no ambiente escolar* (Dissertação de Mestrado). Universidade Federal Fluminense.

8. Araujo, A. T. (2024). *Imunização da criança com transtorno do espectro autista: material educativo para equipe de enfermagem* (Dissertação de Mestrado). Universidade Estadual do Oeste do Paraná.

9. Arksey, H., & O'Malley, L. (2005). Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology, 8*(1), 19-32.

10. Bandura, A. (1994). Self-efficacy. In V. S. Ramachaudran (Ed.), *Encyclopedia of human behavior* (2ª ed., pp. 71-81). Academic Press.

11. Barbosa, C. P. (2018). *Caderneta de saúde da criança no contexto da atenção básica: desenvolvimento e avaliação de software educativo* (Tese de Doutorado). Universidade Federal de Pernambuco.

12. Barra, D. C. C., et al. (2017). Métodos para desenvolvimento de aplicativos móveis em saúde. *Texto & Contexto Enfermagem, 26*(4). https://doi.org/10.1590/0104-07072017002260017

13. Bezerra, F. E. S. E. (2019). *Construção e validação de manual de cuidados à criança em ventilação mecânica domiciliar para enfermeiros da Atenção Primária à Saúde* (Dissertação de Mestrado Profissional). Universidade Estadual do Ceará, Fortaleza.

14. Botelho, L. L. R., Cunha, C. C. D. A., & Macedo, M. (2011). O método da revisão integrativa nos estudos organizacionais. *Gestão e Sociedade, 5*(1), 121-136. Disponível em: https://ges.face.ufmg.br/index.php/gestaoesociedade/article/view/1220

15. Brasil. (2004). *Agenda de compromissos para a saúde integral da criança e redução da mortalidade infantil*. Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Ações Programáticas Estratégicas. Disponível em: https://bvsms.saude.gov.br/bvs/publicacoes/agenda_compro_crianca.pdf

16. Brasil. (2000). Portaria GM n. 693 de 5 de julho de 2000. Norma de orientação para implantação do método Mãe Canguru. *Ministério da Saúde*. Disponível em: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2000/prt0693_05_07_2000.html

17. Brasil. (2011). Portaria nº 2.351 de 5 de outubro de 2011. Altera a Portaria nº 1.459/GM/MS, de 24 de junho de 2011, que institui, no âmbito do Sistema Único de Saúde (SUS), a Rede Cegonha. *Ministério da Saúde*. Disponível em: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2011/prt2351_05_10_2011.html

18. Brum, C. N., et al. (2016). Revisão narrativa da literatura: aspectos conceituais e metodológicos na construção do conhecimento da enfermagem. In M. R. Lacerda & R. G. S. Costenaro (Eds.), *Metodologias da pesquisa para a enfermagem e saúde: da teoria à prática* (pp. 123-142). Porto Alegre: Moriá Editora.

19. Caires, J. C. (2007). *Formação de multiplicadores: Orientações Pedagógicas*. Embrapa Tabuleiros Costeiros, Aracaju.

20. Cakmak, M., et al. (2018). Efeito de informações por meio de vídeo sobre a ansiedade e satisfação de pacientes submetidos à anestesia espinhal. *Brazilian Journal of Anesthesiology, 68*(3), 274-279. https://doi.org/10.1016/j.bjan.2018.01.001

21. Carvalho, B. M. (2021). *Aplicativo móvel sobre a primeira consulta de enfermagem ao recém-nascido na atenção básica: construção e validação* (Dissertação de Mestrado). Universidade de São Paulo, Escola de Enfermagem de Ribeirão Preto.

22. Castro, C. S. C. (2021). *Tecnologia para rastreamento precoce do autismo na consulta de enfermagem na atenção primária* (Dissertação de Mestrado Profissional). Universidade de Fortaleza.

23. Costa, C. I. A. (2023). *Validação de cartilhas educativas para familiares de crianças/adolescentes com leucemia para o cuidado domiciliar* (Dissertação de Mestrado). Universidade do Estado do Rio de Janeiro.

24. Cunha, A. G. A. (2014). *Infecções das vias aéreas superiores: construção e validação de tecnologia educacional com educadoras infantis* (Dissertação de Mestrado). Universidade Federal do Amazonas.

25. Dantas, C. N. (2016). *Software-Protótipo para o acompanhamento do crescimento e desenvolvimento infantil a partir da Classificação Internacional das Práticas de Enfermagem (CIPE)* (Dissertação de Mestrado). Universidade Federal do Rio Grande do Norte.

26. Domingos, C. S., et al. (2017). A aplicação do processo de enfermagem informatizado: revisão integrativa. *Revista Enfermería Global*(48), 620-636. Disponível em: https://scielo.isciii.es/pdf/eg/v16n48/pt_1695-6141-eg-16-48-00603.pdf

27. Errazuriz, G., et al. (2016). Características clínicas y manejo de lactantes menores de 1 año com sospecha de alergia a proteína de leche de vaca. *Revista Chilena de Pediatria, 87*(6), 449-454. http://dx.doi.org/10.1016/j.rchipe.2016.06.007

28. Falkenberg, M. B., et al. (2014). Educação em saúde e educação na saúde: conceitos e implicações para a saúde coletiva. *Ciência & Saúde Coletiva, 19*(3), 847-852. https://doi.org/10.1590/1413-81232014193.01572013

29. Ferreira, F. M. S., et al. (2023). Vacinação infantil em infográfico animado: tecnologia para a educação permanente sobre processo de enfermagem. *Revista da Escola de Enfermagem da USP, 57*, e20220423. Disponível em: https://www.scielo.br/j/reeusp/a/Q8FM39Tn7dNqFhYhq5Cwngn/?format=pdf&lang=p

30. Ferreira, L. S. (2020). *Construção e validação de conteúdo e semântica da escala de percepção de autoeficácia da família no cuidado domiciliar da criança em diálise peritoneal* (Dissertação de Mestrado). Universidade Federal de Mato Grosso do Sul.

31. Freitas, O. (2009). *Equipamentos e materiais didáticos*. Universidade de Brasília.

32. Gaíva, M. A., Alves, M. D., & Monteschio, C. A. (2019). Nursing appointments in puericulture in family health strategy. *Revista Sociedade Brasileira de Enfermagem Pediátrica, 19*(2), 65-73. Disponível em: https://journal.sobep.org.br/wp-content/uploads/articles_xml/2238-202X-sobep-19-2-0065/2238-202X-sobep-19-2-0065.x60241.pdf

33. Hunt, E. A., et al. (2014). Pediatric resident resuscitation skills improve after "rapid 96 cycle deliberate practice" training. *Resuscitation, 85*(7), 945-951. https://doi.org/10.1016/j.resuscitation.2014.02.025

34. Joanna Briggs Institute (JBI). (2015). *The Joanna Briggs Institute reviewers' manual 2015: Methodology for JBI scoping reviews*. Disponível em: http://joannabriggs.org/assets/docs/sumari/Reviewers-Manual_Methodology-for-JBI-Scoping--Reviews_2015_v2.pdf

35. Jorge, M. S. B., & Pedrosa, K. A. (2020). Cartilhas em cuidados e promoção da saúde mental na pandemia da COVID-19 como ferramenta da educação em saúde: revisão de escopo. *Revista Pesquisa, Sociedade e Desenvolvimento, 27*(7). Disponível em: https://rsdjournal.org/index.php/rsd/article/view/30256/26154

36. Lemos, R. A. (2016). *Promoção do desenvolvimento funcional de crianças nascidas prematuras: organização das bases teóricas e operacionais e construção de um guia de apoio à família* (Dissertação de Mestrado). Universidade de São Paulo.

37. Levac, D., Colquhoun, H., & O'Brien, K. K. (2010). Scoping studies: advancing the methodology. *Implementation Science, 5*(69). https://doi.org/10.1186/1748-5908-5-69

38. Lima, A. P. (2018). *Alta Responsável: Tecnologia Educacional para Pacientes e Cuidadores* (Dissertação de Mestrado Profissional). Universidade Federal do Paraná.

39. Lima, C. M. de, et al. (2021). Cuidados à criança com Transtorno do Espectro Autista: uma revisão narrativa. *Revista Internacional de Apoyo a la Inclusión, Logopedia, Sociedad y Multiculturalidad, 7*(2), 63-73. https://doi.org/10.17561/riai.v7.n2.6305

40. Lomba, L., et al. (2014). Impacto da diálise peritoneal na família com doença renal crônica: revisão integrativa da literatura. *Revista de Enfermagem Referência, 6*(3), 139-148. Disponível em: https://www.redalyc.org/articulo.oa?id=388239973013

41. Luz, R. R. (2022). *Tecnologia para orientação de familiar/cuidador de crianças submetidas a procedimentos cirúrgicos* (Dissertação de Mestrado). Universidade Federal do Paraná.

42. Magalhães, V. M. P. C. (2018). *Construção e validação de uma escala de autoeficácia materna na alimentação do lactente* (Dissertação de Mestrado). Universidade Federal de Pernambuco.

43. Más, M. F. F. (2015). *Prevenção do excesso de peso infantil na Atenção Básica: construção e validação de um álbum seriado* (Dissertação de Mestrado Profissional). Universidade de São Paulo.

44. Masetto, M. T. (2010). *O Professor na Hora da Verdade* (1ª ed.). São Paulo: Avercamp.

45. Meakim, C., et al. (2013). Standards of Best Practice: Simulation Standard I: Terminology. *Clinical Simulation in Nursing, 9*(6), s3-s11.

46. Miranda, P. S. (2022). *Elaboração e validação de vídeos sobre primeiros socorros: produção baseada na demanda de saber de professores e funcionários da educação infantil* (Dissertação de Mestrado). Universidade Federal Fluminense.

47. Moura, T. H. M. (2015). *Adaptação transcultural da self-efficacy in infant care scale para o Brasil e validação de conteúdo da versão brasileira* (Dissertação de Mestrado). Universidade Federal de Pernambuco.

48. Muniz, V. de O., Mota, T. N., & Sousa, A. R. (2023). Saúde Digital à Brasileira e a Prática Clínica em Enfermagem: Do Que Estamos Falando? *Enfermagem em Foco, 14*. Disponível em: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1435523

49. Nietsche, E. A., Teixeira, E., & Medeiros, H. P. (2014). *Tecnologias cuidativo-educacionais: uma possibilidade para o empoderamento do/a enfermeiro/a?* Porto Alegre: Moriá.

50. Oliveira, G. T. P. (2019). *Primeira visita domiciliar ao recém-nascido: produção de tecnologia assistencial* (Dissertação de Mestrado). Universidade Federal do Paraná.

51. Pereira, I. C. (2023). *Elaboração de uma cartilha para cuidadores de pacientes pediátricos traqueostomizados na Amazônia Ocidental brasileira: estudo metodológico* (Dissertação de Mestrado). Universidade Federal Fluminense.

52. Piffero, E. L. F., et al. (2020). Metodologias ativas e o ensino de Biologia: desafios e possibilidades no novo ensino médio. *Ensino e Pesquisa, 18*(2), 48-63. Disponível em: https://periodicos.unespar.edu.br/index.php/ensinoepesquisa/article/view/3568/pdf_1

53. Pissaia, L. F., et al. (2017). Tecnologia educacional no processo de formação de enfermeiros. *Cinergis, 18*(3), 185-189. https://doi.org/10.17058/cinergis.v18i3.8865

54. Polit, D. F., & Beck, C. T. (2018). *Fundamentos de pesquisa em enfermagem: avaliação de evidências para prática de enfermagem* (9ª ed.). Porto Alegre: Artemd.

55. Rababah, J. A., Mohammed, M. A. H., & Wafa'a, F. T. (2021). A study of the relationship between nurses' experience, structural empowerment, and attitudes toward computer use. *International Journal of Nursing Sciences, 8*(4), 439-443. https://www.sciencedirect.com/science/article/pii/S235201322100096X?via%3Dihub

56. Ribeiro, P. L. (2019). *Tecnologia educativa para aprendizagem da Fisiologia da Lactação: criação e validação do conteúdo visual* (Dissertação de Mestrado). Universidade Federal de Santa Maria.

57. Rocha, N. L. (2022). *Renal Ped: protótipo de serious game para criança em diálise peritoneal* (Dissertação de Mestrado). Universidade de São Paulo.

58. Rocha, P. K., et al. (2008). Cuidado e tecnologia: aproximações através do Modelo de Cuidado. *Revista Brasileira de Enfermagem, 61*(1). https://doi.org/10.1590/S0034-71672008000100018

59. Rojas, A. P. K., et al. (2016). Tecnologias Disponíveis para acompanhamento do Desenvolvimento Infantil pelo Enfermeiro: Revisão Integrativa da Literatura. *Cadernos da Escola de Saúde, 1*(15), 64-80. Disponível em: https://portaldeperiodicos.unibrasil.com.br/index.php/cadernossaude/article/view/2455

60. Ronquillo, C. E., et al. (2021). Artificial intelligence in nursing: Priorities and opportunities from an international think-tank of the nursing and artificial intelligence leadership collaborative. *Journal of Advanced Nursing, 77*, 3707-3717. Disponível em: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jan.14855?src=getftr

61. Rother, E. T. (2007). Revisão sistemática X revisão narrativa. *Acta Paulista de Enfermagem, 20*(2), v-vi. https://doi.org/10.1590/S0103-21002007000200001

62. Saarinen, K. M., et al. (1999). Alimentação complementar em maternidades e o risco de alergia ao leite de vaca: um estudo prospectivo com 6209 bebês. *Jornal de Alergia e Imunologia Clínica, 2*(104), 457-461.

63. Santos, L. C., et al. (2014). Percepção das mães de prematuros sobre a visita domiciliar antes e após a alta hospitalar. *Investigação Educacional em Enfermagem*, Londrina. http://www.scielo.org.co/scielo.php?pid=S012053072014000300004&script=sci_arttext&tlng=pt Acesso em: 03 jun. 2024.

64. Santos, M. N., et al. (2021). Vivências de enfermeiros na consulta de puericultura: percepção sobre os sinais de risco/atraso para o desenvolvimento infantil. *Revista Uruguaya de Enfermería*, 16(1). https://rue.fenf.edu.uy/index.php/rue/article/view/302/338 Acesso em: 27 mai. 2024.

65. Salbego, C., et al. (2018). Care-educational technologies: an emerging concept of the praxis of nurses in a hospital context. *Revista Brasileira de Enfermagem*, 71(Supl 6), 2666-74. https://www.scielo.br/j/reben/a/zPJy9NvkcDJVw9Jr7ZKhNQs/ Acesso em: 24 mai. 2024.

66. Salbego, C. (2016). Tecnologias cuidativo-educacionais: a práxis de enfermeiros em um hospital universitário [Dissertação]. Universidade Federal de Santa Maria. http://coral.ufsm.br/ppgenf/images/Dissertacoes_alunos/Dissertacao_Cleton_Salbego.pdf Acesso em: 30 mai. 2024.

67. Schmidt, A., & Pazin-Filho, A. (2007). Recursos visuais. *Medicina*, 40(1), 32-41.

68. Silva, F. P. M. A. (2022). Simulação clínica no preparo de familiares de crianças com traqueostomia em processo de alta hospitalar [Dissertação]. Mestrado Profissional em Enfermagem Assistencial, Universidade Federal Fluminense.

69. Silva, M. M., et al. (2020). Atuação do enfermeiro na consulta de puericultura. *Brazilian Journal of Surgery and Clinical Research*, 32(2), 175-179. https://www.mastereditora.com.br/periodico/20201004_092943.pdf Acesso em: 27 mai. 2024.

70. Silva, R. D. M. (2015). Construção e validação de brinquedo e história para o cuidado à criança submetida a cateterismo cardíaco em sessão de brinquedo terapêutico [Dissertação]. Programa de Pós-Graduação em Enfermagem, Centro de Ciências da Saúde, Universidade Federal de Pernambuco.

71. Sawyer, T., et al. (2016). More than one way to debrief: A critical review of healthcare simulation debriefing methods. *Simulation in Healthcare*, 11(3), 209-217.

72. Silva, S. F. (2021). Construção e validação de instrumento de sistematização da assistência de enfermagem à criança com alergia a proteína do leite de vaca [Dissertação]. Mestrado Profissional em Tecnologia e Inovação em Enfermagem, Universidade de Fortaleza.

73. Sousa, S. M. (2020). Construção e validação de cartilha educativa para o manejo e condução de criança com sequelas neurológicas causadas pelo câncer [Dissertação]. Mestrado Profissional em Gestão em Saúde, Programa de Pós-Graduação em Saúde Coletiva, Centro de Ciências da Saúde, Universidade Estadual do Ceará.

74. Souza, M. T. D., Silva, M. D. D., & Carvalho, R. D. (2010). Revisão integrativa: o que é e como fazer. *Einstein (São Paulo)*, 8(1).

75. Teixeira, L. F. S., Rodrigues, I. L. A., & Nogueira, L. M. V. (2021). Tecnologia educativa sobre concepção oral: construção compartilhada com enfermeiras assistência reprodutiva. *Revista Brasileira de Enfermagem*, 75(5). https://www.researchgate.net/publication/330139910_Educational_technology_on_oral_contraception_construction_shared_with_nurses_reproductive_assistance_Tecnologia_educacional_sobre_contracepcao_oral_construcao_compartilhada_com_enfermeiros_da_assisten Acesso em: 23 mai. 2024.

76. Tenório, A. P. S. (2016). Construção e validação de um website sobre cuidados com o prematuro [Dissertação]. Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Centro de Ciências da Saúde, Universidade Federal de Pernambuco.

77. Vasconcelos, V. M., et al. (2012). Puericultura em enfermagem e educação em saúde: percepção de mães na estratégia saúde da família. *Esc Anna Nery*, 16(2), 326-331. https://doi.org/10.1590/S1414-81452012000200017 Acesso em: 02 jun. 2024.

78. Vasques, M. C. M. Z. (2020). Construção e validação de livreto educativo lúdico para realização da visita pré-operatória de enfermagem [Dissertação]. Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Medicina de Botucatu.

79. Wegner, W., et al. (2017). Segurança do paciente no cuidado à criança hospitalizada: evidências para enfermagem pediátrica. *Revista Gaúcha de Enfermagem*, 38, e68020. https://doi.org/10.1590/1983-1447.2017.01.68020 Acesso em: 04 jun. 2024.

80. Weissheimer, G., et al. (2021). Informational support for families of children with autism spectrum disorder. *Revista Gaúcha de Enfermagem*, 42. https://www.scielo.br/j/reben/a/VgmBNksLCTLNxs4cFzcf54r/?format=pdf&lang=pt Acesso em: 04 jun. 2024.

81. Whittemore, R., & Knafl, K. (2005). The integrative review: updated methodology. *Journal of Advanced Nursing*, 52(5), 546-553. https://doi.org/10.1111/j.1365-2648.2005.03621.x Acesso em: 04 jun. 2024.

82. Wightman, A., et al. (2019). Caregiver experience in pediatric dialysis. *Pediatrics*, 143(2), e20182102. https://doi.org/10.1542/peds.2018-2102 Acesso em: 04 jun. 2024.

83. Zavaleta-Ramírez, P., et al. (2014). Confiabilidad interevaluador del K-SADS-PL-2009 / trastornos del espectro autista (TEA). *Salud Mental*, 37(6), 461-466. https://www.researchgate.net/publication/305864645_Confiabilidad_interevaluador_del_KSADS-PL-2009trastornos_del_espectro_autista_TEA Acesso em: 24 mai. 2024.

CHANGES IN HAEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN PATIENTS DUE TO LONG-TERM USE OF OMEPRAZOLE

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Mariana Gomes Vidal Sampaio[1], Andreina Barros dos Santos[2], Arysa Dias Pereira de Melo[3], Lívia Carla Veríssimo Souza[4], Mylene Teles de Lima[5], Maria Ysabell Nascimento Alberto[6] and Teresa Dávila Cruz Matias[7]

ABSTRACT

Introduction: Omeprazole (OMZ) is the most frequently used PPI in conditions of Gastroesophageal Reflux Disease (GERD), gastric/duodenal ulcer, erosive esophagitis, H. pylori infection, in addition to being prescribed as a gastric protector in case of use of Non-Steroidal Anti-inflammatory Drugs (NSAIDs) (Sambugaro et al., 2021). Drugs of this class are often well tolerated, their adverse effects are usually manifested with the prolonged use of PPIs (Haastrup et al., 2018). Biochemical alterations may occur, such as hypocalcemia, hypokalemia, hypomagnesemia (Isse; Hashimoto, 2020). Methodology: For the construction of the present research, a systematic review of the qualitative literature was carried out. In this review study, in the search phase, the search was carried out in journal articles, books and dissertations. Results and discussion: According to the study carried out, the prolonged use of omeprazole can generate a series of complications, among them we can mention the decrease in the absorption of vitamin B12, important for hormonal development and for the formation of red blood cells (red blood cells), and iron deficiency, as its use affects the intestinal absorption capacity of micro-elementary nutrients. In addition to affecting the absorption of vitamins and minerals, prolonged use of omeprazole can cause hematological changes such as MCV (Mean Corpuscular Volume), HCM (Mean Corpuscular Hemoglobin) and MCHC (Mean Corpuscular Hemoglobin Concentration). Conclusion: Taking into account the preference for the use of omeprazole as a proton pump inhibitor in the treatment of acid-peptic disorders, attention should be paid to the harm caused by the prolonged use of this drug.

[1] Doctor in Biological Sciences
Institution: University center Paraíso - (UniFAP)
E-mail: mariana.sampaio@fapce.edu.br
[2] Pharmacy student
Institution: University center Paraíso - (UniFAP)
Email: andreinabarros.m@gmail.com
[3] Pharmacy student
Institution: University center Paraíso - (UniFAP)
Email: arysadiias97@gmail.com
[4] Pharmacy student
Institution: University center Paraíso - (UniFAP)
E-mail: liviacarla015@gmail.com
[5] Pharmacy student
Institution: University center Paraíso - (UniFAP)
E-mail: myleneteles@aluno.fapce.edu.br
[6] Pharmacy student
Institution: University center Paraíso - (UniFAP)
Email: mariaysabell@aluno.fapce.edu.br
[7] Pharmacy student
Institution: University center Paraíso - (UniFAP)
Email: teresadavilacm@aluno.fapce.edu.br

Keywords: Omeprazole. Hematological alterations. Biochemical changes.

INTRODUCTION

The gastrointestinal tract is made up of a set of organs (mouth, pharynx, esophagus, stomach, small intestine, large intestine, rectum and anus) that have the function of promoting the digestion of food, in order to absorb nutrients, such as water, macronutrients, micronutrients and electrolytes, necessary for the full functioning of the body, from the conversion of food into absorbable molecules (Tortora; Derrickson, 2017).

The stomach is a fundamental organ for the functioning of the digestive system. It is composed of four regions (cardia, gastric fundus, gastric body and pylorus), and has gastric glands that help its performance. Peristalsis waves favor the digestion of food in smaller sizes, contributing to the process of digestion and stomach absorption (Tortora; Derrickson, 2017).

The gastric glands, responsible for releasing substances that make up gastric juice, are composed of 3 types of cells: mucous cells of the colon, main and parietal. The mucous cells of the cervix secrete mucus, the main cells secrete gastric lipase and pepsinogen, and the parietal cells produce hydrochloric acid, which transforms pepsinogen into pepsin, the enzyme responsible for the digestion of proteins (Tortora; Derrickson, 2017).

The use of Proton Pump Inhibitors are effective and allow for prolonged therapy, however, users are not exempt from adverse effects over time; calcium deficiency is an adverse effect due to the ability of this class to reduce calcium absorption. Omeprazole (OMZ) is the most frequently used PPI in conditions of Gastroesophageal Reflux Disease (GERD), gastric/duodenal ulcer, erosive esophagitis, *H. pylori infection*, in addition to being prescribed as a gastric protector in case of use of Non-Steroidal Anti-inflammatory Drugs (NSAIDs) (Sambugaro et al., 2021).

Drugs of this class are often well tolerated, their adverse effects are usually manifested with the prolonged use of PPIs, such as the appearance of enteric infections, due to their mechanism of action resulting in hypochlorhydria, which is summarized in a reduction of hydrochloric acid, favoring bacterial colonization; another adverse effect related to hypochlorhydria is its interference in the ionization of calcium that facilitates its absorption, as a consequence of this process hypocalcemia arises, which favors the emergence of other diseases, such as osteoporosis (Haastrup et al., 2018).

Therefore, since the prolonged use of omeprazole results in biochemical alterations, it is necessary to evaluate these parameters in patients with prolonged use of this proton pump inhibitor, because commonly, in this context, biomarkers undergo alterations, such as hypocalcemia, hypokalemia, hypomagnesemia, respectively, reduction of serum calcium

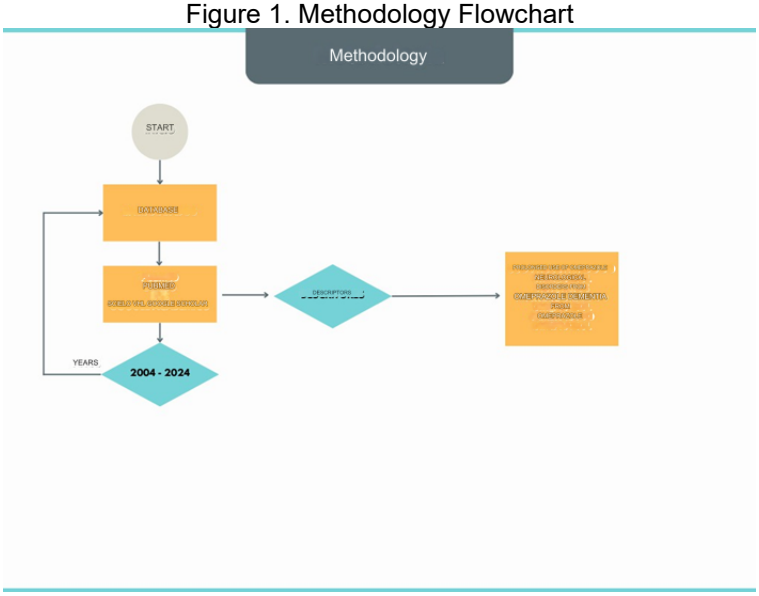
levels, reduction of potassium levels and below-normal levels of magnesium value (Isse; Hashimoto, 2020).

METHODOLOGY

The present work is a systematic review of the qualitative literature. In this review study, in the search for literature, the search was carried out in journal articles, books and dissertations. In this phase, we used descriptors such as "omeprazole", "neurological disorders", "dementia", "PPIs", correlating through the Boolean operator AND. For this, the search engines VHL (Virtual Health Library), Scielo (Scientific Electronic Library Online); PubMed (U.S. National Library of Medicine) and Google Scholar.

Publications between the years 2004 and 2024, articles in English, Portuguese, and Spanish, which directly addressed the mentioned descriptors, and to direct the search, the filter for articles with full and free texts was added. As an exclusion criterion, we eliminated articles that analyzed the theme from another perspective, prior to 2004 and duplicate articles among the databases, totaling 34 articles used for this review.

Figure 1. Methodology Flowchart



Source: The author.

THEORETICAL FRAMEWORK

DRUGS USED IN THE TREATMENT OF ACID-PEPTIC DISORDERS

Disturbances in the secretion of gastric acid or in the action of this compound on the mucosa of the gastrointestinal tract are related to several diseases and aggravations, such as gastric or duodenal ulcers, gastritis, and gastroesophageal reflux disease. Depending on the symptoms, treatment is carried out with proton pump inhibitors or H2 receptor

antagonists. In cases with mild to moderate symptoms, antacids may be used in addition to treatment with antisecretors. They are also used for the treatment of gastric heartburn, a sensation of heat or burning in the stomach (Ministry of Health, 2023).

Gastroesophageal reflux disease (GERD) is a chronic disorder that significantly affects quality of life, requiring effective treatment to relieve symptoms. The first-line drugs are proton pump inhibitors (PPIs), which act by inhibiting gastric acid secretion and increasing intragastric pH. Esomeprazole, the S-isomer of omeprazole, may demonstrate better results compared to other PPIs, as it has a longer half-life, which results in higher plasma concentrations (Lim, 2023).

The global prevalence of heartburn and reflux in adolescents and adults is about 15%. Proton Pump Inhibitors are the standard treatment for patients with persistent heartburn and reflux. They have better symptom control and mucosal healing compared to histamine-2 receptor antagonists (H2RAs). Refractory GERD occurs in patients who have persistent symptoms despite twice-daily PPI administration. In this case, it is indicated to add an H2RA, such as famotidine, as needed before bedtime for patients with nocturnal symptoms (Provenza, 2024).

Children and infants have a relatively high prevalence of gastroesophageal reflux. The most effective therapies are proton pump inhibitors (omeprazole, esomeprazole, pantoprazole, lansoprazole, dexlansoprazole, and rabeprazole), with only esomeprazole approved for use in neonates, pantoprazole can only be used in children >5 years of age, and the other four PPIs in children >1 year of age; and H2 receptor antagonists (ranitidine and famotidine/cimetidine), which are approved for use in children aged ≥1 month and ≥1 year, respectively (Masarwa, 2024).

Proton pump inhibitors (PPIs), such as omeprazole, are widely used in gastrointestinal disorders, such as: ulcers with or without *Helicobacter pylori infection;* prevention of peptic ulcers in patients receiving nonsteroidal inflammatory agents (NSAIDs), treatment of gastroesophageal reflux, Zollinger-Ellison disease, dyspepsia, esophagitis, and gastritis (Forgerini, 2018).

Peptic ulcer disease is the most common cause of intestinal bleeding, accounting for about 50% of episodes. Since gastric acid contributes to the hemorrhagic effect by promoting clot lysis, the use of PPIs is favorable in these cases, as it reduces the risk of recurrent bleeding, in view of the suppressive action on acid secretion (Zhang, 2021).

Proton pump inibiter drugs

The proton pump is responsible for maintaining stomach acidity, which happens by the exchange of hydrogen (H+) and potassium (K+) in an energetic process with the use of ATP. PPIs block the action of the enzyme in the exchange of protons, which confers an increase in the pH of the gastric juice, inhibiting the production of hydrochloric acid. Irreversible inhibition of the enzyme occurs by connecting to the receptor by covalent bonding, ensuring an action of 24 hours to 48 hours (time for the synthesis of a new enzyme to occur) (Morschel et al., 2018).

Within this class, the most commonly used omeprazole (OMZ) stands out among its peers, such as: esomeprazole, lansoprazole, pantoprazole, rabeprazole, with dexlansoprazole being the most recent. They are available in the pharmaceutical market and are known for their metabolism carried out by the isoenzyme CYP2C19 (Picoli et al., 2018).

Omeprazole (OMZ) is the main representative of the class of proton pump inhibitors, in clinical use it is part of the treatment for patients with ulcers, usually duodenal or gastric, such as peptic disease, those that arise from *Helicobacter pylori* infection or from the prolonged use of non-steroidal anti-inflammatory drugs. An ASTRONAUT study, carried out with 541 patients with erosions and ulcers, under drug therapy, obtained healing results of these lesions after eight weeks, and 80% healed with the dose of omeprazole 20mg/day (Wannmacher, 2004).

Two endocrine cells are important for the maintenance of gastric acid secretion, G and D cells. Therapy using PPIs contributes to an increase in serum gastrin levels, due to the emergence of acid inhibition and an increase in gastrin (which is produced by G cells), this alteration deregulates the mechanism for the synthesis of hydrochloric acid. Increased gastrin levels are usually higher in PPI users for more than 3 years (Camilo et al., 2020).

According to Chinzon et al (2022), PPIs are (in their chronic use) drugs that strongly interfere with calcium absorption, this is due to the fact that this class acts on its mechanism of action, raising gastric pH, this interference is due to the fact that salts are insoluble at basic pH, this relationship favors bone mining density (Chinzon et al., 2022).

PPIs have similar efficacy, but the levels of improvement in the condition of some pathologies change from drug to drug of this class, pantoprazole, for example, has greater efficacy after 8 weeks of treatment to treat duodenal ulcer, reflux esophagitis (obtaining the highest percentage of efficacy), with about 90-96% (Costa et al., 2023).

Pantoprazole in association with antibiotic therapy, as an adjuvant in the prevention of symptoms in relation to *Helicobacter pylori* infection, can reach 100% efficacy, which

suggests that it is an ideal adjuvant of choice to accompany its eradication, in the same sense, in second place of efficacy with 90% is esomeprazole, followed by rabeprazole (77%) and omeprazole in last place with 75%. Pharmacokinetic processes are related to the efficacy of PPIs (Costa et al., 2023).

CONSEQUENCES OF LONG-TERM USE OF PROTON PUMP INHIBITORS

Long-term use of proton pump inhibitors has been associated with adverse consequences, including chronic kidney injury, acute kidney injury, acute interstitial nephritis, hypomagnesemia, *Clostridium difficile* infection, community-acquired pneumonia, bone fracture, and increased risks of developing and dying gastric cancer (Yang et al., 2020).

Several studies have suggested an association between long-term use of proton pump inhibitors (PPIs) and potential adverse effects, including iron and vitamin B12 deficiency, hypomagnesemia, risk of bone fracture, particularly hip fracture, *Clostridium difficile* infections, cognitive impairment, and dementia in elderly patients (Mumtaz, et al 2022).

PPIs are often prescribed to people who have already received other medications, and while considered safe, several concerns have been raised about their safety in long-term use (Cena et al., 2020).

According to numerous studies, PPIs have been linked to hyperprolactinemia, which can lead to a variety of sexual and reproductive problems (Ashfaq, et al 2022).

Other studies have commented that PPIs can substantially affect sperm quality parameters, including sperm count, sperm motility, sperm viability, and capacitation, which can lead to male infertility (Mumtaz et al., 2022).

Although serious side effects are very rare, they include liver problems, joint pain due to subacute cutaneous lupus erythematosus due to prolonged use, and allergic reaction (Hadeel et al., 2022).

PPI users tend to have a less healthy gut microbiota than non-users, with a significant increase in *Enterococcus*, *Streptococcus*, *Staphylococcus,* and *Escherichia coli* (Yang et al., 2020).

The change in gastric acidity can also affect the intestinal absorption capacity of micro elemental nutrients in a way that can result in iron deficiency and decreased concentration of zinc, selenium and copper (Hadeel et al., 2022).

In view of this, we postulate that chronic PPI use can lead to the accumulation of unhealthy gut microflora and disrupt the normal functions of the gallbladder and bile ducts, inducing biliary tract diseases (Yang et al., 2020).

Other signs of long-term use may include a decrease in blood magnesium levels after taking omeprazole for more than 3 months. (Hadeel et al., 2022).

Dementia and Other Neurological Disorders Associated with Long-Term Use of Omeprazole

Proton pump inhibitors (PPIs) are widely recognized as one of the most commonly prescribed classes of drugs globally for the control of stomach acidity. These medications play a crucial role in managing conditions associated with excess stomach acid, such as gastritis, gastric ulcers, and reflux esophagitis. Among the various drugs available within this class, omeprazole stands out for its remarkable effectiveness. This drug is able to reduce stomach acid production by up to 95%, offering significant relief from symptoms related to hyperacidity and promoting the healing of gastric and esophageal lesions (Hoefler et al., 2009).

Long-term use can lead to the occurrence of adverse reactions of concern and unknown to the majority of the population. For example, use for a period equal to or greater than 2 years can lead to a decrease in the absorption of vitamin B12, an important vitamin for hormonal development and for the formation of red blood cells (red blood cells). Clinically, the effects caused by vitamin B12 deficiency can manifest as dementia, neurological problems, anemia and other complications, sometimes irreversible (Santos, 2016).

The prolonged use of omeprazole by the elderly impairs the absorption of essential vitamins for its nutrition, as the elderly have a slightly deficient immune system, the absence of these vitamins increases the possibility of the emergence of serious diseases, such as dementia and Alzheimer's (Liotti et al., 2015).

In this sense, it is possible to perceive an important contraindication regarding the prolonged use of Omeprazole by the elderly, since it may end up contributing to the advancement or aggravation of a series of complications that already exist or that at least it is already a predetermination, requiring constant care and adequate medical follow-up in order not to aggravate already complicated conditions (Liotti et al, 2015).

In addition, long-term use of omeprazole can lead to significant complications, including severe changes in the balance of electrolytes in the body, particularly hypomagnesemia. This condition, characterized by low levels of magnesium in the blood,

may, in some cases, not have evident symptoms. However, in more severe situations, it can result in a variety of clinical symptoms. Among them are episodes of vomiting, diarrhea, and, in more severe cases, neuromuscular symptoms such as tetany — a condition marked by involuntary muscle spasms and pain (Miyares et al., 2020).

Magnesium is the most abundant divalent cation in the human body. Approximately 60% of magnesium is stored in bones, 38% intracellularly in soft tissues, and approximately only 2% in extracellular fluid, including plasma (Huang et al., 2007). Hypomagnesemia can result in neurological signs and symptoms including lethargy, tremors, confusion, fasciculation, tetany, ataxia, and tremors (Ghosh et al., 2008).

Acidic gastric secretion is necessary for the absorption of vitamin B12 from food. Vitamin B12 is an essential nutrient that needs to be acquired from the diet, it is present in protein-bound foods and the presence of gastric acid is necessary for pancreatic proteases to separate vitamin B12 from proteins, allowing its association with intrinsic factor (IF) and absorption in the terminal ileum (Mccoll, 2009).

Vitamin B12 deficiency can cause neurological diseases, including neuropathy, spinal cord degeneration, gait disorders leading to falls, depression, and dementia, which if diagnosed in time are reversible (Werder, 2010).

Although there is an association between the use of Omeprazole and the risk of dementia, especially Alzheimer's, although the mechanism responsible for its development is not fully understood, prolonged hypochlorhydria seems to potentiate cognitive decline, as well as the increase in β-amyloid levels in the brain, after PPI crosses the blood-brain barrier, leading to degradation and promotion of the formation of anomalous aggregates of TAU protein, abundant proteins in the central nervous system (Viegas; Nabais, 2017).

CHANGES IN LABORATORY TESTS OF PATIENTS UNDERGOING PROLONGED USE OF OMEPRAZOLE

The blood count is one of the most requested laboratory tests by health professionals. This, in turn, evaluates the individual's health in general, providing important information that can help diagnose pathologies such as leukemias, infectious processes, and several other hematological disorders such as anemia, thalassemias, and polycythemias (Rosenfeld et al., 2019).

Studies show that the prolonged use of omeprazole can cause changes in hematimetric indices such as MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Hemoglobin) and MCHC (Mean Corpuscular Hemoglobin Concentration) and in biochemical

parameters, for example the dosage of vitamin B12, Vitamin D and Calcium (Ricardo et al., 2023).

Vitamin B12 is a water-soluble micronutrient, acquired exogenously in foods of animal origin. Its deficiency is common among the elderly, vegetarians, and individuals who adopt a low protein diet or have gastrointestinal absorption problems. In addition, the deficiency may be due to prolonged use of omeprazole. In this way, its deficiency can harm the hematopoietic and nervous system, interfering with the development of cell maturation, which leads to cell lysis. Thus, they can lead to pathological conditions, such as megaloblastic anemia and lesions in the nervous system (Haefliger et al., 2021).

According to Ricardo et al. (2023), the prolonged use of omeprazole may be related to the occurrence of megaloblastic anemia, which leads to reduced absorption of calcium, vitamin B12, and vitamin D. Vitamin B12 is part of the production of blood cells and acts in the synthesis of deoxyribonucleic acid (DNA), which is the genetic material of cells. Therefore, vitamin B12 deficiency causes a delay in the maturation process of the nucleus of cells and results in a lower number of erythrocytes. Consequently, it causes the appearance of abnormally large cells, leading to a condition called megaloblastic anemia.

In addition to vitamin B12, calcium as a fundamental nutrient for the body, also suffers a reduction in absorption with prolonged use of omeprazole. Calcium is an essential mineral for the mineralization of bones and teeth and for the regulation of intracellular events in various tissues (Natasha et al. 2018).

In view of the pointing out of studies on the reduction of nutrients and vitamins due to the prolonged use of omeprazole, it is important to correlate and show the importance of performing laboratory tests to assess people's health, since they provide data and information that allow diagnoses, prognosis, and the characterization of risks for various pathologies (Ricardo et al. 2023).

RESULTS AND DISCUSSION

A study carried out by Oliveira et al. (2019) states that the continuous use of omeprazole, the proton pump inhibitor (PPI), reduces the absorption of vitamin B12 in the body, given that this drug raises stomach pH and interferes with the absorption process, causing a shortage of this nutrient.

Ferreira (n.d.) mentions that the administration of omeprazole is recommended one hour before or two hours after the diets of elderly patients with foods rich in Vitamin B12 (such as meat, chicken and milk), since when administered near or during meals, its absorption is reduced, prevailing the risks of dementia and megaloblastic anemia.

Hipólito et al. (2016) report in their study that patients aged between 60 years and over are the ones who most use omeprazole, due to the high use of drugs with age, increased morbidity and life expectancy, intensifying the use of health services in this population.

Table 1. Profile data of patients who take omeprazole for a long time.

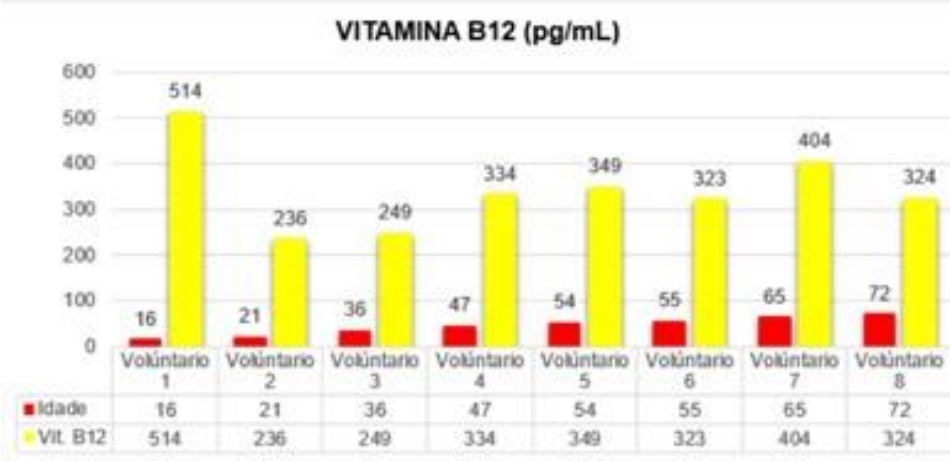
Dados	Voluntário 1	Voluntário 2	Voluntário 3	Voluntário 4	Voluntário 5	Voluntário 6	Voluntário 7	Voluntário 8
Idade	65 anos	74 anos	21 anos	16 anos	36 anos	47 anos	54 anos	54 anos
Sexo	Feminino	Feminino	Feminino	Feminino	Feminino	Feminino	Masculino	Feminino
Escolaridade	Fundamental Incompleto	Fundamental Incompleto	Ensino Médio Completo	Ensino Médio cursando	Superior Completo	Fundamental Incompleto	Ensino médio Completo	Ensino Fundamental Incompleto
Ocupação	Pensionista	Aposentada	Gerente	Estudante	Professora	Dona de casa	Auxílio Doença	Dona de casa
Tempo de uso do omeprazol e posologia	5 anos. 1 comp. 20mg	15 anos. 2 comp. por dia manhã e noite de 40 mg	4 anos. 1 comp. /dia de 20 mg	2 meses 1 comp. de manhã em jejum	10 anos. 1 comp. manhã/ noite 20mg	10 anos. 1 comp./ dia 20 mg	3 anos. 2 comp. /dia 40 mg	5 anos. 3 comp. /dia de 20 mg
Motivo	Gastrite	Gastrite, esofagite e úlcera	Esofagite erosiva grau A, pangastrite	Dor no estômago	Refluxo e hérnia de hiato no esôfago	Gastrite crônica devido aos outros medicamentos	Úlcera e *H. pilory* duodenal	Para poder tomar os outros medicamentos
Outros medicamentos	Losartana 50mg	Rivotril, Losartana, Citalopram	Cloridrato de Fluoxetina	Buscopan e ansiedade	Losartana potássica 50 mg	Danazol, Fluoxetina, Icatibanto e Firazyr (quando crise)	Nilotinibe	Losartana 50 mg, Glibenclamida 5 mg, Metformina 850 mg
Acompanhamento de exames laboratoriais	Não faz	Não faz	Não faz	Não faz	Só quando solicitado pelo médico	Não faz	Faz uso periodicamente para oncologia	Uma vez ao ano

Fonte: Ricardo et al., (2023).

Among the 8 patients interviewed, only two undergo periodic exams, and the male patient, volunteer 7, uses it due to the oncologist's prescription. Prolonged use of the drug ranges from 6 months to 15 years.

Graph 1 shows the result of the age-related vitamin B12 analysis of the selected volunteers on the profile of omeprazole users. However, there were no significant changes in serum vitamin B12 dosages in relation to the prolonged use of omeprazole, regardless of the age of the patients.

Graph 1. Results of vitamin B12 analysis related to the age of the patients.



Fonte: Ricardo et al., (2023).

Araújo et al. (2017) conducted a research related to prescriptions and chronic use of omeprazole. A total of 88 omeprazole prescriptions were analyzed, all of which were chronically used. Regarding age, the age group was between 60 and 69 years old with 45.45%, which intensifies the risk of bone demineralization and the predisposition to fractures. It was observed that females were the ones who most used omeprazole, representing a percentage of 76.13%.

According to Costa and Damascena (2020), women are pointed out as the biggest users of medicines, since they are more careful with their health than men, as they use health services more, and consequently, they are more medicated than men.

CONCLUSION

Therefore, taking into account the preference for the use of omeprazole as a proton pump inhibitor in the treatment of acid-peptic disorders, attention should be paid to the harm caused by the prolonged use of this drug.

In addition, through the research carried out, some of these harmful effects on the patient's health were found, including chronic kidney injury, acute kidney injury, acute interstitial nephritis, hypomagnesemia, other alterations, for example, in laboratory tests, including alterations in hematimetric indices such as MCV (Mean Corpuscular Volume), HCM (Mean Corpuscular Hemoglobin) and CHCM (Mean Corpuscular Hemoglobin Concentration) and in biochemical parameters, for example the dosage of vitamin B12, Vitamin D and Calcium.

In addition, some authors show that the prolonged use of omeprazole can lead to megaloblastic anemia, as well as other harms already mentioned regarding the loss of nutrients and vitamins, requiring laboratory monitoring of this patient.

The empirical and frequent use of PPIs is what results in the adverse effects mentioned above, however, when used rationally, they are the best choice for treatment, prevention and symptoms of gastrointestinal tract diseases, since in general they have a good cost-benefit ratio, in addition to a good absorption and lasting inhibition of gastric acid secretion.

REFERENCES

1. ARAÚJO, C. V., et al. (2017). Perfil das prescrições e uso crônico de omeprazol. In I Congresso Brasileiro de Ciências Farmacêuticas (6. ed., Resumo). Foz do Iguaçu-PR: Conselho Federal de Farmácia. Disponível em: https://shre.ink/DwFp. Acesso em: 7 jun. 2024.

2. BRITO, A. L. S., MOREIRA, E. S., & GONÇALVES, K. A. M. (2021). Os riscos da utilização inadequada do omeprazol: uma revisão bibliográfica. *Brazilian Journal of Development*, 7(12), 113207-113215.

3. CAMILO, S., ALMEIDA, É., SOUSA, J., CAMILO, L., & ETCHEBEHERE, R. (2020). Uso crônico de inibidores de bomba de prótons e a quantidade de células G, D e ECL no estômago. *ABCD. Arquivos Brasileiros de Cirurgia Digestiva*, 33(2).

4. CHINZON, D., DOMINGUES, G., TOSETTO, N., & PERROTTI, M. (2022). Safety of long-term proton pump inhibitors: facts and myths. *Arq Gastroenterol*, 59(2).

5. COSTA, A. L., RAIOL, S., & DINIZ, D. (2023). Farmacocinética, efeitos colaterais e eficácia dos IBPS: uma revisão integrativa. *Research, Society and Development*, 12(8).

6. COSTA, M. P., & DAMASCENA, R. S. (2020). Perfil de usuários de omeprazol e considerações sobre seu uso racional: uma revisão bibliográfica. *ID on line Revista de Psicologia*, 14(50), 1185-1196.

7. CUESTA MIYARES, J., LÓPEZ CALEYA, J. F., & MARTÍN RODRIGO, L. (2020). Hipomagnesemia e hipocalcemia associadas a toma crônica de omeprazol. *SEMERGEN, Soc. Esp. Med. Rural Gen.*, e1-e2.

8. FERREIRA, J. V. D., et al. Uso contínuo do omeprazol e seus efeitos na absorção de vitamina B12 em idosos. In *X Congresso Internacional de Envelhecimento Humano*. CIEH: [s.d.].

9. HAASTRUP, P. F., et al. (2018). Side effects of long-term proton pump inhibitor use: a review. *Basic Clin Pharmacol Toxicol*, 123(2), 114-121. Disponível em: https://onlinelibrary.wiley.com/doi/10.1111/bcpt.13023. Acesso em: 15 maio 2024.

10. HIPÓLITO, P., et al. (2016). Perfil de usuários com prescrição de omeprazol em uma unidade básica de saúde do Sul do Brasil: considerações sobre seu uso racional. *Rev Bras Med Fam Comunidade*, 11(38), 1-10. Disponível em: https://rbmfc.org.br/rbmfc/article/view/1153/768. Acesso em: 8 jun. 2024.

11. HOEFLER, R., & LEITE, B. F. (2009). Segurança do uso contínuo de inibidores da bomba de prótons. *Farmacoterapêutica*, 14(01/02), 1-3.

12. ISSE, N., & HASHIMOTO, M. (2020). Omeprazole-induced hypomagnesaemia, causing renal tubular acidosis with hypokalaemia, hypocalcaemia, hyperlactacidaemia and hyperammonaemia. *BMJ Case Rep*, 13(7). Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7348324/. Acesso em: 15 maio 2024.

13. LIOTTI, A. C. C., & AMBROSIO, P. A. (2015). Riscos da má absorção de vitamina B12 e cálcio causados pelo uso prolongado do omeprazol em idosos. Centro de Pós-Graduação Oswaldo Cruz.

14. MORSCHEL, C., MAFRA, D., & CARRARO, J. (2018). A relação entre inibidores da bomba de prótons e doença renal. *Brazilian Journal of Nephrology*, 40.

15. OLIVEIRA, P. C. J., et al. (2019). Deficiência da vitamina B12 relacionada ao uso prolongado do omeprazol. In *I Jornada Científica da Biomedicina*. Guaraí-TO.

16. PICOLI, M., DE BONA, C., & HORN, A. (2011). Inibidores da bomba de prótons: revisão e análise farmacoeconômica. *Ahead of print*, 73(2).

17. RICARDO, G., et al. (2023). Alterações nos parâmetros hematológicos e bioquímicos em pacientes com uso prolongado de omeprazol. *Ries - Revista Interdisciplinar de Estudos em Saúde da Uniarp*, Caçador Brasil, SC, 38-45. Disponível em: https://abrir.link/JgXKZ. Acesso em: 8 jun. 2024.

18. SAMBURAGO, J., et al. (2021). Prescrições de omeprazol para idosos em unidades de saúde de Curitiba: análise segundo os critérios de Beers. *Geriatr Gerontol Aging*. Disponível em: https://cdn.publisher.gn1.link/ggaging.com/pdf/gga131221a02.pdf. Acesso em: 15 maio 2024.

19. SANTOS, L. C. O. Omeprazol: consequências do uso prolongado.

20. TORTORA, G., & DERRICKSON, B. (2017). *Corpo Humano: Fundamentos de Anatomia e Fisiologia* (10. ed.). ARTMED EDITORA LTDA. Disponível em: https://books.google.com.br/books?hl=pt-BR&lr=&id=z5K4DQAAQBAJ&oi=fnd&pg=PR1&dq=Tortora&ots=6KXV9GglVM&sig=UFg8mwZcZIsiUHKNtU_KojKz1yI#v=onepage&q=Tortora&f=false. Acesso em: 15 maio 2024.

21. VIEGAS, A., & NABAIS, S. (2017). Associação entre os inibidores da bomba de protões e o risco de demência. *Revista Portuguesa de Medicina Geral Familiar*, 33(1), 79-80.

22. WANNMACHER, L. (2004). Inibidores da bomba de prótons: indicações racionais. In *Uso racional de medicamentos: temas selecionados* (Vol. 2, nº 1). Brasília.

EFFECTS OF LASER PHOTOBIOMODULATION ON TUMOR CELLS

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Jéssica Lucio da Silva[1], Ana Flávia Spadaccini Silva de Oliveira[2], Danielle Gregório[3], Ellen Greves Giovanini[4], Regina Célia Poli[5], Rodrigo Antonio Carvalho Andraus[6] and Luciana Prado Maia[7]

ABSTRACT

Considering the beneficial and non-invasive effects of laser as a therapy, the possibility of using it in cancer patients would be of great interest to the clinical area. However, the available literature is still scarce for the definition of the ideal dosimetric parameters of photobiomodulation (FBM) in cancer cells, and when considering the use of the therapy as a bioinhibitory treatment in this cell type, more studies are needed to elucidate the main factors responsible for the different behaviors in these cells, since in specific parameters this therapy can promote biostimulation or even cell inhibition, It should be used with caution in clinical practice, avoiding increasing existing cancerous tissue.

Keywords: Photobiomodulation (FBM). Cancer. Biostimulation. Bioinhibitory therapy.

[1] Doctor, Graduate Program in Rehabilitation Sciences, Pitágoras University UNOPAR Anhanguera, Londrina, Paraná, Brazil.
[2] Doctor, Graduate Program in Rehabilitation Sciences, Pitágoras University UNOPAR Anhanguera, Londrina, Paraná, Brazil.
[3] Doctor, Graduate Program in Dentistry, Universidade Anhanguera Uniderp, Campo Grande, Mato Grosso do Sul, Brazil.
[4] Master's degree, Graduate Program in Dentistry, Universidade Anhanguera Uniderp, Campo Grande, Mato Grosso do Sul, Brazil.
[5] Doctor, Graduate Program in Rehabilitation Sciences, Pitágoras University UNOPAR Anhanguera, Londrina, Paraná, Brazil; Graduate Program in Dentistry, Universidade Anhanguera Uniderp, Campo Grande, Mato Grosso do Sul, Brazil.
[6] Doctor, Graduate Program in Rehabilitation Sciences, Pitágoras University UNOPAR Anhanguera, Londrina, Paraná, Brazil.
[7] Doctor, Graduate Program in Dentistry, Uniderp Anhanguera University, Campo Grande, Mato Grosso do Sul, Brazil; Graduate Program in Rehabilitation Sciences, Pitágoras University UNOPAR Anhanguera, Londrina, Paraná, Brazil.

INTRODUCTION

Cancer is a serious global public health problem, characterized by the uncontrolled proliferation of a group of cells within the body, and is one of the main causes of morbidity and mortality in many parts of the world. (1)

According to the estimates of Fitzmaurice et al. (2), in 2015 there were at least 17.5 million cases of cancer in the world, with at least 8.7 million deaths and according to the World Health Organization this number will reach 21 million by 2030. (3)

This disease has multiple causes, and can be triggered by etiological factors, such as age, endocrine alterations and genetics. (4,5) and several risk factors that predispose to the disease, with 90% of cases being related to environmental factors.

When it comes to antineoplastic treatment, new less invasive therapies have been investigated and have generated great interest in the health area, seeking a better prognosis and fewer side effects. One of the current therapies under investigation is Photobiomodulation (FBM) (6). This therapy has also been suggested in cases of sequelae of antineoplastic treatment, such as in cases of osteonecrosis associated with bisphosphonates. (7,8)

However, there are controversies regarding the use of FBM during the neoplastic process. Some studies show that this therapy can favor an increase in cell proliferation and differentiation, since it has significant biomodulatory effects, being a form of therapy contraindicated in regions with the presence of tumors (9). However, it is known that this process will depend on the parameters that will be applied (10).

Although the studies are not conclusive, the literature shows that there is a tendency for higher doses to lead to tumor cell death (11). However, in this context, when using FBM in high doses, while some authors have demonstrated that it can inhibit the tissue repair process (4), causing aggressive effects at the cellular level, other studies have shown satisfactory results in the repair process. (9,12).

There is a lack of evidence on the effects of FBM in conditions of malignancy, both in relation to the parameters to be used and in relation to the biological mechanisms resulting from irradiation at the cellular level (13). Considering the beneficial and non-invasive effects of laser as a therapy, the possibility of using it in cancer patients would be of great interest to the clinical area, and it could be used as an adjuvant in the treatment of cancer patients.

LITERATURE REVIEW

CANCER

Cancer is understood as a disease that is characterized by the uncontrolled proliferation of a group of cells within the body, much faster than that of normal cells (4,14). These cells attack tissues and organs, dividing rapidly and tend to be very aggressive and uncontrollable, leading to the formation of tumors, which can spread to other regions of the body. (15)

Cancer is the leading public health problem in the world and is already among the four leading causes of premature death in most countries (1). It is a disease of multiple causes, and can be caused by factors such as age, endocrine changes and genetics. (18,19). In addition, several risk factors predispose to the disease, and 90% of the cases are related to environmental factors, those that can be modified by changes in behavior and lifestyle habits, such as: exposure to radiation and chemical products, smoking, alcoholism, inadequate diet, obesity and physical inactivity. (5,16,17)

When it takes on an advanced form, cancer can evolve into a condition that cannot be cured, with the presence of uncontrollable signs and symptoms such as pain, fatigue, nausea, vomiting, anorexia, anxiety, depression, among others. The manifestations may be related to tumor invasion, as well as to the adverse effects of the treatment being performed, causing intense discomfort to the patient and a negative impact on quality of life. In view of this, the care provided to cancer patients is no longer curative and becomes palliative. (20)

This disease is considered a global public health problem, with a 20% high incidence in the last decade (21). Most of the time, the diagnosis of cancer is interpreted as a disease with a negative stigma considered as synonymous with suffering and death(22) and this image that the disease conveys is a consequence of its impact on the patient's life, since there is impairment in the physical, psychological, social, economic and spiritual aspects. (22,23)

Currently, cancer is the second leading cause of mortality in developed countries and, in a few decades, it will become the main cause of morbidity and mortality in the poorest regions of the planet (17). It stands out among chronic non-communicable diseases, reaching alarming levels, and is considered a global public health problem. (25)

According to research by the World Health Organization, by 2030 cancer will reach approximately 27 million incident cases, 17 million deaths, and 75 million people with an annual diagnosis worldwide, with 50% of cases being metastatic (26). In Brazil, statistical data made available by the National Cancer Institute (INCA), 2020 showed an incidence of

about 626 thousand new cases of cancer, thus revealing the magnitude of the problem in the country. (5,20,25)

Although the number of individuals diagnosed is increasing, it is believed that 1/3 of the cases are preventable. Thus, there is a need to incorporate new habits into the lifestyle so that the organic defenses can be able to fight against mutated cells and capable of developing a tumor mass. (27)

In this sense, it seems urgent to implement public health policies aimed at the most affected populations, associated with the reduction of social inequities and access to primary prevention, early diagnosis and treatments, in order to reduce disparities in cancer mortality in Brazil. (17)

Osteossarcoma

Osteosarcoma (OS) is a primary malignant bone tumor, originating from mesenchymal stem cells, characterized by a high rate of metastasis (36), high mortality, and a high rate of disability (29). It originates from mesenchymal tissue and acquires features of strong early metastasis, which are associated with a poor prognosis. (30)

Epidemiological data indicate that its incidence is 30% of bone tumor cases in Ireland, while in the United States it is approximately 1.7 cases per million inhabitants per year, representing 600 to 900 new cases annually. In Brazil, it is believed that the incidence is approximately 400 to 600 new cases per year. (31)

The disease has a bimodal incidence, predominantly affecting children and adolescents (primary osteosarcomas) (32) during the period of greatest growth, with a second peak incidence in adults over 65 years of age (secondary osteosarcomas), (33,34) in which men are affected more frequently than women, in a ratio of 1.6:1.

As for its etiology, studies indicate that the origin of osteosarcoma is still unclear, however, it is known that certain environmental factors, such as irradiation and hereditary conditions, such as Li-Fraumeni syndrome, familial retinoblastoma, and Rothmund-Thomson syndrome, are associated with germline mutations in the TP53, RB1, and RECQL4 genes, respectively, which predispose to osteosarcoma. (35)

The tumor can affect any bone, but it is usually located in the metaphyseal regions of the long bones. The distal region of the femur and the proximal region of the tibia and humerus are the most frequently affected locations. More than 50% of cases occur near the knee. (36)

The typical presentation includes the appearance of pain and expansion of the affected bone, and a hallmark of the pain is that it is sufficiently intense to awaken the

patient from sleep. Occasionally, patients will present with the onset of severe pain or other signs associated with a pathologic fracture. Approximately 15% to 20% of patients will have clinically detectable metastases, and more than 85% of metastatic disease occurs in the lung, the most common site of metastasis. (32)

A study conducted by Mirabello et al. (28) showed that osteosarcoma metastasis is one of the leading causes of treatment failure and patient death. The mechanism of metastasis of malignant tumors is that tumor cells that break off from the lesion enter the blood or lymphatic system and circulation of the body and proliferate and form metastatic focus in the metastatic organs, which is basically consistent with the mechanism of metastatic osteosarcoma. (29)

Traditionally, the gold standard for primary bone malignancies located in extremities has been amputation (32). In recent decades, therapy has shifted to salvaging limbs with intact local function in order to improve patients' quality of life. (37)

Thus, the current standard treatment of osteosarcoma consists of surgery associated with chemotherapy (38), leading to a 70% survival at 5 years in patients with non-metastatic disease. However, the 5-year survival rate of patients with metastatic disease is about 20%, emphasizing the importance of developing new therapeutic strategies (34). However, the effectiveness of these therapeutic strategies is limited, and some of them can cause serious complications and adverse effects.

In recent years, scientific evidence on FBM has been pointing to a better understanding of its effects, and researchers and clinicians have begun to investigate its use in increasingly innovative applications. Among these new clinical approaches are its application to repair damaged bone tissue and its place in oncology as an adjunct treatment, slowing or even leading to cancer cell death. (11)

Cancer cells

Cancer cells are thought to be altered normal cells, formed by cellular transformation (39) and they differ from healthy cells due to a multitude of molecular changes (40,41), many of which may be mechanically linked to metabolic reprogramming.

These cells have some special characteristics, such as unlimited proliferation capacity, loss of response to growth inhibition factors, evasion of apoptosis (programmed cell death), ability to invade other tissues (metastases), production of new blood vessels (angiogenesis), (42) ability to produce a greater number of reactive oxygen species and greater dependence on an antioxidant defense system. (43)

As for the development of a cancer cell, initially the cell is stimulated, either by a hormone or growth factor, and its division process is no longer normal and becomes permanent. Next, the "safety brakes" that prevent excessive cell division must be eliminated and these brakes are controlled by two main genes: RB1 and TP53, also known as P53. When these genes are mutated, they prevent apoptosis, thus allowing a tumor mass to form. Making these changes is enough for the cells to become cancerous. (4)

The Inactivation of the *RB1* It is reported in 20-40% of sporadic cases of osteosarcoma and is associated with a poor disease outcome. Its inactivation has also been associated with abnormalities of cell differentiation, cell death, angiogenesis, metastasis, and senescence (44). The mutants of the *TP53* they lose the ability to inhibit cell growth, gain the ability to proliferate and transform, and possibly lead to malignancy.

Nakase et al.(45) They transfected the gene P53 in osteosarcoma cells *in vitro* and *in vivo,* which apparently leads to the establishment of tumor growth. However, the functions of these gene mutants P53 in different osteosarcoma cell lines are not completely consistent and further investigation is needed.

LOW-POWER LASER

The term Laser - *Light Amplification By Stimulated Emission of Radiation* (light amplification by stimulated emission of radiation) (46) it was initially described by Albert Einstein in 1917, in a theoretical way, but it was only in 1960 that Theodore H. Maiman announced its operation for therapeutic purposes (47), being applied clinically for wound healing, pain relief, inflammation, and various orthopedic conditions. (48)

In 1967, Dr. Endre Mester was the first scientist to discover that a low-power laser had a stimulating effect on hair growth in mice and since then, low-power laser has been applied in various conditions to increase physiological function in humans and animals. (49)

Radiation is characterized by electromagnetic waves, visible or invisible, in which the applied energy performs work in the tissue area to be treated. Its purpose is the photoactivation of cellular mechanisms that help in the rehabilitation of injured areas. (50)

Among all the existing low-power laser types, the most commonly reported devices are: helium-neon gas (HeNe), gallium arsenide (GaAs), yttrium aluminum garnet (YAG), aluminum gallium arsenide (GaAlAs), aluminum aluminum gallium diode laser (AlGaInP). (51)

This radiation has unique characteristics, such as coherence: ordered displacement of waves in relation to time with their equal amplitudes; collimation: photons travel in

parallel, moving great distances; and monochromaticity: which is characterized by presenting a pure color, being a single color. (52)

Currently, the term FBM has replaced the old low-power laser, and FBM was introduced as a descriptor in PUBMED in 2015 (49). This form of irradiation has gained great prominence worldwide in health science due to the search for less invasive forms of treatment. A variety of pathological conditions using FBM are described in the literature, such as modulation of the inflammatory process, acceleration of the tissue repair process, pain relief, and treatment of some neurological disorders. (54,61)

FBM has become a widely used method in most countries and has been studied worldwide, one of the reasons for its popularity is related to its less invasive, athermal, painless, low-cost action (66) and with a shorter applicability time than other physical therapy resources. (67)

Therefore, taking into account its efficacy and non-invasive action, FBM has been studied as an adjuvant treatment option for cancer. (49,68)

Dosimetry

Multiple variables affect the clinical therapeutic effects of FBM, such as wavelength (λ), energy density (dE), power density (DP), and treatment time (53), because when applied it exposes cells or tissue to both a biostimulatory and bioinhibitory effect. (6)

Wavelength is considered an essential parameter for beneficial application results, as it determines the ability of the laser to penetrate the tissue (54) And depending on the wavelength the light can be classified as visible or red (380 to 750nm) and invisible or infrared (above 750nm) (55), although there is still divergence in the literature regarding these values. What is worth mentioning is that the longer the wavelength, the greater the depth of penetration of the energy into the tissue (54). De acordo com Huang et al.(56), wavelengths in the range of 700-1000 nm are most often used to treat deep tissue because of their deep penetration.

Regarding the dispersion, it is inversely proportional to the wavelength, the longer the wavelength, the lower the dispersion. (57)

The energy radiated in Joule (J) corresponds to the amount of energy employed during the treatment time. Another important factor is energy density, which is defined as the total amount of energy (J) per radiated area (cm^2) (57), given in Joule per square centimeter (J/cm^2), which will designate the irradiation time and its power, presented in Watts (W). (58,59)

It is important to highlight that energy cannot be confused with dose, as it presupposes reciprocity (the inverse relationship between power and time). It is calculated as: Energy (J) = Power (W) x Time (s). Energy density or fluence is an important dose descriptor, which assumes a reciprocal relationship between irradiance and time, obtained according to the following equation: FROM = $\frac{PxT}{A}$. (82,83)

Power (P) can be calculated by the following equation: P = , where E = radiated energy (dose) (in J) and T = irradiation time (in s). The power density (DP) or irradiance is related to the power (W) per unit area (A) radiated (in W/cm²), and can be calculated by the following equation: $\frac{E}{T}DP = \frac{P}{A}$. (60,61)

Knowledge of these parameters is essential to establish safe and adequate doses, according to the physiological characteristics and objectives of each individual.

It is known that if incorrect parameters are applied, the treatment is likely to be ineffective. There is a biphasic dose response curve in that when very low or very high doses (fluence (J/cm²), irradiance (mW/cm²), delivery time or number of repetitions may lead to no significant effect or sometimes excessive light delivery may lead to undesired inhibitory effects (62). Underdosing results in poor cellular response, but overdosing can paradoxically inhibit cell proliferation or induce apoptosis. (63)

Mechanisms of Action of Photobiomodulation

Several studies *in vitro* and *in vivo* report the effects of FBM on cell proliferation, metabolism, angiogenesis, apoptosis, and inflammation (9,12,63) and that FBM is correlated with accelerated wound healing due to the stimulation of cellular processes, such as cell migration and differentiation. It is also found that the respiratory chain in the mitochondria is stimulated by FBM, which results in an increase in the production of adenosine triphosphate (ATP) and thus increased synthesis of Deoxyribonucleic Acid (DNA), Ribonucleic Acid (RNA), and proteins.

Mitochondria contain chromophores that absorb photons from FBM. The primary chromophore that absorbs red light is the enzyme cytochrome c oxidase, the site of action of FBM being the main receptor and transducer of photosignal (63), is located in unit IV of the mitochondrial respiratory chain, resulting in the activity of several molecules, such as nitric oxide, promotes the production of ATP, calcium ions, reactive oxygen species, and several other signaling molecules. (71)

As for ATP production, they are promoted due to the FBM-stimulating electrons in the chromophores, and then electron carriers such as the cytochrome C oxidase chromophore,

deliver these electrons to their final electron acceptors, while a proton gradient is made, as well as creating a proton gradient that increases ATP production. (71)

Regarding mitochondrial alterations that increase the release of reactive oxygen species, this alteration is capable of inducing transcriptional alterations and production of nuclear factor-κB (NF-κB). NF-κB induces anti-apoptotic proteins along with cell proliferation and migration. (63)

Action of Photobiomodulation on Tumor Cells

The effects of FBM on cell proliferation and differentiation were investigated *in vitro* in different malignant cell lines and generated conflicting data when exploring a wide diversity of tumor parameters and cell lines. (49,51)

Werneck et al.(94) described that the tumor cell has a nutritional deficiency, due to its intense metabolic activity, and is therefore susceptible to the action of FBM.

The mechanism of FBM is based directly on the application of biostimulatory light energy to cells. Cellular photoreceptors absorb light, and can transfer it to the mitochondria to produce ATP (73). With increased vasodilation via ATP synthesis, the use of oxygen is increased and the activity of cytoplasmic enzymes with nucleic acids stimulates cell mitosis, which can likewise induce negative outcomes by proliferating cancer cells. (4)

In fact, studies *in vitro* show that, depending on the light parameters and cell type, pre-exposure to FBM can modulate the cytotoxic response of cancer cells exposed to irradiation. (74)

The cellular proliferative potential of irradiation has attracted some negative speculation that it could also increase tumor growth in neoplastic diseases. (13)

Studies *in vitro* and *in vivo* have demonstrated that FBM presents biomodulatory results on different cell types, characterized by increased viability, gene and protein expression by cells submitted to irradiation. (10,64)

The proliferation of both normal and tumor cells can be stimulated, and this process will depend on the parameters of the laser and the rate of cell proliferation at the time of irradiation. Depending on the parameters used, the use of FBM during this neoplastic process may favor an increase in cell proliferation and differentiation, since it has significant biomodulatory effects, and this is not a desirable effect in neoplasms. (9)

In order to elucidate the biological mechanism of cell proliferation, Sroka et al.(75) evaluated the effect of FBM on cells of different origins and different degrees of malignancy, comparing them with normal cells. An increase in the mitotic pattern was observed in benign and malignant cells after irradiation with doses in the range of 4 to 8 J/cm².

However, a reduction in the rate of cell proliferation was observed when the dose exceeded this energy range, regardless of the wavelength.

Carnevalli, et al.76), demonstrated in their study that CHO K-1 cells cultured and irradiated with low-intensity laser (830 nm and 2 J/cm²) exhibited greater ATP synthesis and mitotic capacity when subjected to nutritional stress when compared to non-irradiated cells in the control group.

Renno, and collaborators (77) investigated the effects of laser irradiation of 670, 780 and 830 nm on the proliferation of cells from human osteosarcoma and found that only the dose of 10 J/cm² at 830 nm was able to increase the proliferation of osteoblasts, while the energy densities of 1, 5 and 10 J/cm² at 780 nm decreased proliferation. Osteosarcoma cells were not affected by laser irradiation at 830 nm, while laser at 670 nm had a mild proliferative effect.

Frigo, and collaborators (13) used B16F10 murinho melanoma cells for irradiation with the laser emitting a wavelength of 660 nm, power of 50 mW and irradiance of 2.5 W/cm² at energy densities 150 J/cm² and 1050 J/cm², fractioning the energy delivered in 3 consecutive days, 9 J and 63 J respectively. After performing the exclusion test with tripan blue, they did not identify a statistically significant difference in relation to the control group.

Pinheiro, and collaborators (78) conducted a study analyzing the effect of FBM on malignant cells *in vitro*. In particular, they studied epithelial-type cancer cells, exposing them to irradiation at wavelengths of 635 and 670 nm. They found that the irradiated cells (both wavelengths) proliferated more than the non-irradiated control group. The group exposed to 670 nm proliferated more than the group at 635 nm. The authors concluded, therefore, that exposure to laser light could significantly increase the proliferation of cancer cells.

A recently published systematic review by da Silva et al.(11)suggested that FBM can be used in cancerous lesions in order to decrease the proliferation of cancer cells, depending on the parameters used; however, the lack of standardization of laser irradiation protocols for investigations does not allow the establishment of optimal parameters for this purpose, so FBM should be used with caution in cancer patients until further studies are conducted.

Thus, it is important to seek a better therapeutic approach for osteosarcoma, taking into account the need to minimize adverse effects, reduce the incidence of metastases, increase survival time and provide better quality of life to patients, considering that depending on the energy density applied to these cells, FBM can stimulate metastasis, being a form of therapy contraindicated, as it will lead to an increase in the disease, or it

can inhibit cell proliferation, being considered a favorable therapy that can be used as an adjuvant in the treatment of cancer patients.

CONCLUSION

The available literature is still scarce for the definition of the ideal dosimetric parameters of photobiomodulation in cancer cells and when considering the use of the therapy as a bioinhibitory treatment in this cell type, more studies are needed to elucidate the main factors responsible for the different behaviors in these cells, since in specific parameters this therapy can promote biostimulation or even cell inhibition and should be used with caution in practice clinic, avoiding increasing existing cancerous tissue.

REFERENCES

1. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 68(6), 394–424.

2. Fitzmaurice, C., Allen, C., Barber, R., Barregard, L., Bhutta, L., & Brenner, H. (2018). Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A systematic analysis for the Global Burden of Disease Study. *JAMA Oncology*, 3(4), 524–548.

3. Kara, C., Selamet, H., Gökmenoğlu, C., & Kara, N. (2018). Low level laser therapy induces increased viability and proliferation in isolated cancer cells. *Cell Proliferation*, 51(2), 1–6.

4. Kara, C., Selamet, H., Gökmenoğlu, C., & Kara, N. (2017). Low level laser therapy induces increased viability and proliferation in isolated cancer cells. *Cell Proliferation*, (November), 1–6.

5. De Oliveira, M. M., Malta, D. C., Guauche, H., De Moura, L., & Azevedo e Silva, G. (2015). Estimativa de pessoas com diagnóstico de câncer no Brasil: Dados da pesquisa nacional de saúde, 2013. *Revista Brasileira de Epidemiologia*, 18, 146–157.

6. Crous, A., & Abrahamse, H. (2016). Low-intensity laser irradiation at 636 nm induces increased viability and proliferation in isolated lung cancer stem cells. *Photomedicine and Laser Surgery*, 34(11), 525–532.

7. Akens, M. K., Wise-Milestone, L., Won, E., Schwock, J., Yee, A. J. M., Wilson, B. C., et al. (2014). In vitro and in vivo effects of photodynamic therapy on metastatic breast cancer cells pre-treated with zoledronic acid. *Photodiagnosis and Photodynamic Therapy*, 11(3), 426–433. https://doi.org/10.1016/j.pdpdt.2014.04.002

8. Basso, F. G., Turrioni, A. P. S., Soares, D. G., Bagnato, V. S., Hebling, J., & De Souza Costa, C. A. (2014). Low-level laser therapy for osteonecrotic lesions: Effects on osteoblasts treated with zoledronic acid. *Supportive Care in Cancer*, 22(10), 2741–2748.

9. Renno, A. C. M., Mcdonnell, P. A., Crovace, M. C., Zanotto, E. D., & Laakso, L. (2010). Effect of 830 nm laser phototherapy on osteoblasts grown in vitro on biosilicate® scaffolds. *Photomedicine and Laser Surgery*, 28(1), 131–133.

10. Incerti Parenti, S., Checchi, L., Fini, M., & Tschon, M. (2014). Different doses of low-level laser irradiation modulate the in vitro response of osteoblast-like cells. *Journal of Biomedical Optics*, 19(10), 108002.

11. Da Silva, J. L., Silva-de-Oliveira, A. F. S., Andraus, R. A. C., & Maia, L. P. (2019). Effects of low level laser therapy in cancer cells—a systematic review of the literature. *Lasers in Medical Science*.

12. Bashardoust Tajali, S., MacDermid, J. C., Houghton, P., & Grewal, R. (2010). Effects of low power laser irradiation on bone healing in animals: A meta-analysis. *Journal of Orthopaedic Surgery and Research*, 5(1), 1–10.

13. Frigo, L., Luppi, J. S. S., Favero, G. M., Maria, D. A., Penna, S. C., & Bjordal, J. M., et al. (2009). The effect of low-level laser irradiation (In-Ga-Al-AsP - 660 nm) on melanoma in vitro and in vivo. *BMC Cancer*, 9, 1–8.

14. Sudhakar, A. (2009). History of cancer, ancient and modern treatment methods. *Journal of Cancer Science & Therapy*, 01(02), i–iv.

15. Balasopoulou, A., Kokkinos, P., Pagoulatos, D., Plotas, P., Makri, O. E., Georgakopoulos, C. D., et al. (2017). Symposium: Recent advances and challenges in the management of retinoblastoma globe-saving treatments. *BMC Ophthalmology*, 17(1), 1.

16. Maresso, K. C., Tsai, K. Y., Brown, P. H., Lippman, S., Hawk, E., & Sciences, P., et al. (2016). Molecular cancer prevention: Current status & future. *CA: A Cancer Journal for Clinicians*, 65(5), 345–383.

17. Ribeiro, B. I., do Céu, C. C. Í., Milagros, B. P. M., & de Souza, L. B. (2016). Desigualdades socioeconômicas e mortalidade por câncer: um estudo ecológico no Brasil. *Revista Brasileira em Promoção da Saúde*, 29(3), 350–356.

18. Brenner, D. R., Brockton, N. T., Kotsopoulos, J., Cotterchio, M., Boucher, B. A., Courneya, K. S., et al. (2016). Breast cancer survival among young women: A review of the role of modifiable lifestyle factors. *Cancer Causes & Control*, 27(4), 459–472.

19. Gurgel, D. C., Capistrano Junior, V. L. M., Nogueira, I. C., & Neto, P. P. (2018). Atividade física e câncer: Intervenções nutricionais para um melhor prognóstico. *Motricidade*, 14(1), 398–404.

20. Freire, M. E. M., da Costa, S. F. G., de Lima, R. A. G., & Sawada, N. O. (2018). Health-related quality of life of patients with cancer in palliative care. *Texto e Contexto Enfermagem*, 27(2), 1–13.

21. Stewart, B. W., & Wild, C. P. (2015). *World cancer report 2014*. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press. *Advances in Nutrition*, 7(2), 418–419.

22. Şengül, M. C. B., Kaya, V., Şen, C. A., & Kaya, K. (2014). Association between suicidal ideation and behavior, and depression, anxiety, and perceived social support in cancer patients. *Medical Science Monitor*, 20, 329–336.

23. Souza, M. G. G. (2008). O olhar que olha o outro... Um estudo com familiares de pessoas em quimioterapia antineoplásica. *Revista Brasileira de Cancerologia*, 54(1), 31–41.

24. Sette, C. P., & Capitão, C. G. (2018). Efeito moderador do suporte social em pacientes oncológicos. *Revista Brasileira de Cancerologia*, 19(2), 265–277.

25. Guerra, M. R., Bustamante-Teixeira, M. T., Corrêa, C. S. L., De Abreu, D. M. X., Curado, M. P., Mooney, M., et al. (2017). Magnitude e variação da carga da mortalidade por câncer no Brasil e unidades da federação, 1990 e 2015. *Revista Brasileira de Epidemiologia*, 20(25000192049), 102–115.

26. Petrellis, M. C., da Fonseca, G. A. M. D., de Barros Pinto, A., Rosa, F. O., Maria, D. A., Shibli, J. A., et al. (2020). Laser-photobiomodulation on experimental cancer pain model

in Walker tumor-256. *Journal of Photochemistry and Photobiology B: Biology*, 210(July), 111979. https://doi.org/10.1016/j.jphotobiol.2020.111979

27. Gray, J. M., Rasanayagam, S., Engel, C., & Rizzo, J. (2017). State of the evidence 2017: An update on the connection between breast cancer and the environment. *Environmental Health: A Global Access Science Source*, 16(1), 1–61.

28. Mirabello, L., Yeager, M., Mai, P. L., Gastier-Foster, J. M., Gorlick, R., Khanna, C., et al. (2015). Germline TP53 variants and susceptibility to osteosarcoma. *Journal of the National Cancer Institute*, 107(7), 5–8.

29. Chen, X., & Zhang, Y. (2019). Bmp-2 and mir-29c in osteosarcoma tissues on proliferation and invasion of osteosarcoma cells. *Oncology Letters*, 17(6), 5389–5394.

30. Xie, C., Chen, B., Wu, B., Guo, J., & Cao, Y. (2018). LncRNA TUG1 promotes cell proliferation and suppresses apoptosis in osteosarcoma by regulating the miR-212-3p/FOXA1 axis. *Biomedicine & Pharmacotherapy*, 97(250), 1645–1653.

31. Tanaka, M. H., Penna, V., Chung, W. U. T. U., & Lopes, A. (1994). Tumores malignos primários dos ossos. *Arquivos Católicos de Medicina*, 26, 18–21.

32. Isakoff, M. S., Bielack, S. S., Meltzer, P., & Gorlick, R. (2015). Osteosarcoma: Current treatment and a collaborative pathway to success. *Journal of Clinical Oncology*, 33(27), 3029–3035.

33. Tempelaere, C., Biau, D., Babinet, A., & Anract, P. (2019). Osteosarcoma after the age of fifty: A clinicopathological study. *European Journal of Surgical Oncology*, 45(7), 1288–1292.

34. Geary, R. L., Corrigan, L. R., Carney, D. N., & Higgins, M. J. (2019). Osteosarcoma and second malignant neoplasms: A case series. *Irish Journal of Medical Science*.

35. Negri, G. L., Grande, B. M., Delaidelli, A., El-Naggar, A., Cochrane, D., Lau, C. C., et al. (2019). Integrative genomic analysis of matched primary and metastatic pediatric osteosarcoma. *Journal of Pathology*.

36. Cavalcante, E. T. M., Oliveira, L. L. P., Andrade, L. C., Vieira, V. da F., & Galloti, F. C. M. (2020). OSTEOSSARCOMA: INTERFERÊNCIA DA. *Revista*.

37. Carina, V., Costa, V., Sartori, M., Bellavia, D., De Luca, A., Raimondi, L., et al. (2019). Adjuvant biophysical therapies in osteosarcoma. *Cancers (Basel)*, 11(3).

38. Ma, J., Gao, W., & Gao, J. (2019). sCLU as prognostic biomarker and therapeutic target in osteosarcoma. *Bioengineered*, 10(1), 229–239.

39. Dong, Q. L., & Xing, X. Y. (2018). Cancer cells arise from bacteria. *Cancer Cell International*, 18(1), 1–9. https://doi.org/10.1186/s12935-018-0699-4

40. Cavallo, F., De Giovanni, C., Nanni, P., Forni, G., & Lollini, P. L. (2011). The immune hallmarks of cancer. *Cancer Immunology, Immunotherapy*, 60(3), 319–326.

41. Kroemer, G., & Pouyssegur, J. (2008). Tumor cell metabolism: Cancer's Achilles' heel. *Cancer Cell*, 13(6), 472–482.

42. Martinez, M. A. R., Francisco, G., Cabral, L. S., Ruiz, I. R. G., & Neto, C. F. (2006). Genética molecular aplicada ao câncer cutâneo não melanoma. *Anais Brasileiros de Dermatologia*, 81(5), 405–419.

43. Li, T., Copeland, C., & Le, A. (2021). Glutamine metabolism in cancer. *Advances in Experimental Medicine and Biology*, 1311, 17–38.

44. Burkhart, D. L., & Sage, J. (2008). Cellular mechanisms of tumour suppression by the retinoblastoma gene. *Nature Reviews Cancer*, 8(9), 671–682.

45. Nakase, M., Inui, M., Okumura, K., Kamei, T., Nakamura, S., & Tagawa, T. (2005). P53 gene therapy of human osteocarcinoma using a transferrin-modified cationic liposome. *Molecular Cancer Therapeutics*, 4(4), 625–631.

46. Davidovich, L. (2015). Os quanta de luz e a ótica quântica. *Revista Brasileira de Ensino de Física*, 37(4).

47. Bayat, M., Virdi, A., Rezaei, F., & Chien, S. (2018). Comparison of the in vitro effects of low-level laser therapy and low-intensity pulsed ultrasound therapy on bony cells and stem cells. *Progress in Biophysics and Molecular Biology*, 133, 36–48. https://doi.org/10.1016/j.pbiomolbio.2017.11.001

48. Hamblin, M. R., Nelson, S. T., & Strahan, J. R. (2018). Photobiomodulation and cancer: What is the truth? *Photomedicine and Laser Surgery*, 36(5), 241–245.

49. Bensadoun, R. J., Epstein, J. B., Nair, R. G., Barasch, A., Raber-Durlacher, J. E., Migliorati, C., et al. (2020). Safety and efficacy of photobiomodulation therapy in oncology: A systematic review. *Cancer Medicine*, 1–22.

50. Baxter, D. (2003). Laserterapia de baixa intensidade. In *Eletroterapia: Prática Baseada em Evidências* (pp. 171–186).

51. Zecha, J. A. E. M., Raber-Durlacher, J. E., Nair, R. G., Epstein, J. B., Sonis, S. T., Elad, S., Hamblin, M. R., Barach, A., Migliorati, C. A., Milstein, D. M. J., Genot, M.-T., Lansaat, L., & Brink, R. van der. (2016). Low level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: Part 1: Mechanisms of action, dosimetric, and safety considerations. *HHS Public Access*, 24(6).

52. Moskvin, S. V. (2017). Low-level laser therapy in Russia: History, science and practice. *Journal of Lasers in Medical Sciences*, 8(2), 56–65. http://dx.doi.org/10.15171/jlms.2017.11

53. Bensadoun, R. J., & Nair, R. G. (2012). Low-level laser therapy in the prevention and treatment of cancer therapy-induced mucositis: 2012 state of the art based on literature review and meta-analysis. *Current Opinion in Oncology*, 24(4), 363–370.

54. Cheng, W., Yao, M., Sun, K., & Li, W. (2020). Progress in photobiomodulation for bone fractures: A narrative review. *Photobiomodulation, Photomedicine, and Laser Surgery*, 38(5), 260–271.

55. Catorze, M. G. (2009). Laser: Fundamentos e indicações em dermatologia. *Medicina Cutânea Ibero-Latino-Americana*, 37(1), 5–27.

56. Huang, Q., Ou, Y. S., Tao, Y., Yin, H., & Tu, P. H. (2016). Apoptosis and autophagy induced by pyropheophorbide-α methyl ester-mediated photodynamic therapy in human osteosarcoma MG-63 cells. *Apoptosis*, 21(6), 749–760.

57. Cavalcanti, T. M., de Almeida-Barros, R. Q., Catão de MHC de V., Feitosa, A. P. A., & Lins, R. D. A. U. (2011). Conhecimento das propriedades físicas e da interação do laser com os tecidos biológicos na odontologia. *Anais Brasileiros de Dermatologia*, 86(5), 955–960.

58. Loreti, E. H., Pascoal, V. L. W., Nogueira, B. V., Silva, I. V., & Pedrosa, D. F. (2015). Use of laser therapy in the healing process: A literature review. *Photomedicine and Laser Surgery*, 33(2), 104–116.

59. Heckler, M. C. T., Barberini, D. J., & Amorim, R. M. (2014). Low level laser therapy on cell cultures. *Revista Brasileira de Ciência Animal*, 7(14), 541–565.

60. Castano, A. P., Dai, T., Yaroslavsky, I., Cohen, R., Apruzzese, W. A., Smotrich, M. H., et al. (2007). Low-level laser therapy for zymosan-induced arthritis in rats: Importance of illumination time. *Lasers in Surgery and Medicine*, 39(6), 543–550.

61. Enwemeka, C. S. (2009). Intricacies of dose in laser phototherapy for tissue repair and pain relief. *Photomedicine and Laser Surgery*, 27(3), 387–393.

62. de Freitas, L., & Hamblin, M. R. (2016). Proposed mechanisms of photobiomodulation or low-level light therapy. *IEEE Journal of Selected Topics in Quantum Electronics*, 22(3), 1–37.

63. Tam, S. Y., Tam, V. C. W., Ramkumar, S., Khaw, M. L., Law, H. K. W., & Lee, S. W. Y. (2020). Review on the cellular mechanisms of low-level laser therapy use in oncology. *Frontiers in Oncology*, 10, 1–11.

64. Stein, C., Fernandes, R. O., Miozzo, A. P., Coronel, C. C., Baroni, B. M., Belló-Klein, A., et al. (2018). Acute effects of low-level laser therapy on patients' functional capacity in the postoperative period of coronary artery bypass graft surgery: A randomized, crossover, placebo-controlled trial. *Photomedicine and Laser Surgery*, 36(3), 122–129.

65. de Oliveira, P., Fernandes, K. R., Sperandio, E. F., Pastor, F. A. C., Nonaka, K. O., Parizotto, N. A., et al. (2012). Comparação dos efeitos do laser de baixa potência e do ULTRASSOM de baixa intensidade associado ao Biosilicato® no processo de reparo ósseo em tíbias de ratos. *Revista Brasileira de Ortopedia*, 47(1), 102–107.

66. Lins, R. D. A. U., Dantas, E. M., Lucena, K. C. R., Catão, M. H. C. V., Granville-Garcia, A. F., & Carvalho Neto, L. G. (2010). Biostimulation effects of low-power laser in the repair process. *Anais Brasileiros de Dermatologia*, 85(6), 849–855.

67. Baxter, G. D., Liu, L., Petrich, S., Gisselman, A. S., Chapple, C., Anders, J. J., et al. (2017). Low level laser therapy (Photobiomodulation therapy) for breast cancer-related lymphedema: A systematic review. *BMC Cancer*, 17(1), 833.

68. AlGhamdi, K. M., Kumar, A., & Moussa, N. A. (2012). Low-level laser therapy: A useful technique for enhancing the proliferation of various cultured cells. *Lasers in Medical Science*, 27(1), 237–249.

69. Djavid, G. E., Bigdeli, B., Goliaei, B., Nikoofar, A., Hamblin, M. R., Hospital, F., et al. (2018). HHS Public Access. *Journal of Biophotonics*, 10(12), 1732–1742.

70. Gomes Henriques, Á. C., Ginani, F., Oliveira, R. M., Keesen, T. S. L., Galvão Barboza, C. A., Oliveira Rocha, H. A., et al. (2014). Low-level laser therapy promotes proliferation and invasion of oral squamous cell carcinoma cells. *Lasers in Medical Science*, 29(4), 1385–1395.

71. Dompe, C., Moncrieff, L., Matys, J., Grzech-Leśniak, K., Kocherova, I., Bryja, A., et al. (2020). Photobiomodulation—underlying mechanism and clinical applications. *Journal of Clinical Medicine*, 9(6), 1–17.

72. Werneck, C. E., Barbosa Pinheiro, A. L., Tavares Pacheco, M. T., Pacheco Soares, C., & Freire De Castro, J. L. (2005). Laser light is capable of inducing proliferation of carcinoma cells in culture: A spectroscopic in vitro study. *Photomedicine and Laser Surgery*, 23(3), 300–303.

73. Murayama, H., Sadakane, K., Yamanoha, B., & Kogure, S. (2012). Low-power 808-nm laser irradiation inhibits cell proliferation of a human-derived glioblastoma cell line in vitro. *Lasers in Medical Science*, 27(1), 87–93.

74. Ramos Silva, C., Cabral, F. V., de Camargo, C. F. M., Núñez, S. C., Mateus Yoshimura, T., de Lima Luna, A. C., et al. (2016). Exploring the effects of low-level laser therapy on fibroblasts and tumor cells following gamma radiation exposure. *Journal of Biophotonics*, 9(11–12), 1157–1166.

75. Sroka, R., Schaffer, M., Fuchs, C., Pongratz, T., Schrader-Reichard, U., Busch, M., et al. (1999). Effects on the mitosis of normal and tumor cells induced by light treatment of different wavelengths. *Lasers in Surgery and Medicine*, 25(3), 263–271.

76. Carnevalli, C. M. M., Soares, C. P., Zângaro, R. A., Pinheiro, A. L. B., & Silva, N. S. (2003). Laser light prevents apoptosis on CHO K-1 cell line. *Journal of Clinical Laser Medicine & Surgery*, 21(4), 193–196.

77. Renno, A. C., McDonnell, P. A., Parizotto, N. A., & Laakso, E. L. (2007). The effects of laser irradiation on osteoblast and osteosarcoma cell proliferation and differentiation in vitro. *Photomedicine and Laser Surgery*, 25(4), 275–280.

78. Pinheiro, A. L. B., Carneiro, N. S., Vieira, A. L. de B., Brugnera, A. J., Zanin, F. A., Barros, R. A., et al. (2002). Effects of low-level laser therapy on malignant cells: In vitro study. *Journal of Clinical Laser Medicine & Surgery*, 20(1), 23–26.

79. Petros, A. M., Olejniczak, E. T., & Fesik, S. W. (2004). Structural biology of the Bcl-2 family of proteins. *Biochimica et Biophysica Acta - Molecular Cell Research*, 1644(2–3), 83–94.

80. Wang, Q., Zhang, L., Yuan, X., Ou, Y., Zhu, X., Cheng, Z., et al. (2016). The relationship between the Bcl-2/Bax proteins and the mitochondria-mediated apoptosis pathway in

the differentiation of adipose-derived stromal cells into neurons. *PLoS ONE*, 11(10), 1–16.

81. Moazami-Goudarzi, M., Farshdousti-Hagh, M., Hoseinpour-Feizi, A., Talebi, M., Movassaghpour-Akbari, A. A., Shams-Asanjan, K., et al. (2016). The acute lymphoblastic leukemia prognostic scoring: Whether it is possible by BCL-2, BAX gene promoter genotyping. *Caspian Journal of Internal Medicine*, 7(2), 105–113.

82. Sun, M., Zhou, C., Zeng, H., Puebla-Osorio, N., Damiani, E., Chen, J., et al. (2015). Hiporfin-mediated photodynamic therapy in preclinical treatment of osteosarcoma. *Photochemistry and Photobiology*, 91(3), 533–544.

83. Adams, J. M., & Cory, S. (2007). The Bcl-2 apoptotic switch in cancer development and therapy. *Oncogene*, 26(9), 1324–1337.

84. Peña-Blanco, A., & García-Sáez, A. J. (2018). Bax, Bak and beyond — mitochondrial performance in apoptosis. *FEBS Journal*, 285(3), 416–431.

85. O'Neill, K. L., Huang, K., Zhang, J., Chen, Y., & Luo, X. (2016). Inactivation of prosurvival Bcl-2 proteins activates Bax/Bak through the outer mitochondrial membrane. *Genes & Development*, 30(8), 973–988.

86. Tossounian, M. A., Zhang, B., & Gout, I. (2020). The writers, readers, and erasers in redox regulation of GAPDH. *Antioxidants*, 9(12), 1–21.

87. Zhong, X. Y., Yuan, X. M., Xu, Y. Y., Yin, M., Yan, W. W., Zou, S. W., et al. (2018). CARM1 methylates GAPDH to regulate glucose metabolism and is suppressed in liver cancer. *Cell Reports*, 24(12), 3207–3223. https://doi.org/10.1016/j.celrep.2018.08.066

88. Park, J. B., Park, H., Son, J., Ha, S. J., & Cho, H. S. (2019). Structural study of monomethyl fumarate-bound human GAPDH. *Molecular Cells*, 42(8), 597–603.

89. Jayaguru, P., & Mohr, S. (2011). Nuclear GAPDH: Changing the fate of Müller cells in diabetes. *Journal of Ocular Biology, Diseases, and Informatics*, 4(1–2), 34–41.

90. Zhang, J. Y., Zhang, F., Hong, C. Q., Giuliano, A. E., Cui, X. J., Zhou, G. J., et al. (2015). Critical protein GAPDH and its regulatory mechanisms in cancer cells. *Cancer Biology & Medicine*, 12(1), 10–22.

91. Tristan, C. (2012). The diverse functions of GAPDH. *Cellular & Molecular Life Sciences*, 23(2), 317–323.

92. Jo, H. Y., Kim, Y., Park, H. W., Moon, H. E., Bae, S., Kim, J., et al. (2015). The unreliability of MTT assay in the cytotoxic test of primary cultured glioblastoma cells. *Experimental Neurobiology*, 24(3), 235.

93. Artilheiro, P. P., Barbosa, J. L. P., Fernandes, K. P. S., Oliveira, T. S. de, Bussadori, S. K., & Mesquita-Ferrari, R. A. (2012). Análise comparativa dos efeitos do ultrassom terapêutico e laser de baixa potência sobre a proliferação de células musculares durante a diferenciação celular. *Fisioterapia em Movimento*, 25(1), 21–29.

94. Riss, T. L., Moravec, R. A., Niles, A. L., Duellman, S., Benink, H. A., Worzella, T. J., et al. (2004). Cell viability assays. *Assay Guidance Manual*.

95. Mosmann, T. (1983). Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays. *Journal of Immunological Methods*, 65(1–2), 55–63.

96. McKinnon, K. M. (2019). Flow cytometry instrumentation – An overview. *Current Protocols in Cytometry*, 87(1), 1–16.

97. Todd, R. T., Braverman, A. L., & Selmecki, A. (2018). Flow cytometry analysis of fungal ploidy. *Current Protocols in Microbiology*, 50(1), 1–32.

98. Dominical, V., Samsel, L., & McCoy, J. P. (2017). Masks in imaging flow cytometry. *Methods*, 112, 9–17.

99. Phinney, D. A., & Cucci, T. L. (1989). Flow cytometry and phytoplankton. *Cytometry*, 10(5), 511–521.

100. Rieger, A. M., Nelson, K. L., Konowalchuk, J. D., & Barreda, D. R. (2011). Modified annexin V/propidium iodide apoptosis assay for accurate assessment of cell death. *Journal of Visualized Experiments*, (50), 3–6.

101. Crowley, L. C., Marfell, B. J., Scott, A. P., & Waterhouse, N. J. (2016). Quantitation of apoptosis and necrosis by annexin V binding, propidium iodide uptake, and flow cytometry. *Cold Spring Harbor Protocols*, 2016(11), 953–957.

102. VanGuilder, H. D., Vrana, K. E., & Freeman, W. M. (2008). Twenty-five years of quantitative PCR for gene expression analysis. *Biotechniques*, 44(5), 619–626.

103. Pyo, S. J., Song, W. W., Kim, I. R., Park, B. S., Kim, C. H., Shin, S. H., et al. (2013). Low-level laser therapy induces the expressions of BMP-2, osteocalcin, and TGF-β1 in hypoxic-cultured human osteoblasts. *Lasers in Medical Science*, 28(2), 543–550.

104. Lorenz, T. C. (2012). Polymerase chain reaction: Basic protocol plus troubleshooting and optimization strategies. *Journal of Visualized Experiments*, (63), 1–15.

105. Novais, C., Pires-Alves, M., & Silva, F. (2004). PCR em tempo real. *Revista Brasileira de Biotecnologia e Ciências do Movimento*, 11, 10–14.

106. Zhang, C., Wang, Y. Q., Jin, G., Wu, S., Cui, J., & Wang, R. F. (2017). Selection of reference genes for gene expression studies in human bladder cancer using SYBR-green quantitative polymerase chain reaction. *Oncology Letters*, 14(5), 6001–6011.

107. Steibel, J. P., Poletto, R., Coussens, P. M., & Rosa, G. J. M. (2009). A powerful and flexible linear mixed model framework for the analysis of relative quantification RT-PCR data. *Genomics*, 94(2), 146–152.

108. Valones, M. A. A., Guimarães, R. L., Brandão, L. A. C., De Souza, P. R. E., De Albuquerque Tavares Carvalho, A., & Crovela, S. (2009). Principles and applications of polymerase chain reaction in medical diagnostic fields: A review. *Brazilian Journal of Microbiology*, 40(1), 1–11.

109. Livak, K. J., & Schmittgen, T. D. (2001). Analysis of relative gene expression data using real-time quantitative PCR and the 2-ΔΔCT method. *Methods*, 25(4), 402–408.

110. Qu, R., Miao, Y., Cui, Y., Cao, Y., Zhou, Y., Tang, X., et al. (2019). Selection of reference genes for the quantitative real-time PCR normalization of gene expression in *Isatis indigotica* Fortune. *BMC Molecular Biology*, 20(1), 1–12.

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