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*Annals of Olinda Medical School*

# HEALTH SOCIAL RESPONSIBILITY

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# Summary

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## *Letter to the Editor*

**Inácio de Barros Melo Neto**

Dear Editor,

It is with great pleasure that we present the volume 12 of the Journal Anais da Faculdade de medicina de Olinda (AFMO). This volume is very important because it celebrates the 10th anniversary of the institution, evoking memories of all the challenges faced, the courage to confront them, and the joy of sharing numerous achievements.

This year, we also celebrate the 5th anniversary of the Institutional Development Program for Scientific Initiation (PRODIIC), which promotes knowledge production and a solid scientific foundation for our students. To commemorate this milestone, we had the opportunity to host the Scientific Director of the Foundation for Research Support of the State of Pernambuco, Professor Dr. Helen Jamil Khoury, who reflected with us on "Science and Development: the Case of Pernambuco." It is noteworthy that in just five years, the number of submitted articles increased from 8 in 2019 to 63 in 2024, representing an increase of approximately 80%. This reinforces the hypothesis that we are on the right path by investing in the scientific production of our institution and supporting our researchers and students.

Moreover, our journal has adopted new technologies and provided training and tools to assist the reviewers in the analysis of the submitted articles; thus, streamlining the editorial process. The first meeting of AFMO reviewers was held and fostered the integration, training, and discussion among those responsible for maintaining publication quality: the editorial board and reviewers. The new cover of the journal was also presented along with preparations for the upcoming year.

We must emphasize that internationalization is a key focus in scientific production, and proficiency in another language, particularly English, is essential. In this sense, the AFMO continues its bilingual trajectory. To enhance this component, it is important to highlight the role of the FMO Global Office, which certified the first students participating in in-person English courses; coordinated the English Olympiads during vacation and awarded students, the faculty, and staff; and launched the FMO Global Ambassadors project to certify students with excellence in English proficiency. These initiatives strengthen the crucial pillar of internationalization for knowledge production.

As a grand finale for such a special year, we held the 3rd International Health Congress of the Faculty of Medicine (III CISFMO) as part of an internationalization process and featured two international guests: Professor Dr. Antônio Coca (Spain) and Professor Dr. Joaquim Spinoza (United States of America). With over 500 registrants participating in conferences, panels, and mini-courses, we set a record with more than 140 scientific studies submitted. Additionally, we conducted the first FMO Health Innovation - StartupMed Challenge, which engaged over a hundred students in a competition to provide solutions to real problems faced by managers in the Unified Health System. The III CISFMO also hosted the 1st International Workshop on Down Syndrome, which invited researchers,

specialists, non-governmental organizations, and students of the FMO to provide suggestions and insights for developing the research agenda of the Maria Alcoforado de Barros Melo Institute (Maria Institute).

This demonstrates the significant actions taken by the FMO to fulfill its mission of excellence in education. Apart from distinguishing itself nationally, the institution is making substantial strides toward consolidating its presence internationally while fostering a critical and humanistic perspective among its students — an expansive worldview that creates a conducive environment to develop solutions for local problems with a global outlook.

Anais da Faculdade de Medicina de Olinda
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# Epidemiological and care characteristics and spatial distribution of deaths due to congenital syphilis

## Características epidemiológicas, assistenciais e distribuição espacial dos óbitos por sífilis congênita

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## Abstract

**Objective:** To describe the epidemiological and care characteristics and investigate the spatial distribution of deaths due to congenital syphilis (CS). **Methods:** A descriptive and mixed study with a quantitative and ecological approach was conducted. The investigation and summary records of fetal and infant deaths due to CS registered in the Mortality Information System of Recife between 2013 and 2017 were analyzed. Mortality rates and relative and absolute frequencies were calculated. For spatial analysis, the health districts, areas covered by the Family Health Strategy (FHS), and place of the deaths were superimposed; the kernel density estimator was adopted. **Results:** A total of 2,437 deaths were found: 1,119 (45.9%) were fetal, and 1,318 (54.1%) were infant. Only 198 (8.1%) of the deaths were due to CS, of which 173 (87.4%) were fetal and 25 (12.6%) were infant. The mean fetal and infant mortality rates were 9.7 and 11.5 per 1,000 live births, respectively. In contrast, the mean fetal and infant mortality rates related to CS were 1.5 and 0.2 per 1,000 live births, respectively. A total of 27 (77.1%) out of 35 deaths due to CS in 2017 received prenatal care; of these, 14 (51.8%) started in the second trimester of pregnancy. The mapping showed clusters of deaths in most health districts of areas covered by the FHS. **Conclusion:** The mortality due to CS is associated with the quality of pre-

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natal care, indicating weaknesses in the performance and organization of healthcare teams.

**Keywords:** Congenital syphilis; Child mortality; Fetal mortality; Prenatal care; Spatial analysis.

## Resumo

**Objetivo:** Descrever as características epidemiológicas e assistenciais e a distribuição espacial dos óbitos por sífilis congênita (SC). **Métodos:** Estudo misto, ecológico e descritivo com abordagem quantitativa. Foram analisados todos os registros no Sistema de Informação sobre Mortalidade de **óbitos fetais e infantis por** SC em parturientes residentes no Recife-PE ocorridos entre 2013 e 2017, assim como suas fichas de investigação e fichas síntese. Os coeficientes de mortalidade foram calculados, bem como a frequência relativa e absoluta. Para a análise espacial, foram sobrepostas as camadas de distritos sanitários, as **áreas** atendidas pela Estratégia de Saúde da Família e as residências dos óbitos estudados, e foi adotado o estimador de densidade de Kernel. **Resultados:** Constatou-se a ocorrência de 2.437 óbitos, sendo 1.119 (45,9%) fetais e 1.318 (54,1%) infantis. Dos óbitos analisados, 198 (8,1%) foram por SC, sendo 173 (87,4%) fetais e 25 (12,6%) infantis. O coeficiente médio de mortalidade fetal foi de 9,7 por 1.000 nascimentos, e o infantil foi de 11,5 por 1.000 nascidos vivos. J**á o coeficiente** médio de mortalidade fetal por SC foi de 1,5 por 1.000 nascimentos, e o infantil foi de 0,2 por 1.000 nascidos vivos. Para os óbitos por SC ocorridos em 2017 (35), verificou-se que 27 (77,1%) receberam assistência ao pré-natal, sendo que, desses, 14 (51,8%) só tiveram o início da assistência ao pré-natal no 2° trimestre da gestação. No mapeamento, observou-se aglomerados de óbitos na maioria dos distritos sanitários e que esses estão concentrados em áreas atendidas pela Estratégia de Saúde da Família. **Conclusão:** A persistência da mortalidade por SC está relacionada **à** qualidade da assistência ao pré-natal, o que aponta fragilidades na atuação e na organização das equipes.

**Palavras-chave:** Sífilis congênita; Cuidado pré-natal; Mortalidade fetal; Mortalidade infantil; Análise espacial.

## INTRODUCTION

Congenital syphilis (CS) is a public health issue worldwide. This disease results from the hematogenous transmission of the *Treponema pallidum* in an infected pregnant woman via a transplacental route. CS can be transmitted in any trimester of pregnancy and is responsible for nearly 40% of the perinatal mortality rate, 25% of fetal deaths, and 14% of infant deaths globally[1]. Its vertical transmission is preventable, given the early diagnosis and adequate treatment of the pregnant woman. Thus, prenatal care is crucial to reduce negative outcomes[2].

A study indicated that late initiation of prenatal care, difficulties in diagnosing syphilis during pregnancy, failure to treat the pregnant woman and her partner, and the absence of orientation about the disease and its prevention represent gaps in the provided prenatal care. These factors

reinforce that the understanding of vertical transmission is essential to ensure the quality of prenatal care[3].

A satisfactory prenatal care should include at least six medical appointments, starting in the first trimester of pregnancy. Syphilis testing is highly recommended in the first and third trimesters and before birth[4]. Although the healthcare network provides the means for disease control, socioeconomic, political, and individual factors may hinder population access, favoring CS in vulnerable groups[5, 6].

Studies showed that low income and education level, drug abuse, and history of sexually transmitted infections are risk factors for CS. Furthermore, the lack of partner support during pregnancy, single mothers with multiple partners, or unintended pregnancies may hinder access to prenatal care, favoring CS infection. These vulnerabilities may also influence late prenatal care and lead women to attend fewer medical appointments, reducing the chance of screening for the disease in the first semester[7, 8, 9].

In this context, health departments have been adopting spatial analysis via geoprocessing to understand the characteristics related to the dynamics of CS in the territory and develop interventions to address the disease. Spatiotemporal distribution verifies the spatial patterns of the disease, health services, and the environment. Thus, diseases can be mapped, aggregations detected, and potential risk areas identified to properly guide resource allocation and define target groups for intervention[10, 11].

This study aimed to describe the epidemiological and care characteristics and investigate the spatial distribution of deaths due to CS in Recife (Pernambuco, Brazil) between 2013 and 2017.

## METHODS

A mixed and descriptive study was performed in Recife (Pernambuco), northeastern Brazil, using a quantitative and ecological approach. Recife has an area of 218,435 km² and a population of 1,637,834 distributed across 94 neighborhoods and divided into 8 health districts (HD). The estimated population coverage for primary care is 73%, of which 58% is covered by the Family Health Strategy (FHS) and 14.5% by community health agents. The network of specialized healthcare consists of 18 maternity hospitals, and four of these are managed by the Recife Health Department[12].

Fetal and infant deaths due to CS in Recife between 2013 and 2017 were obtained from the Mortality Information System (SIM). Specifically for 2017, the confidential investigation form and the summary form were used in addition to the SIM to monitor fetal and infant deaths. These data were used to characterize the care provided during prenatal and birth, as well as the occurrence of death. The forms were analyzed until 2017 because this was the last year with complete

records related to death at the time of this study. Data from the mother, pregnancy, and childbirth were also obtained from the SIM.

Data from the SIM were processed and analyzed using the TabWin and Excel® 2013 software. A database was created using the Epinfo software (version 7.2.3.1) to collect data from the forms. Absolute and relative frequencies and fetal, infant, perinatal (total fetal deaths at ≥ 22 pregnancy weeks and deaths of infants aged from zero to six complete days), and total mortality rates related to CS were calculated.

Spatial analysis was carried out using cartographic bases of HD and the FHS coverage. The place of residence where deaths occurred was georeferenced using the Google Earth Pro. Based on geographic coordinates and the Qgis 2.18 software, the kernel density estimator was applied. This parameter creates continuous surface maps and provides estimates of the occurrence across the analyzed area. These estimates are also independent of administrative boundaries and consider the number of occurrences in a defined coverage radius, assigning greater scores to closer points and reducing the importance of distant points.

This study was approved by the human research ethics committee of the Professor Fernando Figueira Institute of Integral Medicine under registration number 3285689.

## RESULTS

A total of 2,437 deaths were recorded: 1,119 (45.9%) fetal and 1,318 (54.1%) infant. Of these, 198 (8.1%) were due to CS, of which 173 (87.4%) were fetal and 25 (12.6%) were infant deaths. The mean fetal mortality rate was 9.7 per 1,000 births, whereas the infant mortality rate was 11.5 per 1,000 live births. The mean fetal and infant mortality rates due to CS were 1.5 and 0.2 per 1,000 live births, respectively (Table 1).

**Table 1.** Fetal, infant, perinatal, and CS mortality rates by year.
Recife (Pernambuco, Brazil), 2013 to 2017.

| Year | Fetal | | | | Infant | | | | Perinatal | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total | | SC | | Total | | SC | | Total | | SC | |
| | N° | CM | Nº | CM | N° | CM | N° | CM | N° | CM | N° | CM |
| **2013** | 235 | 10.0 | 36 | 1.5 | 288 | 12.4 | 8 | 0.3 | 354 | 15.1 | 42 | 1.8 |
| **2014** | 228 | 9.6 | 32 | 1.3 | 280 | 12.0 | 5 | 0.2 | 348 | 14.7 | 33 | 1.4 |
| **2015** | 221 | 9.2 | 34 | 1.4 | 248 | 10.5 | 2 | 0.1 | 332 | 13.9 | 33 | 1.4 |
| **2016** | 219 | 10.1 | 38 | 1.7 | 255 | 12.0 | 8 | 0.4 | 328 | 15.2 | 41 | 1.9 |
| **2017** | 216 | 9.4 | 33 | 1.4 | 247 | 11.0 | 2 | 0.1 | 329 | 14.3 | 29 | 1.3 |
| **Total** | 1119 | 9.7 | 173 | 1.5 | 1318 | 11.5 | 25 | 0.2 | 1691 | 14.6 | 185 | 1.6 |

Fetal and perinatal mortality rates per 1,000 births; infant mortality rate per 1,000 live births.
MR = mortality rate; CS = congenital syphilis.

Moreover, 1,691 perinatal deaths were recorded; 185 (10.9%) were due to CS. The mean perinatal mortality rate (PMR) was 14.6 per 1,000 births, and the mean PMR due to CS was 1.6 per 1,000 births (Table 1); most were observed in pregnant women aged from 20 to 34 years (n = 108; 58.3%).

Regarding education level, over half of the deaths (n = 143; 77.3%) were related to mothers who complete high school and were without income (n = 140; 75.7%). Regarding the PMR, a higher risk of death due to CS was observed in pregnant women aged < 19 years (3.4 per 1,000 births), with complete high school (2.3 per 1,000 births), and without income (2.2 per 1,000 births) (Table 2).

**Table 2.** Sociodemographic, epidemiological, clinical, and care profile of pregnant women and their infants who suffered perinatal death due to CS. Recife, Pernambuco, Brazil, 2013 to 2017

| Variables | N | % | PMR* |
|---|---|---|---|
| **Age group** | | | |
| < 19 years | 63 | 34.0 | 3.4 |
| 20 to 34 years | 108 | 58.3 | 1.3 |
| ≥ 35 years | 14 | 7.5 | 1.4 |
| **Education level** | | | |
| No education | 0 | - | - |
| Elementary school | 7 | 3.8 | 1.4 |
| Middle school | 27 | 14.6 | 1.0 |
| High school | 143 | 77.3 | 2.3 |
| Bachelor's degree | 2 | 1.1 | 0.1 |
| Ignored | 6 | 3.2 | - |
| **Occupation** | | | |
| With remuneration | 41 | 22.2 | 0.7 |
| Without remuneration | 140 | 75.7 | 2.3 |
| Ignored | 4 | 2.1 | - |
| **History of previous pregnancies**** (1) | | | |
| Live births | 124 | 67.0 | - |
| Fetal losses and abortions | 104 | 56.2 | - |
| Ignored | 2 | 1.0 | - |
| **Gestational week at birth** | | | |
| Premature (< 37weeks) | 166 | 89.7 | 11.8 |
| Full-term (≥ 37 weeks) | 19 | 10.3 | 0.2 |
| **Type of pregnancy** | | | |
| Single | 181 | 97.8 | 1.6 |
| Twin | 4 | 2.2 | 1.6 |
| **Type of birth** | | | |
| Vaginal | 168 | 90.8 | 3.1 |
| Cesarean | 15 | 8.1 | 0.2 |
| Ignored | 2 | 1.1 | - |

| | | | |
|---|---|---|---|
| **Sex of the infant** | | | |
| Male | 95 | 51.3 | 1.6 |
| Female | 87 | 43.8 | 1.5 |
| Ignored | 3 | 1.5 | - |
| **Race of the infant**** (1) | | | |
| Non-black (white) | 1 | 4.7 | - |
| Black (black + brown) | 17 | 81.0 | - |
| Ignored | 3 | 16.0 | - |
| **Weight at birth** | | | |
| Low (< 2500 g) | 148 | 80.0 | 15.0 |
| Normal (≥ 2500 g) | 34 | 18.4 | 0.3 |
| Ignored | 3 | 1.6 | - |

* Ignored variables were excluded from the calculation.
**Variable with more than one answer.
***Only for infant deaths.
(1) Perinatal mortality rate was not calculated for this variable.
CS = congenital syphilis; PMR = perinatal mortality rate.

Among all perinatal deaths due to CS, over half of pregnant women (n = 104; 56.2%) had a previous fetal loss or abortion. Most of these deaths were observed from premature births (n = 166; 89.7%, PMR of 11.8 per 1,000 births), single pregnancies (n = 181; 97.8%, PMR of 1.6 per 1,000 births), and vaginal birth (n = 168; 90.8%, PMR of 3.1 per 1,000 births). Additionally, 95 (51.3%) deaths due to CS occurred in male infants and with low weight at birth (n = 148; 80.0%, PMR of 15.0 deaths per 1,000 births). Furthermore, 17 (81.0%) deaths occurred in infants assigned as black (Table 2).

In 2017, 35 deaths due to CS were registered; 27 (77.1%) pregnant women received prenatal care. Fourteen (51.8%) of these women initiated prenatal care in the second trimester of pregnancy, and 23 (85.1%) received care at a basic health unit through the FHS. Furthermore, 23 (85.2%) pregnant women attended fewer than six prenatal appointments (Table 3).

Among the pregnant women who received prenatal care, seven (25.9%) were tested for syphilis and six (22.2%) did not undergo any testing. However, the investigation and summary forms of 14 (51.9%) deaths lacked records of syphilis testing, and 20 (74.1%) had no information concerning visits by a community health agent (Table 3).

All births occurred in hospitals or maternities: 33 (94.3%) were public healthcare facilities, 30 (85.7%) were premature births, and 33 (94.3%) were from single pregnancies. Additionally, 30 (85.7%) were vaginal births, and 100% underwent a rapid syphilis testing (Table 3).

**Table 3.** Characteristics of prenatal care, birth, and fetal and infant deaths due to CS. Recife, Pernambuco, Brazil, 2017.

| Section | Variables | N | % |
|---|---|---|---|
| Perinatal | **Complete prenatal care** | | |
| | Yes | 27 | 77.1 |
| | No | 8 | 22.9 |
| | **Start of prenatal care** | | |
| | First trimester | 8 | 29.6 |
| | Second trimester | 14 | 51.8 |
| | Third trimester | 4 | 14.8 |
| | Ignored | 1 | 3.7 |
| | **Facility where prenatal care was conducted** | | |
| | Family Health Strategy | 23 | 85.1 |
| | High-risk prenatal care unit | 1 | 3.7 |
| | Multiple facilities | 1 | 3.7 |
| | Ignored | 2 | 7.4 |
| | **Number of medical appointments** | | |
| | < 6 | 23 | 85.2 |
| | ≥ 6 | 4 | 14.8 |
| | **Testing for syphilis** | | |
| | Yes | 7 | 25.9 |
| | No | 6 | 22.2 |
| | Ignored | 14 | 51.9 |
| | **Visit from a community health agent during pregnancy** | | |
| | Yes | 7 | 25.9 |
| | Ignored | 20 | 74.1 |
| Birth | **Place of birth** | | |
| | Hospital/maternity | 35 | 100.0 |
| | Other health facilities | 0 | - |
| | **Gestational age** | | |
| | Premature (< 37 weeks) | 30 | 85.7 |
| | Full-term (≥ 37 weeks) | 4 | 11.4 |
| | Ignored | 1 | 2.8 |
| | **Type of pregnancy** | | |
| | Single | 33 | 94.3 |
| | Twin | 2 | 5.7 |
| | **Rapid syphilis testing at the maternity** | | |
| | Yes | 35 | 100.0 |
| | No | 0 | - |
| | **Type of birth** | | |
| | Vaginal | 30 | 85.7 |
| | Cesarean | 5 | 14.3 |
| | **Time spent by the newborn in the maternity*** | | |
| | ≥ 28 days | 1 | 50.0 |
| | Ignored | 1 | 50.0 |

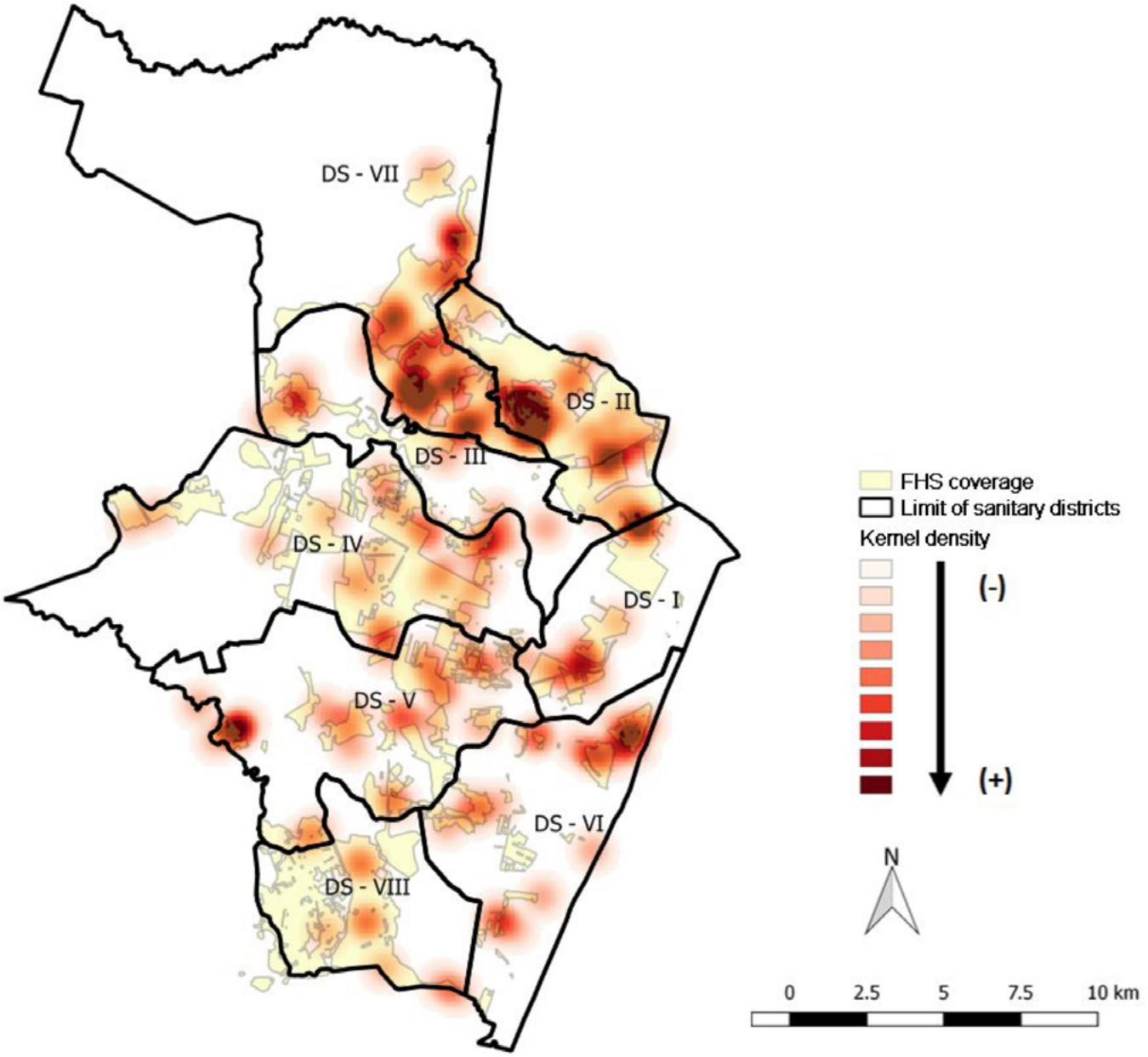
| | | | |
|---|---|---|---|
| **Occurrence of death** | **Place of death** | | |
| | Hospital/maternity | 35 | 100.0 |
| | Other health facilities | 0 | - |
| | **Type of facility** | | |
| | Public | 33 | 94.3 |
| | Private | 2 | 5.7 |

*Infant death.

CS = congenital syphilis .

Although fetal and infant deaths due to CS were observed throughout the territory of Recife, a higher density was found in the adjacency of the HD II and VII (north of the city). Death clusters were observed in the central region of the city (HD I), which is predominantly commercial, has a lower demographic density, and is mostly composed of a socially vulnerable population. Places of residence with deaths due to CS were mainly observed in unfavored socioeconomic regions of the HD V (west) and VI (south), which are areas with high population density. Interestingly, all clusters were identified in regions covered by the FHS (Figure 1).

**Figure 1.** Spatial distribution of fetal and infant deaths due to congenital syphilis. Recife (Pernambuco, Brazil), 2013 to 2017.




Source: Authors.

## DISCUSSION

In Recife, the PMR due to CS was 1.6 per 1,000 births; more than 85% were fetal deaths. Studies performed in all Brazilian regions showed that fetal and infant mortality rates due to CS indicated precarious basic maternal and infant care, reinforcing the hypothesis that these deaths could predict the quality of prenatal care[13, 14].

As CS is a preventable disease, a minimum threshold for mortality rate does not exist.

Thus, any death is unacceptable and indicates a failure in the public healthcare system. Nevertheless, the Pan American Health Organization and the Brazilian defined a rate of 0.5 per 1,000 live births as goal to eradicate CS[15] Ministry of Health[16].

Although most perinatal deaths from CS were observed in pregnant women aged from 20 to 34 years, the highest risk was detected in women aged < 19 years with completed high school and without income[17]. A study conducted in the state of Paraná (Brazil) demonstrated that adolescents were more susceptible to contracting syphilis due to developmental and emotional immaturity and early sexual activity without contraceptive methods. Additionally, pregnancy during adolescence often impair or interrupts education, hindering access to paid work[17].

Also, most perinatal deaths from CS were observed in infants assigned as black race. Race is a risk factor for infant death due to its association with the social context, both affected by limited access to healthcare services. The relationships between race and sociodemographic characteristics of the mother indicate that this profile is generally associated with an unfavorable socioeconomic condition and minimum access to healthcare services[17, 18].

Most deaths due to CS were observed in women with a history of fetal losses and abortions. Depending on the cause, the risk of fetal death in the following pregnancies is two to ten times higher, and fetal death in multiparous women is associated with a highly active syphilis[19].

Prematurity and low weight at birth must be highlighted in this study because of the higher risk of perinatal death due to CS. Low weight at birth may be associated with prematurity since it is considered an adverse event of CS. Death before 37 weeks of pregnancy depend on the stage of maternal infection and gestational age at which vertical transmission occurred, highlighting the importance of prevention. Therefore, testing for syphilis in the first trimester (especially at the first appointment) and at the beginning of the third trimester is essential. Nevertheless, when diagnosis cannot be performed, immediate treatment of the pregnant woman and her partner is recommended to prevent reinfection[4, 17].

The analysis of prenatal care in 2017 indicated that over a quarter of fetal and infant deaths did not receive treatment. However, 77% of the pregnant women received prenatal care, primarily through the FHS. This finding suggests a weakness in prenatal care, as over half of the pregnant women initiated it in the second trimester and attended fewer appointments than recommended by the Ministry of Health, hindering diagnosis and appropriate treatment. This result supports the findings of a study conducted in the state of Minas Gerais (Brazil), which correlated CS and late prenatal care to the failure to diagnose the disease in the first trimester of pregnancy[8].

Despite the high FHS coverage, prevention measures for CS are still poor. Specialized prenatal care is essential to reduce CS mortality[20]. Appropriate management to prevent vertical transmission involves early detection and appropriate treatment. In this sense, an active search

for pregnant women in the communities is needed to initiate prenatal care by the 12th week of pregnancy and implement interventions recommended by the Ministry of Health to timely eliminate maternal syphilis and vertical transmission. Promoting health and sexual and reproductive orientation is also necessary[17, 19].

In this study, many women ignored the question regarding syphilis testing during pregnancy and visits by a community health agent. These prenatal variables assessed in the form are important to investigate fetal and infant death, ensure a better understanding of the provided prenatal care, allow for a correct classification of preventable deaths, and propose measures to prevent further deaths[16, 21].

Although few participants responded to the question related to syphilis testing in the forms, 22.2% of the pregnant women who received prenatal care did not undergo any testing. This may indicate a failure in prenatal care since rapid and efficient testing for syphilis is available in healthcare services. Syphilis testing provides early access to syphilis results; thus, allowing for an early treatment even if the pregnant woman attends fewer appointments than recommended[22].

All pregnant women were tested for syphilis at the maternity hospital, following the recommendations of the Ministry of Health. Although birth is not the appropriate moment for diagnosis, the protocol includes treponemal and nontreponemal tests to indicate the best approaches for the mother and newborn[23].

The mapping of fetal and infant deaths from CS highlighted clusters in most HD. Recife has a territory composition that ranges from highly economically valued areas to structurally unfavored areas. Special zones of social interest with low-income populations and social and infrastructural vulnerability can also be identified in the territory[12].

This heterogeneity explains the distribution of CS throughout the territory and indicates social vulnerability as risk factor to death. A study conducted in the state of Rio de Janeiro (Brazil) indicated that limited access to services, education, work, and culture increased social vulnerability, reduced responsiveness in risk situations, and increased illnesses among the population[24].

Nonetheless, the result showed that most deaths occurred in areas covered by the FHS, which suggests problems in team performance or organization of the healthcare system that may compromise the quality and efficiency of the prenatal care provided[10].

The resoluteness of primary care depends on ordination in the work process and personnel capacitation to identify and attend to user needs[25]. A study conducted in Fortaleza (Ceará, Brazil) showed that some professionals from family health units were unaware of preventive measures to control CS[26]. Another study carried out in Londrina (Paraná, Brazil) also highlighted that insufficient knowledge of healthcare professionals in preventing vertical transmission hindered efforts to counter CS during prenatal care[27].

As the FHS is essential to counter vertical transmission, investing in permanent education to healthcare professionals may help develop adequate management practices and change the epidemiology scenario[28]. In the state of Paraná, an educational intervention for health professionals of basic health units improved prenatal care, indicated by a decrease in CS transmission and mortality rates[27].

The present study has limitations related to the use of secondary data, which depended on the quality of previous records. Despite this, the database and forms used were reliable, of good quality, and contained trustworthy information[29]. Nevertheless, the lack of studies investigating fetal, infant, and perinatal deaths due to CS using georeferencing tools underscores the importance of this study.

## CONCLUSION

Fetal and infant deaths from CS were observed mostly in black pregnant women aged < 19 years with complete high school and without income. Although most women received prenatal care through the FHS, over half of them started late and had fewer appointments than recommended. A concentration of deaths was observed in areas close to the FHS, suggesting weaknesses in team performance and systematization of health services; thus, impairing maternal and infant qualified healthcare.

The mortality due to CS is not only associated to primary care coverage but also to the quality of primary care provided. This is justified by the deaths, which indicates impaired prenatal care and failure to prevent vertical transmission.

## COMPETING INTERESTS

The authors declare no competing interests.

## AUTHORS CONTRIBUTION

All authors participated in all stages of the manuscript and approved the publication of the final version.

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# Clinical-epidemiological profile of individuals with schistosomiasis in Pernambuco state

## Perfil clínico-epidemiológico de indivíduos portadores de esquistossomose no estado de Pernambuco

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## Abstract

**Objective:** This study aimed to describe the clinical-epidemiological profile of schistosomiasis reported between 2017 and 2021 in Pernambuco state. **Methods:** This cross-sectional study was conducted using data from the Notifiable Diseases Information System, obtained from DATASUS, concerning schistosomiasis cases reported between 2017 and 2021 in Pernambuco, Brazil. Clinical-epidemiological variables analyzed were sex, age, ethnicity, level of education, clinical form, disease progression, quantitative analysis (colposcopy), and qualitative analysis (serological tests). Data was analyzed with descriptive statistics using Microsoft Excel® software. **Results:** A total of 906 cases of schistosomiasis were reported in Pernambuco, predominantly in males (53.1%) aged between 40 and 59 years (33.3%) and with Black ethnicity (68.7%). The most common clinical presentation was intestinal (31.6%), and 48.3% progressed to cure, while 11.0% died. Quantitative analysis showed the absence of eggs in 57.4% of individuals, and 39.9% tested positive in qualitative analysis. **Conclusion:** This study highlights schistosomiasis as a public health concern in Pernambuco state. Focus on educational efforts and control measures for vulnerable individuals is crucial to early detection, appropriate treatment,

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and review strategies of public health to fight schistosomiasis effectively in different regions.

**Keywords:** Schistosomiasis, Epidemiology, Neglected diseases, Brazil.

## Resumo

**Objetivo:** Este trabalho objetivou descrever o perfil clínico-epidemiológico dos casos notificados de esquistossomose no estado de Pernambuco (PE) entre 2017 e 2021. **Métodos:** Esse estudo transversal utilizou dados do Sistema de Informação de Agravos de Notificação (Sinan), obtidos no TABNET DATASUS, referentes a todos os casos de esquistossomose notificados em Pernambuco entre 2017 e 2021. Para o estudo, foram designadas variáveis clínico-epidemiológicas, como sexo, idade, raça/cor, escolaridade, forma clínica, evolução da doença, análise quantitativa (exame coproscópico) e análise qualitativa (testes sorológicos). Para a análise dos dados utilizou-se estatística descritiva simples, calculada no software de planilha eletrônica Microsoft Excel®. **Resultados:** Durante o período, houve 906 casos de esquistossomose em Pernambuco, com predominância em homens (53,1%), na faixa etária de 40 - 59 anos (33,3%) e em indivíduos negros (68,7%). A forma clínica mais comum foi a intestinal (31,6%). Do total, 48,3% evoluíram para a cura e 11,0% para o óbito. A análise quantitativa revelou que 57,4% dos casos não apresentaram ovos no exame, enquanto 39,9% tiveram resultado positivo na análise qualitativa. **Conclusão:** Este estudo evidenciou a esquistossomose como um problema de saúde pública em Pernambuco. É essencial direcionar esforços educativos e ações de controle para grupos vulneráveis, priorizando a detecção precoce e o tratamento adequado, além de revisar estratégias de saúde pública em diferentes regiões para combater a esquistossomose prontamente.

**Palavras-chave:** Esquistossomose, Epidemiologia, Doenças negligenciadas, Brasil.

## INTRODUCTION

Schistosomiasis is a parasitic disease with chronic progression caused by the helminth *Schistosoma mansoni*, also known as bilharziasis, snail fever, and water belly in Brazil[1]. Transmission requires a favorable environment and susceptible hosts. Humans are the definitive hosts, and infection occurs with skin penetration of cercariae, which evolves and migrates to the heart, lungs, and liver via circulatory and lymphatic systems. After maturation in the host, adult schistosomes reproduce, and the eggs become widespread in the environment with feces. These eggs are the active infective stage for the intermediate host, the snails of the genus *Biomphalaria*, which restart the transmission cycle when cercariae is release into freshwater[1, 2, 3].

Some factors contribute to the incidence and prevalence of schistosomiasis, such as the lack of basic sanitation, health education, control of snail populations, and contamination of water

sources of recreation, domestic activities, or agriculture. Additionally, adequate sunlight and high temperatures are favorable environmental conditions, contributing to transmission cycle[1, 2, 3, 4].

The World Health Organization estimates that schistosomiasis affects 240 million people worldwide, with over 700 million living in endemic areas at risk of disease[3]. Schistosomiasis is a neglected tropical disease associated with poverty and lack of resources for its eradication[4].

Schistosomiasis is prevalent in the Northeast and Southeast regions of Brazil, mainly in Alagoas, Bahia, Pernambuco, Rio Grande do Norte, Paraíba, Sergipe, Espírito Santo, Maranhão, and Minas Gerais[5]. In Pernambuco, the transmission of *S. mansoni* is endemic in 102 of the 186 municipalities, especially in coastal rainforest zones and coastal regions[6].

The Schistosomiasis Surveillance and Control Program Information System records data in endemic areas. Whereas, in non-endemic areas, a positive diagnosis requires mandatory notification by the Notifiable Diseases Information System using the schistosomiasis investigation form. Monitoring enhances the understanding of the epidemiological scenario to improve public policies[5]. Therefore, this study aimed to describe the clinical-epidemiological profile of schistosomiasis cases between 2017 and 2021 in Pernambuco state.

## METHODOLOGY

This cross-sectional study used secondary data from the Notifiable Diseases Information System, obtained from DATASUS, to analyze all reported cases of schistosomiasis between 2017 and 2021 in Pernambuco, Brazil. Clinical-epidemiological variables (sex, age, ethnicity, level of education, clinical form, disease progression), quantitative analysis (colposcopy), and qualitative analysis (serological tests) were analyzed.

After data collection, tabulation was followed by simple descriptive analysis using Microsoft Excel®software. Absolute and relative frequency were calculated and presented in tables. Given the exclusive use of data from the public domain, this study was free from submission to the research ethics committee. All procedures followed resolution no. 466/2012 of the National Health Council of Brazil.

## RESULTS

A total of 906 cases of schistosomiasis were identified, 481 (53.1%) were males, 302 (33.3%) aged between 40 and 59 years, and 622 (68.7%) self-identified as Black (Table 1). Regarding level of education, 306 (33.7%) had completed or incomplete elementary school, 79 (8.7%) were illiterate, and 348 (38.4%) did not answer.

**Table 1.** Epidemiological profile of individuals with schistosomiasis between 2017 and 2021 in Pernambuco state

| Variables | N=906 | % |
|---|---|---|
| **Sex** | | |
| Male | 481 | 53.1 |
| Female | 425 | 46.9 |
| **Age group (years)** | | |
| <1 ano | 4 | 0.4 |
| 1-4 | 5 | 0.5 |
| 5-9 | 15 | 1.7 |
| 10-14 | 18 | 2.0 |
| 15-19 | 15 | 1.7 |
| 20-39 | 257 | 28.4 |
| 40-59 | 302 | 33.3 |
| 60-64 | 81 | 8.9 |
| 65-69 | 80 | 8.8 |
| 70-79 | 71 | 7.9 |
| 80+ | 57 | 6.3 |
| Not answered | 1 | 0.1 |
| **Ethnicity** [1] | | |
| Balck | 622 | 68.7 |
| Non-black | 183 | 20.2 |

Source: Notifiable Diseases Information System - DATASUS

[1] Ethnicity: 9 Yellow (1.0%), 2 Indigenous (0.2%), 90 did not answer (9.9%).

The most prevalent clinical presentation observed was the intestinal form, with 286 (31.6%) cases, followed by hepatosplenic, with 122 (13.5%) cases. The disease progression showed 438 individuals (48.3%) that evolved to cure and 100 (11%) to death. Due to missing data (marked as not answered), the disease outcome was unknown in 266 (29.4%) cases.

Regarding quantitative analysis, 520 (57.4%) individuals with schistosomiasis did not present fecal eggs in the examination, indicating a low parasite load. Qualitative analysis showed that 362 (39.9%) results were positive, while 190 (21%) did not perform the serological test (Table 2).

**Table 2.** Clinical profile of individuals with schistosomiasis between 2017 and 2021 in Pernambuco state

| Variables | N=906 | % |
|---|---|---|
| **Notified clinical form** | | |
| Intestinal | 286 | 31.6 |
| Hepatointestinal | 82 | 9.0 |
| Hepatosplenic | 122 | 13.5 |
| Acute | 24 | 2.6 |
| Other forms | 67 | 7.4 |
| Not answered | 325 | 35.9 |
| **Disease progression** | | |
| Cure | 438 | 48.3 |
| No Cure | 63 | 7.0 |
| Death due to schistosomiasis | 100 | 11.0 |
| Death due to other causes | 39 | 4.3 |
| Not answered | 266 | 29.4 |
| **Quantitative analysis** | | |
| Zero egg | 520 | 57.4 |
| One or more eggs | 386 | 42.6 |
| **Qualitative analysis** | | |
| Positive | 362 | 39.9 |
| Negativ2 | 59 | 6.5 |
| Not analyzed | 190 | 21.0 |
| Not answered | 295 | 32.6 |

Source: Notifiable Diseases Information System - DATASUS

## DISCUSSION

The results of this study emphasize the persistence of schistosomiasis cases in Pernambuco state. The male population was the most prevalent, corroborating previous studies[7, 8]. The distribution of cases by sex may be attributed to behavioral differences or risk exposure, such as cultural resistance to health education initiatives among male and their prevalence in agriculture and fishing activities, with more exposure to potentially contaminated water[8 ,9].

Regarding age group, most cases occurred between 40 and 59 years. However, studies in the Northeast region of Brazil indicated a prevalence between ages of 20 and 39 years, with ages of 31 to 40 years being the most affected in Pernambuco[8, 10]. Despite differences among data, these ages encompass economically active individuals and might be related to the riverside population, which is more exposed to contamination factors due to their occupation[11].

The assessment of ethnicity showed a predominance of Black individuals. Furthermore, the level of education demonstrated that individuals had complete or incomplete primary education. These results are consistent with previous studies, emphasizing their importance to the de-

velopment of public policies and highlighting the need for broader and more effective educational campaigns since a lower level of education may increase susceptibility to diseases[6, 12, 13].

The most prevalent clinical presentation of schistosomiasis was the intestinal form, followed by the hepatosplenic form, which is more complex and severe, affecting intestine, liver, and spleen. Both forms occur in the chronic phase of the disease, leading to late diagnosis or ineffective treatment[1]. A study conducted between 2011 and 2020 in Minas Gerais state reported similar rates, with prevalence of intestinal form[13].

Concerning disease progression, cure was observed in most cases, which was consistent with other studies[12, 14]. Vale ressaltar que os indivíduos curados continuam suscetíveis à reinfecção, visto que, Cured individuals remain susceptible to reinfection since usually the only available water source in the region is contaminated[10]. These findings highlight the importance of early detection, proper treatment, health education, and the need to eliminate the intermediate host.

Moreover, 11% of cases evolved to death. According to the epidemiological bulletin of 2022, schistosomiasis caused 6,130 deaths from 2010 to 2022 in Brazil, with 472 deaths per year[5]. Schistosomiasis continues to present in severe forms that lead to death[1, 2, 15]despite being an easily diagnosed and treatable disease (single oral dose of praziquantel). This underscores the negligence regarding this parasitic disease, which occurs in areas of low visibility and limited political support, adding to the lack of interest of the pharmaceutical industry to develop more effective treatments despite advances in medicine[2, 16].

Regarding quantitative analysis, 42.6% of positive cases demonstrated a low parasite load (one to four eggs). This finding corroborates studies performed in Paraíba[16] and Bahia[17] from 2004 to 2014 and from October 2016 to November 2016, respectively. Parasite load, determined using the Kato-Katz method, is essential to confirm the diagnosis and assess the intensity of the disease, monitoring treatment efficacy. Individuals with low parasite load (below 16 eggs per gram of feces) frequently experience intestinal symptoms, such as bleeding and diarrhea. Conversely, high parasite load (above 17 eggs per gram of feces) frequently presents severe symptoms, including hepatosplenomegaly and pulmonary and renal imparment[1, 2, 17, 18].

Furthermore, qualitative analysis indicates only the presence or absence of parasite eggs and relies on indirect methods, depending on clinical, immunological, and biochemical parameters associated with the disease. Complementary serological tests (e.g., enzyme-linked immunosorbent assay and indirect immunofluorescence for immunoglobulin M) are recommended in non-endemic and low-prevalence areas, especially for individuals with immunodeficiency or lower parasitemia[1, 15, 18].

Due to a lack of data, the outcome of parasitic disease was not answered in 29.4% of cases. This absence of information could be associated with changes in policies and engagement of

individuals, in addition to the focus of health services on the COVID-19 pandemic between 2020 and 2022[6, 19]. Incompleteness of data should not be underestimated, resulting in null or ignored values in records of the Integrated Health System[20,21]

Data on the level of education and clinical profile variables[21,22]demonstrated a gap that may compromise the accuracy of analyses and interpretations, highlighting the importance of complete and consistent data collection and analysis. The appreciation of these stages improves quality of notification systems providing an accurate and comprehensive overview of schistosomiasis that guides effective interventions and health policies in prevention and treatment.

## CONCLUSION

The epidemiological profile of schistosomiasis in Pernambuco state was characterized by Black male individuals aged between 40 and 59 years with completed or incomplete elementary school. Additionally, the intestinal form was the most prevalent, with low parasite load, and individuals evolved to cure. Therefore, schistosomiasis remains a public health issue in Pernambuco state. Consequently, educational efforts and control actions need to target the identified vulnerable individuals, reducing the incidence and promoting preventive education.

Furthermore, besides medical aspects, socioeconomic and behavioral factors significantly influence disease spread. Consequently, prevention and control strategies need to incorporate approaches that consider these factors and aim to mitigate inequalities and promote universal access to healthcare.

Therefore, continuous epidemiological surveillance and completeness of information systems are essential for a comprehensive and effective response, allowing a flexible and agile reaction to changes in disease profile and socioeconomic conditions of individuals.

## CONFLICT OF INTEREST

Nothing to disclosure.

## AUTHOR CONTRIBUTIONS

**AVF** - conceptualization, methodology development, results validation, drafting of the original manuscript, article review and editing; **COB** - literature review, data collection, and validation, and article writing; **ACLC** - participated in the conceptualization of introduction; **JBSN** and **VVFP** - data validation, supervision and guidance of execution of the article, correction and final drafting of the manuscript. All authors approved the final version.

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# Morphometric analysis of the internal auditory canal and its clinical-surgical implications

## Análise morfométrica do meato acústico interno e suas implicações clínico-cirúrgicas

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## Abstract

**Introduction**: The internal auditory canal (IAC) is a short and narrow bone canal close to some bone openings, such as the jugular foramen, allowing the passage of important structures. **Objective**: To assess the morphometric measures of the IAC in human skulls, analyse its microanatomy, and elucidate clinical-surgical implications associated with this canal. **Methods**: This cross-sectional, descriptive, and comparative study analysed 30 human skulls regardless of sex, age, or ancestry. Statistical analysis was conducted using SPSS software. **Results**: The vertical diameter of the IAC was 3.5 ± 0.92 mm in the right antimere (RA) and 3.7 ± 0.92 mm in the left antimere (LA), while the horizontal diameter was 4.8 ± 1.01 mm in the RA and 4.6 ± 1.20 mm in the LA. The upper length of the IAC was 10.3 ± 1.76 mm in the RA and 10.40 ± 1.56 mm in the LA, while the lower length was 9.1 ± 1.72 mm in the RA and 9.6 ± 1.54 mm in the LA. **Conclusions**: The right and left antimeres showed significant differences in three specific variables: upper length of the IAC, distance from the lateral or external edge of the IAC to the groove of the sigmoid sinus, and distance from the lateral or external edge of the IAC to the external opening of the vestibular aqueduct.

**Keywords:** Anatomy; Anthropometry; Ear canal; Temporal bone.

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## Resumo

**Introdução:** O meato acústico interno (MAI) é um canal ósseo curto e estreito próximo a algumas aberturas ósseas, como o forame jugular, e que dá passagem a estruturas importantes. **Objetivo**: Avaliar as medidas morfométricas do MAI em crânios humanos secos, proporcionar uma análise detalhada da microanatomia da região e elucidar as implicações clínico-cirúrgicas associadas ao canal. **Métodos:** Trata-se de um estudo transversal e descritivo comparativo no qual foram analisados 30 crânios humanos, sem distinção de sexo, idade e ancestralidade. A análise estatística foi conduzida utilizando o software SPSS. **Resultados:** O diâmetro vertical do MAI foi 3,5 ± 0,92 mm no antímero direito (AD) e 3,7 ± 0,92 mm, no antímero esquerdo (AE). O diâmetro horizontal do MAI foi 4,8 ± 1,01 mm no AD e 4,6 ± 1,20 mm no AE. O comprimento superior do MAI foi 10,3 ± 1,76 mm no AD e 10,4 ± 1,56 mm no AE. O comprimento inferior do MAI foi 9,1 ± 1,72 mm no AD e 9,6 ± 1,54 mm no AE. **Conclusões:** Foram encontradas diferenças estatisticamente significativas entre os lados direito e esquerdo em três variáveis específicas: o comprimento superior do MAI, a distância da borda lateral ou externa do MAI até o seio do sulco sigmoide e a distância da borda lateral ou externa do MAI até a abertura externa do aqueduto vestibular.

**Palavras-chave:** Anatomia, Antropometria, Meato acústico; Osso temporal.

## INTRODUCTION

The internal auditory canal (IAC) is a short and narrow bone canal located approximately one centimeter from the internal part of the temporal bone and closed by a thin perforated bone plate that separates it from the inner ear[1]. Also, the IAC is close to bone openings (e.g., jugular foramen) and allows the passage of important structures, such as the facial and vestibulocochlear nerves (VII and VIII nerves, respectively), labyrinthine artery, and vestibular ganglion, which are crucial for the auditory and vestibular systems[1,2].

The VII pair innervates the facial mimicry, stapedius, stylohyoid, and posterior belly of the digastric muscles through a motor root forming the nerve[3,4]. The nervus intermedius (also known as intermediate nerve of Wrisberg) is the sensitive and visceral root responsible for innervating the lacrimal, submandibular, and sublingual glands, controlling the production of tears and saliva[3,4]. It also conducts the taste to the anterior two-thirds of the tongue and provides sensibility to part of the external ear, ear canal, and posterior areas of the nasal cavities and soft palate[3,4]. The vestibular portion of the VIII pair influences the ocular and cephalic movements and trunk and limb muscles, contributing to the maintenance of balance, while the cochlear portion is responsible for hearing sensitivity[3,4].

Clinically, the IAC has structural relevance in forming cavernous angiomas, neuromas, malformations, or cavernomas, which may influence the functions of the related cranial nerves[3,4].

Considering the advances in endoscopic surgery and microsurgery, the topographic study associating cranial nerves with IAC has been impacting the understanding of possible anatomic variations and their clinical implications[5,6]. Some studies observed variations in the length, width, and shape (e.g., funnel, cylindrical, or round), and these parameters are important for the safety and efficacy of the surgical procedures involving the IAC[5,6].

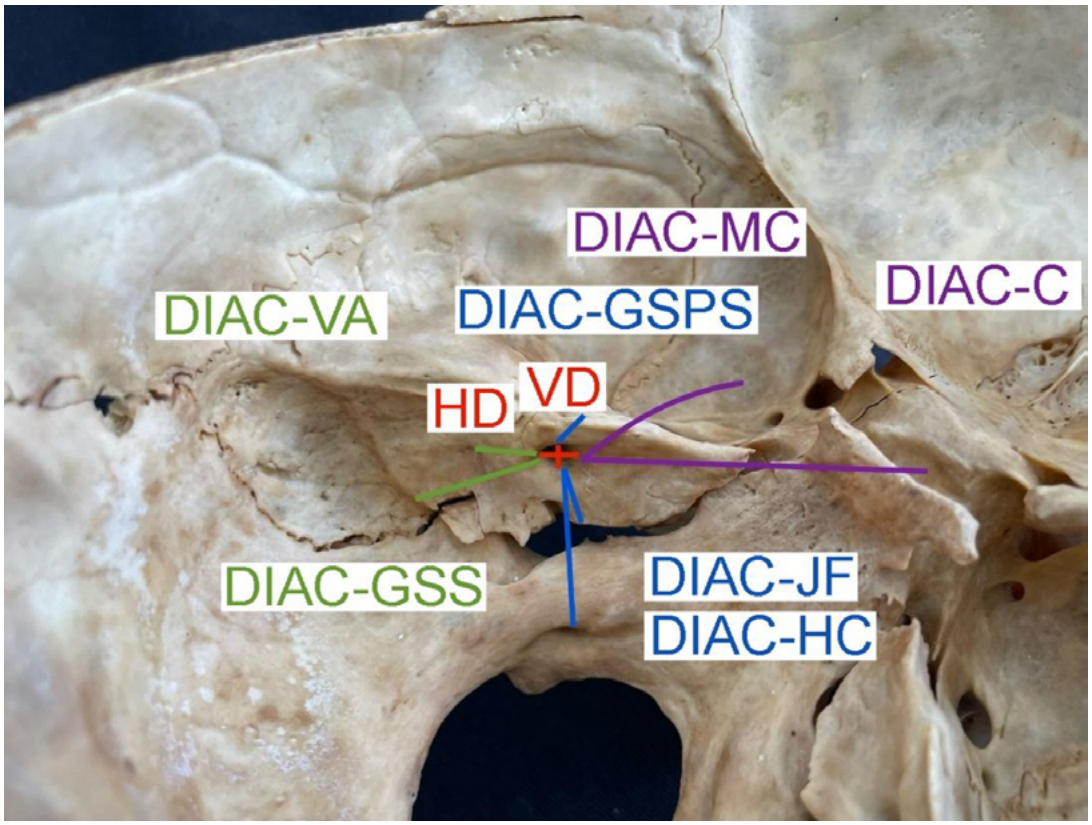
Despite the current evidence, a lack of data was observed in literature regarding the morphometric assessment of the IAC in human skulls and their distances from the adjacent structures. Thus, the present study aimed to assess the morphometric measures of the IAC in human skulls, providing a detailed analysis of its microanatomy and elucidating the clinical-surgical implications associated with this canal.

## METHODS

This cross-sectional, comparative, and descriptive study analysed 30 human skulls (60 cm) regardless of sex, age, or ancestry from cadaveric pieces of a higher education institution using a non-probability and convenience sampling. All damaged skulls were excluded from the study, and both antimeres were analysed to measure the variables.

The present study was organized into two steps: morphologic classification and morphometric measures. Regarding the morphometric measures, the following parameters (Figures 1 and 2) were obtained in the right and left antimeres using a Castroviejo-type curved dry-point compass and a caliper:

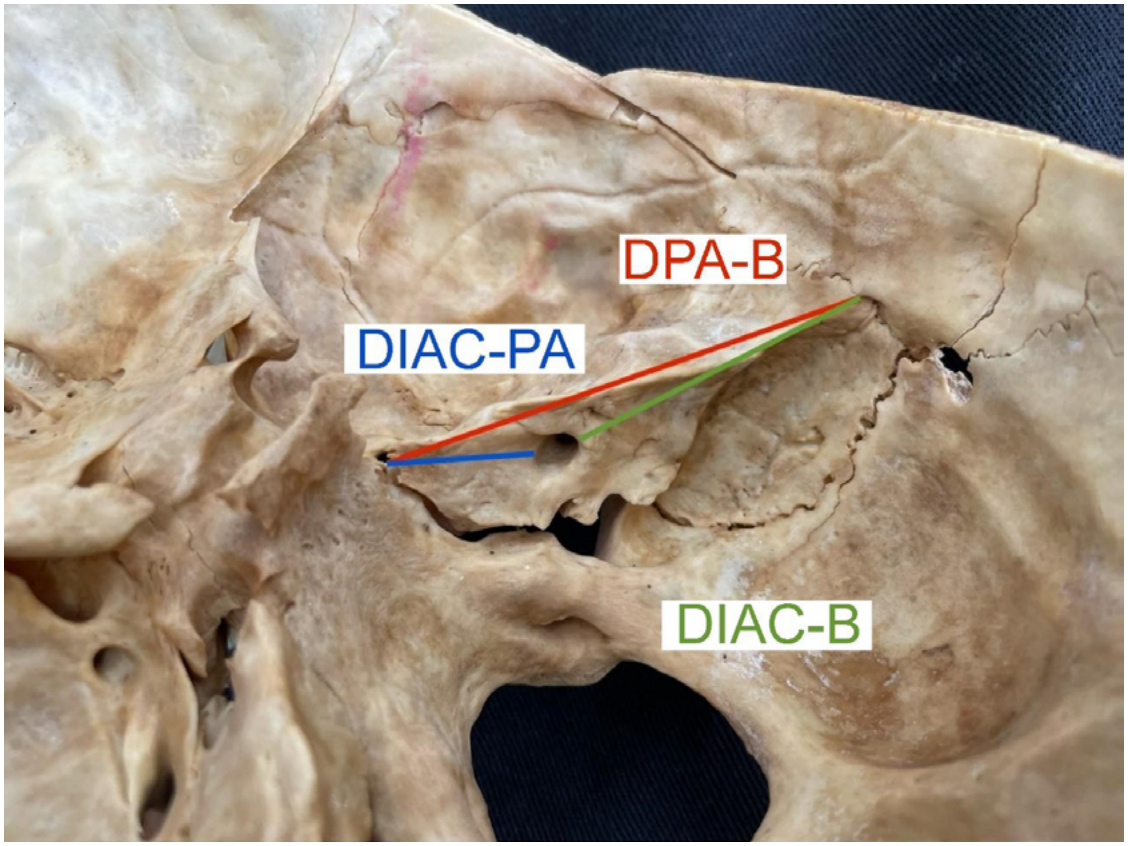
**Figure 1.** Superomedial view of the left temporal bone showing the morphometric measures.




VD: vertical diameter of the internal auditory canal (IAC); HD: horizontal diameter of the IAC; DIAC-JF: distance between the IAC and jugular foramen; DIAC-HC: distance between the IAC and hypoglossal canal; DIAC-GSPS: distance between the IAC and groove for the superior petrosal sinus; DIAC-gSS: distance between the IAC and groove of the sigmoid sinus; DIAC-VA: distance between the IAC and vestibular aqueduct; DIAC-C: distance between the PAI and clivus; DIAC-MC: distance between the PAI and Meckel's cave.

1. VD: vertical diameter (superior-inferior or dorsoventral) of the internal auditory canal (IAC);
2. HD: horizontal diameter (anteroposterior or rostral-caudal) of the IAC;
3. Upper length of the IAC: distance from the superior margin of the IAC to the most lateral point at the bottom in the region of the cribriform plate for the superior vestibular nerve;
4. Lower length of the IAC: distance from the inferior margin of the IAC to the most lateral point at the bottom in the region of the cribriform plate for the inferior vestibular nerve;
5. DIAC-JF: distance between the inferior edge of the IAC and jugular foramen (jugular notch of the temporal bone);
6. DIAC-HC: distance from the inferior edge of the IAC to the hypoglossal canal;
7. DIAC-GSPS: distance from the superior edge of the IAC to the groove for the superior petrosal sinus (superior edge of the petrosal triangle);
8. DIAC-GSS: distance from the lateral or external edge of the IAC to the groove of the sigmoid sinus;
9. DIAC-VA: distance from the lateral or external edge of the IAC to the external opening of the vestibular aqueduct;
10. DIAC-C: distance from the medial or internal edge of the IAC to the clivus;
11. DIAC-MC: distance from the medial or internal edge of the IAC to the Meckel's cave;
12. DPA-B: distance from the petrous apex to the base of the petrous part of the temporal bone;
13. DIAC-PA: distance from the medial or internal edge of the IAC to the petrous apex;
14. DIAC-B: distance from the lateral or external edge of the IAC to the base of the intracranial petrous part of the temporal bone.

**Figure 2.** Superomedial view of the right temporal bone showing morphometric measures.




DPA-B: distance between the petrous apex and base of the petrous part of the temporal bone; DIAC-PA: distance between the internal auditory canal (IAC) and petrous apex; DIAC-B: distance between the IAC and base of the petrous part of the temporal bone.

The format of the IAC was observed as a non-morphometric parameter, which can be classified as type I to VI, according to Unur *et al*. (2007):

Type I: round

Type II: oval

Type III: U-shaped

Type IV: fissure

Type V: irregular

Type VI: V-shaped

The SPSS® software (IBM Corp., Chicago, EUA) was used for statistical analyses. The paired *t*-test was used for comparison between means, and statistical significance was set at $p < 0.05$.

## RESULTS

Table 1 presents the results of measures and variations. VD varied from 1.5 to 5.5 mm (3.50 ± 0.92 mm) in the right antimere and from 2.50 to 5.50 mm (3.70 ± 0.92 mm) in the left antimere, while the HD varied from 3 to 7.50 mm (4.80 ± 1.01 mm) in the right antimere and from 2 to 8.50 mm (4.60 ± 1.20 mm) in the left antimere. The upper length of the IAC varied from 8 to 15 mm (10.30 ± 1.76 mm) in the right antimere and from 8 to 14 mm (10.40 ± 1.56 mm) in the left antimere, while the lower length varied from 6 to 13 mm (9.10 ± 1.72 mm) in the right antimere and from 7 to 12 mm (9.60 ± 1.54 mm) in the left antimere.

**Table 1.** Comparison of diameters, lengths, and distances of the IAC in the right and left antimeres.

| Measure | Right antimere (mean ± SD) | Left antimere (mean ± SD) | *t*-test | p-value |
|---|---|---|---|---|
| VD | 3.5 ± 0.92 | 3.7 ± 0.92 | -1.507 | 0.143 |
| HD | 4.8 ± 1.01 | 4.6 ± 1.20 | 1.718 | 0.097 |
| ULIAC | 10.3 ± 1.76 | 10.4 ± 1.56 | -0.571 | 0.573 |
| LLIAC | 9.1 ± 1.72 | 9.6 ± 1.54 | -2.151 | 0.040* |
| DIAC-JF | 6.2 ± 1.36 | 6.5 ± 1.36 | -1.730 | 0.094 |
| DIAC-HC | 19.7 ± 2.38 | 19.5 ± 2.42 | 1.101 | 0.280 |
| DIAC-GSPS | 4.8 ± 0.90 | 4.6 ± 1.03 | 1.087 | 0.286 |
| DIAC-GSS | 22.1 ± 2.46 | 23.4 ± 2.46 | -3.060 | 0.005* |
| DIAC-VA | 10.2 ± 2.49 | 11.3 ± 2.55 | -2.488 | 0.019* |
| DIAC-C | 35.8 ± 2.96 | 35.1 ± 2.78 | 1.287 | 0.208 |
| DIAC-MC | 32.5 ± 3.39 | 31.9 ± 2.66 | 1.357 | 0.185 |
| DPA-B | 57.0 ± 4.02 | 56.1 ± 4.20 | 1.766 | 0.088 |
| DIAC-PA | 19.2 ± 2.93 | 18.7 ± 2.68 | 1.438 | 0.161 |
| DIAC-B | 35.9 ± 3.23 | 34.8 ± 3.91 | 1.994 | 0.056 |

* Statistically significant ($p < 0.05$) – t-test.

VD: vertical diameter of the internal auditory canal (IAC); HD: horizontal diameter of the IAC; ULIAC: upper length of the IAC; LLIAC: lower length of the IAC; DIAC-JF: distance between the IAC and jugular foramen; DIAC-HC: distance between the IAC and hypoglossal canal; DIAC-GSPS: distance between the IAC and groove for the superior petrous sinus; DIAC-GSS: distance between the IAC and groove of the sigmoid sinus; DIAC-VA: distance between the IAC and vestibular aqueduct; DIAC-C: distance between the IAC and clivus; DIAC-MC: distance between the IAC and Meckel's cave; DPA-B: distance between the petrous apex and base of the petrous part of the temporal bone; DIAC-PA: distance between the IAC and petrous apex; DIAC-B: distance between the IAC and the base of the petrous part of the temporal bone; SD: standard deviation.

The following measures were obtained in the antimeres: DIAC-JF varied from 4 to 9.5 mm (6.20 ± 1.36 mm) in the right and from 4 to 9.5 mm (6.50 ± 1.36 mm) in the left; DIAC-HC varied from 14.5 to 24.5 mm (19.7 ± 2.38 mm) in the right and from 15 to 24 mm (19.5 ± 2.42 mm) in the left; DIAC-GSPS varied from 2.5 to 6.5 mm (4.80 ± 0.90 mm) in the right and from 2.5 to 6.5 mm (4.60 ± 1.03 mm) in the left; DIAC-GSS varied from 16.50 to 28 mm (22.10 ± 2.46 mm) in the right and from 17 to 28.50 mm (23.40 ± 2.46 mm) in the left; DIAC-VA varied from 7 to 18.5 mm (10.20 ± 2.49 mm) in the right and from 7.5 to 17 mm (11.30 ± 2.55 mm) in the left; DIAC-C varied from 29.50 to 41.5 mm (35.80 ± 2.96 mm) in the right and from 30 to 40.5 mm (35.10 ± 2.78 mm) in the left; DIAC-MC varied from 25 to 37.5 mm (32.50 ± 3.39 mm) in the right and from 28 to 37 mm (31.90 ± 2.66 mm) in the left; DPA-B varied from 46 to 66 mm (57 ± 4.02 mm) in the right and from 48 to 64 mm (56.10 ± 4.20 mm) in the left; DIAC-PA: varied from 12 to 24.50 mm (19.20 ± 2.93 mm) in the right and from 11 to 23 mm (18.70 ± 2.68 mm) in the left; and DIAC-B varied from 27 to 42 mm (35.90 ± 3.23 mm) in the right and from 25.50 to 42 mm (34.80 ± 3.91 mm) in the left.

A comparative analysis of the diameters, lengths, and distances was performed on both antimeres using the paired *t*-test, and the results are presented in Table 1 as mean and standard deviation. Significant differences between the right and left antimeres were observed in three specific variables: upper length of the IAC, DIAP-GSS, and DIAP-VA.

The most common type of IAC was the oval, present in 36.6% (n = 22) of all temporal bones, followed by the round, found in 30% (n = 18). The oval type was the most common in the right IAC, corresponding to 44.3% (n = 13), while the oval and round types showed the same frequency in the left IAP, with 3% each (n = 9). The irregular (i.e., the least common) type was not observed in temporal bones.

## DISCUSSION

Considering the embryological aspect, the IAC is developed from the chondrification and ossification of the mesodermal layer, which surrounds the VII and VIII nerves at the petrous part of the temporal bone in the posterior cranial fossa[2,7]. Although the IAC lengthens as the skull increases in size until approximately ten years old, the diameter of the medial opening only increases slightly during the first year of life[2].

Most individuals present only one canal; however, literature describes approximately 21 rare cases of doubled IAC associated with inner ear malformations and frequently related to stenosis in this region[7]. Thus, an adequate morphometric assessment of the IAC is essential to develop a database related to the anatomy of intracranial pathologies. It may also support microsurgery techniques to approach the cerebellopontine angle and vestibular schwannoma, enhancing the protection of the related structures (e.g., inner ear and VII and VIII nerves)[8].

The assessment of anatomical patterns of the IAC may determine the need for a surgical

approach[8] in specific conditions, such as congenital abnormalities, cranial trauma, and peripheral nerves and ear pathologies. The IAC measures also indicate pathologies (e.g., tumors and stenosis), confirming the relevance of its morphometry in both antimeres[8]. Also, literature has described regional and ethnic aspects and variations between antimeres as factors for morphometric differences of the IAC[8].

A study using high-resolution computed tomography in 128 patients (83 with inner ear malformations and 45 without changes) showed a mean diameter of the IAC of approximately 5.5 mm, corroborating the left antimere of the present study, but higher than the diameter observed in the right antimere[9]. A measure of approximately 2 mm width is considered adequate for a neurovascular bundle, and a smaller diameter indicates a narrow canal related to aplasia of the cochlear portion of the VIII nerve and congenital sensorineural hearing loss. Also, studies reported that a difference > 2 mm in the diameter between IAC antimeres might be a tumor marker[1,6,9]. The largest left HD found in this study was 8.5 mm; a diameter > 8 mm is considered enlarged and may be associated with tumors, such as vestibular schwannomas and facial neuromas (less frequent)[6,10].

A retrospective study with 142 healthy individuals (18 to 60 years old) showed that the mean length of IAC was 9.71 mm (right) and 9.92 mm (left), and the diameter was 3.97 mm (right) and 3.95 mm (left), corroborating the present study. Differences in the IAC morphometry may be due to ethnic and regional aspects and variations between antimeres, and a study reported a difference related to sex, which is still unclear[1].

The morphometric data of the IAC are important to assess patients with pathologies in this region, such as vestibular schwannoma (i.e., the most common tumor), due to its proximity with the cerebellopontine angle[2]. Although benign, vestibular schwannomas may cause microvascular compression in the VII and VIII nerves, leading to tinnitus, vertigo, and hemifacial spasms. Also, these tumors present a high potential to expand to the cerebellopontine angle[2,11], and the retrosigmoid approach is indicated in these cases. However, the unawareness of the morphometry of IAC and related structures may cause injuries on the anterior inferior cerebellar artery and VII, IX, and X nerves[8].

Understanding the IAC parameters and orientation and position in the petrous part of the temporal bone is important for translabyrinthine approaches since the unawareness of these data may lead to VII nerve injury[12]. The diameter and length are also relevant for the most recent approaches, such as the minimally invasive transcanal transpromontorial through the external ear canal[13]. In addition, the morphometry of the IAC supports the understanding of its development in pediatric patients, ensuring safety in procedures involving this region[12].

Considering the relevance of morphometric data of the IAC, procedures involving this region have become safer. This is mainly due to the advance of imaging exams associated with en-

doscopic techniques through the canal, especially through the middle cranial fossa by the Fisch approach, which has been improved and performed since 1970[14].

## CONCLUSION

The present study found differences between the right and left antimeres in three specific variables: mean upper length of the IAC (10.30 and 10.40 mm in the right and left, respectively); DIAC-GSS (22.10 and 23.40 mm in the right and left, respectively); and DIAC-VA (10.20 and 11.30 mm in the right and left, respectively). These findings highlighted the anatomical characteristics between the antimeres of IAC, and the discrepancies should be considered when interpreting results and planning clinical interventions.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTIONS

**FAP** - conceptualization, data curation, investigation, methodology, project management, resources, supervision, writing (initial manuscript), revision, and edition; **BBAL** - investigation, writing (initial manuscript), revision, and edition; **BPG** – investigation and writing (initial manuscript); **JNRM -** data curation, investigation, writing (initial manuscript), revision, and edition; **DRB -** investigation, writing (initial manuscript), revision, and edition; **TJMBSV –** supervision, writing (initial manuscript), revision, and edition; and **IFGG -** supervision, writing (initial manuscript), revision, and edition. All authors approved the final version to be published.

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# Morphometric analysis of mastoid foramen and possible clinical and surgical implications

## Análise morfométrica do forame mastóideo e suas possíveis implicações clínicas e cirúrgicas

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## Abstract

**Introduction:** The mastoid foramen (MF) is a narrow fissure in the mastoid process and exhibits considerable anatomical variability. The mastoid emissary vein and the meningeal branch of the occipital artery are important structures that pass through the MF. Despite its anatomical importance, morphological and morphometric analyses of the MF remain scarce. **Objectives:** To investigate the morphological and morphometric aspects of the MF. **Method:** This observational cross-sectional study analyzed 78 human skulls. Measured variables included the diameter of the MF, the presence, number, and the location of MF in relation to the occipitomastoid suture, the position of MF in relation to the Frankfurt plane, and the distances between MF and specific anatomical points. **Results:** All skulls presented at least one MF. However, in 7.69% of the specimens, the MF was absent on one side. MF was present on the right side in 98.72% of specimens and on the left side in 93.59%. The MF pattern most frequently observed was four foramina, independent of laterality, in 23.08% of the skulls. No statistically significant differences were identified across the variables studied. **Conclusion**: This study described relevant morphometric and morphological parameters of the MF.

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Given the importance of the structures passing through this foramen, understanding its anatomic variations and measurements is essential.

**Keywords:** Anatomy; Mastoid foramen; Clinical relevance; Neurosurgery.

## Resumo

**Introdução:** O forame mastóideo (FM), uma pequena abertura localizada no processo mastoide, pode apresentar diversas variações. Por ali passam estruturas relevantes, como a veia emissária mastoidea e o ramo meníngeo da artéria occipital. Apesar da importância do FM, há na literatura uma relativa escassez de dados morfológicos e morfométricos sobre essa estrutura. **Objetivos:** investigar os aspectos morfométricos e morfológicos do FM, bem como suas repercussões clínico-cirúrgicas. Método: Trata-se de um estudo observacional e transversal. Foram incluídos 78 crânios humanos no estudo, que analisou, em relação ao FM, a presença, a quantidade, a localização em relação à sutura occipitomastoidea, os diâmetros, a posição em relação ao plano de Frankfurt e as distâncias até pontos anatômicos específicos. **Resultados:** Dentre os achados do estudo, destaca-se a prevalência do forame, observado em pelo menos um dos lados de todos os crânios analisados. Em 7,69% observou-se a ausência da estrutura em um dos lados. O forame estava presente no lado direito em 98,72%. No lado esquerdo, estava presente em 93,59%. O padrão encontrado com mais frequência foi de quatro forames, independentemente do lado, em 23,08% dos crânios. Não foram identificadas diferenças estatisticamente significativas em todas as variáveis estudadas. **Conclusão:** O estudo descreve importantes parâmetros morfométricos e morfológicos do FM. Devido à relevância das estruturas que o percorrem, é essencial ter um conhecimento adequado da morfometria e da morfologia do FM.

**Palavras-chaves:** Anatomia; Forame mastóideo; Neurocirurgia; Relevância clínica.

## INTRODUCTION

The temporal bone (TB) exhibits significant morphological complexity due to its various bone accidents, and anomalies and developmental variations are described in the literature[1]. Among these variations, the mastoid foramen (MF) is a small aperture located in the mastoid process (MP) of the TB or along the occipitomastoid suture. However, the MF may be absent or present in a singular or multiple occurrence[1].

The MF variability can also encompass laterality, sex, age, quantity, location, and diameter[2]. These variations are attributed to the structures that pass through the MF, including the mastoid emissary vein (MEV) and the meningeal branch of the occipital artery. From a neurosurgical perspective, understanding the location of these structures is essential as the MF can be a potential source of bleeding during procedures involving the MP, as is the case of retrosigmoid craniotomy[2,3].

Detailed anatomical understanding of the MF and its associated structures remains scarce

despite technological advances. Furthermore, the literature offers limited data on the potential clinical and surgical implications related to these structures[1,4,5,6]. Therefore, this study aimed to analyze the morphological and morphometric characteristics of MF using human skulls specimens and discuss potential clinical and surgical implications.

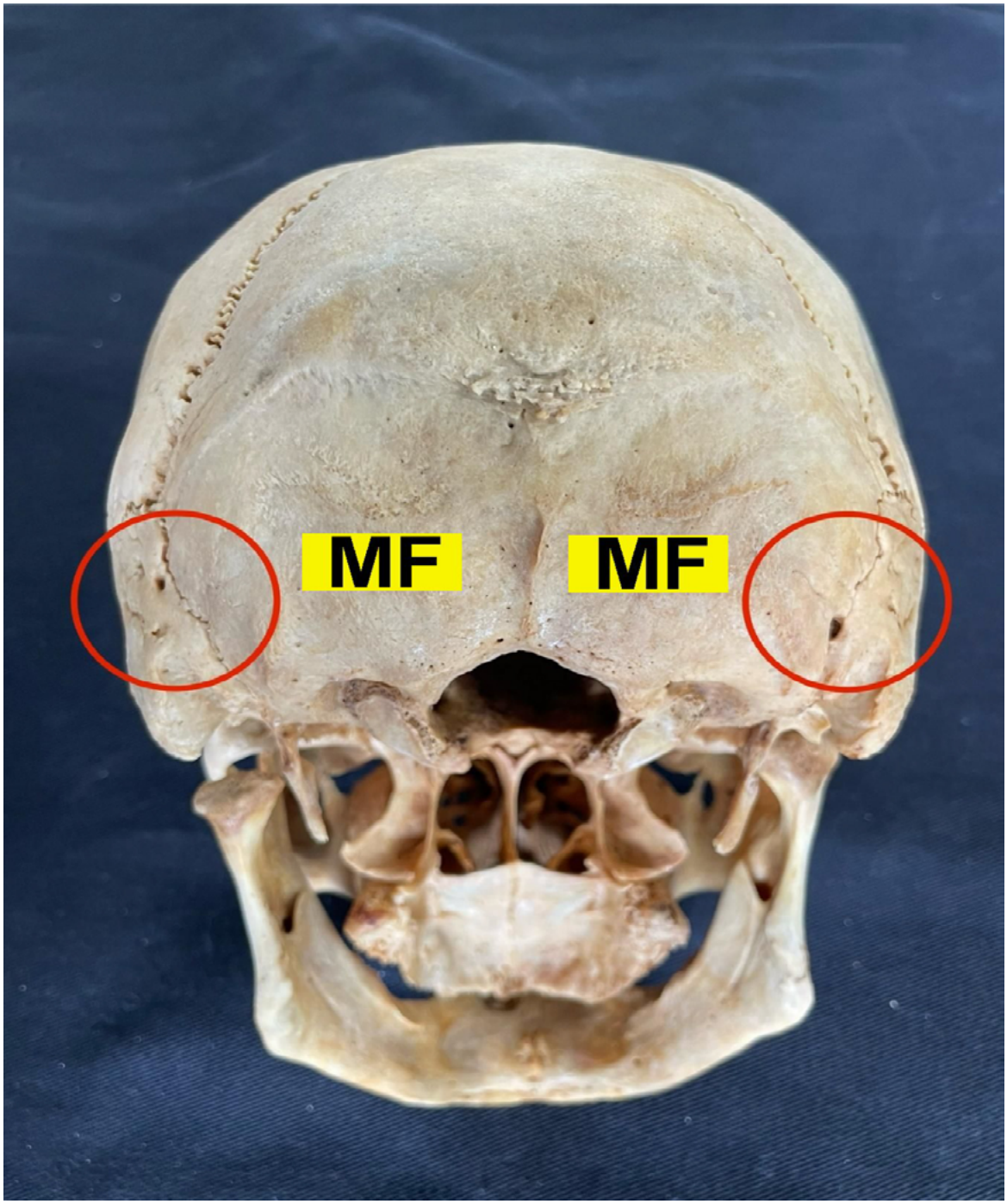
## METHOD

Morphological and morphometric measurements of the MF were performed in articulated and disarticulated human skulls from the anatomy laboratory of a higher education institution. Inclusion criteria required human skulls to be cataloged with documented information regarding sex. A total of 100 human skulls were initially considered for analysis, but only 78 met the criteria. Moreover, the remaining skulls were also excluded due to inadequate bilateral visualization of the studied structures or loss of morphological integrity caused by the decomposition process.

The morphometric analysis was conducted using a thickness compass, a Castroviejo type curved dry point compass, and a digital caliper.

The analyzed variables were MF presence or absence, number, location relative to the occipitomastoid suture, diameter, position in relation to the auriculo-orbital plane (Frankfurt plane), and distance in relation to the apex of the MP, to the foramen magnum, and the asterion. All variables were analyzed bilaterally (Figures 1 and 2).

**Figure 1.** Posteroinferior view of the human skull showing the right and left MFs.



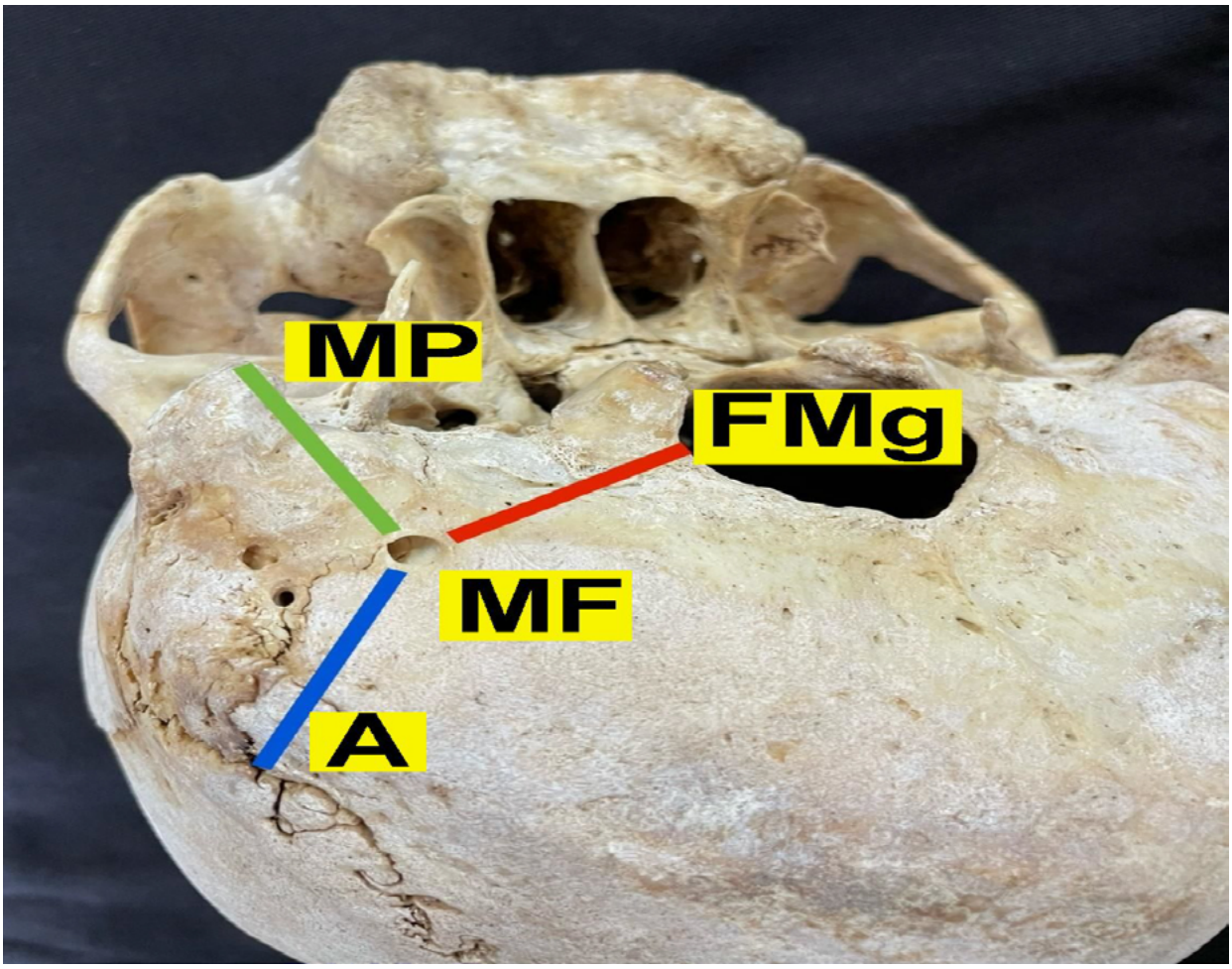

**Legend:** MF - mastoid foramen.

The data were tabulated, processed, and statistically analyzed using the SPSS® software (IBM, Chicago, USA). The Kolmogorov-Smirnov test evaluated the normality and homogeneity of the data. For non-normal data, descriptive statistics were expressed using measures of central tendency (mean, minimum, and maximum) and dispersion (standard deviation). The significance

level was set as 5%, with a 95% confidence interval and a maximum variability of 0.5.

In this study, the chi-square test of independence evaluated potential associations between categorical variables, such as the presence of MF on the right and left sides and differences in its location in relation to the mastoid suture and the auriculo-orbital plane, which may differ by antimere. The paired Wilcoxon test investigated differences in the number of foramina on the right and left sides and in their diameters and distances.

**Figure 2.** Defined surface landmarks and their distances from the MF: green, apex of the MP-MF; red, foramen magnum-FMg; blue, asterion-MF.




**Legend:** asterium (A); foramen magnum (FMg); mastoid foramen (MF); and mastoid process (MP).

## RESULTS

The MF was present in all analyzed human skulls (n = 78). However, 7.69% (n = 6) of the sample exhibited a unilateral MF. Of the total sample, the MF was present on the right side in 98.72% (n = 77) of specimens, whereas in only 1.28% (n = 1) of absence was observed. The MF

was present on the left side in 93.59% (n = 73) specimens, whereas 6.41% (n = 5) of absence was observed. No statistically significant difference was found in the presence of MF between the right and left sides (p = 0.105).

The most frequent MF pattern across the skull sample was four foramina, irrespective of side, observed in 23.08% (n = 18) of the specimens. Both right and left sides presented two foramina in 38.46% (n = 30) and 34.62% (n = 27) of specimens, respectively. The findings enhance the understanding of the variability of this morphological feature of MF, emphasizing the most common patterns identified in the study. No statistically significant difference was observed in the number of MFs between the right and left sides (p = 0.534).

When present on the right side, the MF was located laterally to the occipitomastoid suture in 55.84% (n = 43) of the specimens, medially in 14.29% (n = 11), and at the suture in 29.87% (n = 23). When present on the left side, the MF was lateral to the suture in 57.53% (n = 42) of the specimens, medial in 8.22% (n = 6), and at the suture in 34.25% (n = 25). No statistically significant difference was observed in the location of the MF relative to the occipitomastoid suture between the right and left sides (p = 0.482).

The MF diameter was measured on both sides. For the MFs on the right side, the mean upper-bottom diameter (UBD) was 0.23 cm (SD ± 0.23), and the laterolateral diameter (LLD) was 0.18 cm (SD ± 0.12). For the MFs on the left side, the mean UBD was 0.25 cm (SD ± 0.24), and the LLD was 0.22 cm (SD ± 0.16). Although the UBD was slightly smaller on the right side and the LLD was slightly larger on the left side, no statistically significant differences were found between the right and left sides (p = 0.310 for UBD and p = 0.155 for LLD).

The MF position was classified as below, on, or above in relation to the auriculo-orbital plane (Frankfurt plane). A below MF was found in 94.8% (n = 73) of the specimens on the right side and 97.3% (n = 72) on the left side. No statistically significant differences were found in the MF position in relation to the auriculo-orbital plane between the right and left sides (p = 0.192).

In relation to other anatomical measurements, the distance between the MF and the apex of the MP (MF-MP) had mean values of 3.05 cm (SD ± 0.52 cm) on the right side and 3.03 cm (SD ± 0.59 cm) on the left side. Furthermore, the distance between the MF and the foramen magnum (MF-FMg) had a mean of 4.02 cm (SD ± 0.60 cm) on the right side and 4.00 cm (SD ± 0.52 cm) on the left side. Lastly, the distance between MF and asterion (MF-AA) had a mean of 2.01 cm (SD ± 0.53 cm) on the right side and 2.02 cm (SD ± 0.60 cm) on the left side. No statistically significant differences were found in the distances between the MF and MP (p = 0.533), foramen magnum (p = 0.584), or asterion (p = 0.781).

## DISCUSSION

Our results indicate that the mastoid foramen is typically located in the mastoid process of the temporal bone. However, Patel et al. reported that the MF was in the occipitomastoid suture in 40% of the sample[7]. The authors analyzed 100 human skulls and also observed the presence of two MF of the specimens, 2% on the right side and 16% on the left side. Lastly, they observed a single MF on the left side in 26% of the specimens and in 16% on the left[8]. In another study conducted in 96 human skulls, three MFs were found in 6.2% of the cases. In one case described by Sehmi S., four MFs were observed on the right side[10].

Tsutsumi et al. analyzed magnetic resonance images of the skulls of 96 individuals, demonstrating that the MF was located at an average distance of 21.44 mm from the asterion and 33.65 mm from the tip of the MP[6]. Furthermore, another study, including a sample of 103 human skulls, measured the MF diameter and showed that the widest diameters were found in males, with an average value of 1.2 mm[11].

The MF can be classified into five types, differentiated by the number of external openings (types I to IV, with type 0 representing the absence of MF). In an analysis of 22 human skulls conducted by Chaiyamoon *et al*.[12], type I was the most prevalent (50%)[12]. In contrast, Hampl et al. found a higher frequency of type II (41.2%) in an analysis of 295 human skulls[7].

Although there is an apparent predominance of MF types I, II, III, and IV on the right side and a significantly higher absence of MF on the left side, further elucidation on the reasons behind these differences is needed[12]. For example, some authors suggest that laterality and sex may be related to MF types[12].

The MF is the means by which the meningeal branch of the occipital artery is transmitted to the dura mater and the MEV to the sigmoid sinus, connecting it to the suboccipital venous plexus, extending posteriorly to MP[13,14]. The sigmoid sinus drains the vertebral plexus in the upright position and the internal jugular vein in the supine position[14].

However, the vein extending into the sigmoid sinus has no valve structures and receives slow blood flow, which enhances its role in drainage. When this vein is dilated, as is the case in patients with intracranial hypertension and aplasia or hypoplasia of the internal jugular vein, it leads to high-flow vascular malformations in the venous connections. In certain procedures, these malformations can become an important hemorrhagic source[14].

In addition, the MEV is responsible for blood drainage from the posterior cranial fossa, particularly during otological and neurological procedures (e.g., mastoidectomy, epithympanectomy, and retrosigmoid craniotomy)[7,14,15]. Veins of this type are also a source of bleeding during ear surgeries and skull base operations, especially in the lateral and retrosigmoid approaches[16]. Surgical procedures in the mentioned areas can also lead to thrombosis and embolization due to

the bidirectional blood flow near the sigmoid sinus[16].

A better understanding of the MEV can help to prevent surgical complications. For example, in craniofacial surgeries (e.g., craniosynostosis), the MEV may be the only drainage pathway for the brain[16]. In this procedure, the volume of bleeding in lesions in the MEV depends on its diameter and, consequently, on the MF diameter, i.e., smaller bleedings occur in smaller MF[14]. Small bleeding can be managed using electrocautery or bone wax. However, larger MF diameters can lead to significant bleeding, which is challenging to control and increases the risk of sigmoid sinus rupture, shock, infection, and thrombosis[5]. Of note, larger diameters of the MEV can be found in cases of otitis and labyrinthine dysplasia, primarily due to vascular malformations in the internal jugular vein and sigmoid sinus[15].

A detailed study of the morphology and morphometry of the MF during the preoperative period of specific surgical procedures may reduce the risk of damage to the anatomical structures in the region, thus mitigating the occurrence of complications.

## CONCLUSION

The present study described the morphometric and morphological parameters of the mastoid foramen. Given the relevance of the anatomical structures passing through this foramen, an adequate understanding of its morphology and morphometry is essential for improved outcomes in surgical interventions, in addition to potentially reducing the risk of perioperative and postoperative complications.

## CONFLICT OF INTEREST

Nothing to declare.

## CONTRIBUTIONS OF THE AUTHORS

**IFGG -** conceptualization, investigation, manuscript writing and writing – revision and editing; **MMV -** writing – revision and editing; **TJMBSV -** conceptualization, investigation, manuscript writing and writing – revision and editing; **JMSD -** writing – revision and editing; **AAISG -** writing – revision and editing; **RCFC** - resources, writing – revision and editing; **FAP** - conceptualization, data curation, investigation, methodology, project administration, resources, manuscript writing, supervision and writing – revision and editing. All authors approved the final version to be published.

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# Microbiological analysis of chitosan membranes with n-acylydrazone associations: evaluation of efficiency

## Análise microbiológica de membranas de quitosana com associações de n-acilidrazona: avaliação da eficiência

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## Abstract

**Objective:** To verify the potential and bactericidal activity of chitosan (CS) films combined with N-acylhydrazone (JR19) in different concentrations for wound treatment. **Methodology**: Films were developed from chitosan (CS) + polyvinyl acetate (PVA) solutions. The F1 film consisted of CS and the F2 film consisted of CS + PVA in a 1:1 ratio. To incorporate JR19 in the polymeric solutions, 1 mg of sulfadiazine (AgSD) + 8.6 mg of JR19 were added in 10 mL of CS: PVA. Films formed from this solution were named F3, F4, and F5. The antimicrobial activity of films with JR19 derivatives was assessed using the disc diffusion technique in an Agar Müeller Hinton solid culture medium. **Results:** The F1 film was discarded due to strong electrostatic repulsion with solid agar culture medium, deforming the film and hampering the culture. The F2, F3, and F5 films showed bacterial colony formations in front and verse, indicating no microbial inhibitory activity on *Staphylococcus aureus*. **Conclusion:** In the F4 film, the synergy between JR19 and AgSD showed complementary properties that facilitate wound healing. However, the safety and efficacy of this alternative therapy need further investigation in clinical trials.

**Keywords**: Chitosan; Healing; Membranes; Wounds.

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## Resumo

**Objetivo:** Verificar a potencialidade e a ação bactericida de membranas de quitosana (QTS) com associações de N-acilidrazona (JR19) em diferentes concentrações para o tratamento de feridas. **Metodologia:** Os filmes foram desenvolvidos a partir das soluções de QTS e acetato de polivinila (PVA). Foram analisados: FI, filme de QTS; F2, filme de QTS+PVA na proporção de 1:1; F3, filme com 8,6 mg de JR19 adicionados à solução de QTS usada em F1; F4, filme com 8,6 mg de JR19 e 1 mg de Sulfadiazina de prata (AgSD) adicionados a 10 ml da solução de F2; F5, filme com 1 mg de JR19 e 1 mg de AgSD adicionados a 10 ml da solução de F2. A constatação da atividade antimicrobiana dos filmes de polímero de QTS com derivados JR19 foi realizada pela técnica de difusão de discos em meio de cultura sólido Ágar Müeller Hinton. **Resultados:** O F1 foi desprezado devido à forte repulsão eletrostática com meio de cultura sólido ágar, que causou deformação e inviabilizou a cultura. A ausência de atividade inibitória microbiana dos filmes F2, F3 e F5 sobre os S. aureus foi evidenciada pela formação de colônias bacterianas frente e verso sobre os filmes de polímero de QTS com derivados de JR19. **Conclusão:** A sinergia entre JR19 e AgSD na membrana F4 é vantajosa para a cicatrização de feridas devido às suas propriedades complementares. No entanto, a segurança e a eficácia em ensaios clínicos precisam ser mais exploradas para uma terapia alternativa segura e eficaz.

**Palavras-chave:** Cicatrização; Feridas; Membranas; Quitosana.

## INTRODUCTION

By 2050, almost 25% of Western populations may experience chronic wounds This situation worsens when associated with physical impairment, poor quality of life, risk of infection, hospitalization, amputation, and death[1].

Recently, the incidence of skin wounds in health facilities has increased, affecting 42.6% of patients. This increase, independent of age or sex, causes prolonged hospitalizations[2]. Since skin wounds are a major concern in medicine, therapies for wound healing have been developed focusing on effectiveness and positive outcomes[4, 5, 6, 7, 8].

Research has been conducted to develop promising, cost-effective, and highly efficient tools such as polymer membranes. These membranes are easy to handle, not requiring daily maintenance (e.g., dressing changes and wound cleaning), and can replace damaged skin, prevent infections, and absorb exudates[9,10,11].

Several products have been developed to facilitate wound healing. Evidence indicates over 2,000 types of synthetic or biological dressings are available on the international market. These products are biodegradable and biocompatible, and some techniques are used to prevent reabsorption and material failure[12,13,14,15].

Dressings are composed of synthetic and biological polymers, such as hyaluronic acid, al-

ginate, and chitosan (CS). These polymers present adequate safety, compatibility with the human body, natural degradation, and antibacterial properties. Polymers composition includes nanofibers that improve wound healing due to a high-volume ratio, surface area, proliferation, and cell differentiation. These nanofibers can mimic tissue compositions, facilitating cell organization, adhesion, migration, and transport. Also, multiple porous fibers which are randomly[3] dispersed and interconnected facilitate tissue, cartilage, bones, and blood vessel regeneration[12,13,14].

Therefore, this study aimed to evaluate the efficacy and bactericidal action of CS membranes associated with N-acylhydrazone (JR19) at different concentrations for wound healing.

## MATERIALS AND METHODS

### Films development

Films were developed using two polymeric solutions. The first was a CS solution prepared in a 1% (v/v) acetic acid solution, with a final concentration of 1% (m/v). The second was a polyvinyl acetate (PVA) solution prepared in heated water, with a final concentration of 1% (m/v). From these polymeric solutions, two films (F1 and F2) were produced (Table 1). F1 was a CS-only film, and F2 was a CS + PVA film, in a 1:1 ratio. JR19 was incorporated in the polymeric solutions with 1 mg of silver sulfadiazine (AgSD) + 8.6 mg of JR19 in 10 ml of CS: PVA (1:1) under magnetic agitation for 24 hours. This solution produced films named F3, F4, and F5 (Table 1). JR19 quantity was optimized using 1 mg of AgSD + 1 mg of JR19 in 10 ml of a CS: PVA (1:1) solution under the same conditions described for F2. Ten milliliters of the resulting solutions were poured in plastic Petri dishes (5.5 cm diameter) and kept in an oven with air circulation at 50°C for 24 hours to solvent evaporation and film formation. The formulations were developed in the Laboratory of Development and Characterization of Pharmaceutical Products at the Universidade Estadual da Paraíba.

**Table 1.** Samples used in the study

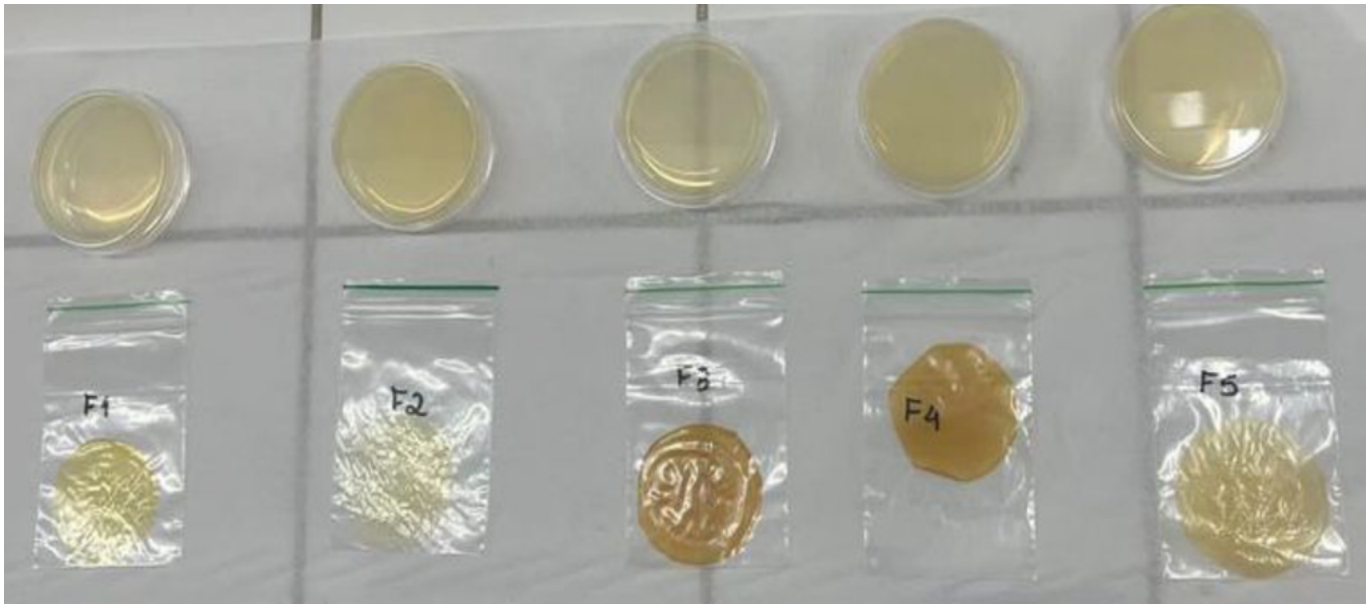
| Sample | CS:PVA ratio (m/m) | JR19 (mg) | AgSD (mg) |
|---|---|---|---|
| F1 | 1:0 | - | - |
| F2 | 1:1 | - | - |
| F3 | 1:0 | 8.6 | - |
| F4 | 1:1 | 8.6 | 1.0 |
| F5 | 1:1 | 1.0 | 1.0 |

CS: chitosan; PVA: polyvinyl acetate; JR19: N-acylhydrazone; AgSD: silver sulfadiazine
Source: research data.

### Antimicrobial activity

The antimicrobial activity of CS polymer films with JR19 derivatives was assessed using an adapted diffusion-disk technique in a solid Agar Müeller Hinton culture medium (Figure 1) on 60 x 15 mm Petri dishes. The bacterial inoculum was seeded with a sterile swab[14,18.]

**Figure 1.** CS films with and without JR19 derivatives.




Source: authors

Antimicrobial sensitivity tests were conducted using the *Staphylococcus aureus* (*S. aureus*) ATCC® 25923 strain. Strains were activated in test tubes containing nutrient agar and kept in an oven at 37 °C for 18 hours. Next, a 0.9% saline solution was prepared, and a bacterial inoculum was adjusted to the MacFarland scale of 0.5, corresponding to approximately $10^8$ CFU/ml [18,19].

From a culture of the selected strain, a single colony was inoculated in BHI broth and incubated at 37 °C for approximately 18 hours. Subsequently, after medium turbidity, with a sterile swab previously dipped in bacterial suspension, the culture was inoculated in streaks onto the Müeller Hinton agar plates in two directions across the entire medium surface. Moreover, the swab was passed around the whole edge of the plate, and the inoculum dried from 5 to 10 minutes[15,17,18]. Last, the CS polymer films with different concentrations of JR19 derivatives were placed in the inoculated plates using sterile forceps.

The F1 film showed strong repulsion towards the agar medium and was discarded, while the F2 and F4 films showed less repulsion and were hydrated with a saline solution to improve adherence[5, 6, 7]. The plates were incubated at 37 °C for 24 hours in an oven. The results were interpreted following the recommendations of the National Committee for Clinical Laboratory ob-

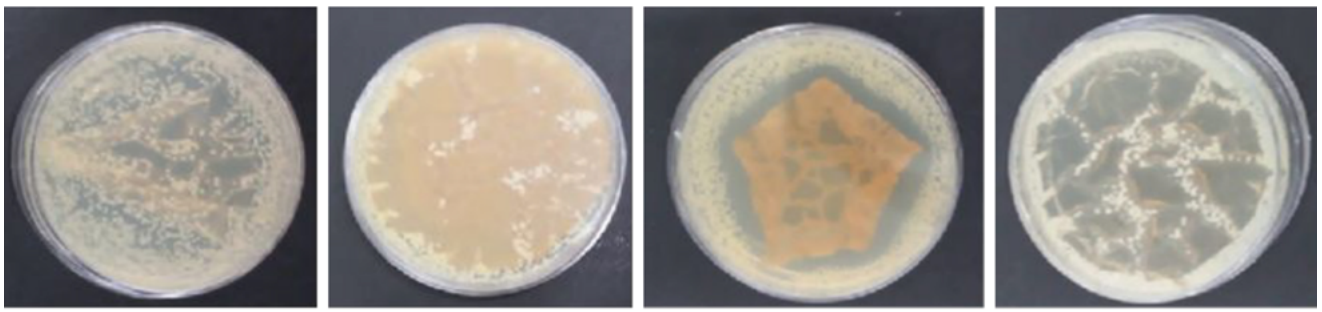
serving isolated colonies around and over the films[2, 3].

The antimicrobial susceptibility profile was conducted in the Laboratory of Microbiology of the Universidade Federal de Pernambuco according to the ISO 17025 and following specific standards for laboratories performing microbiological studies. Strict biosafety protocols were adopted to prevent human and environmental related risks[3, 4].

## RESULTS

After incubation at 37°C for 24 hours, F4 film presented antibacterial activity with no bacterial colonies identified and formed an *S. aureus* inhibition halo (Figure 2)[3, 6, 7]. The F1 film was discarded due to strong electrostatic repulsion against the agar medium, which deformed the film and hampered the culture[10, 11]. The F2, F3, and F5 films showed no antibacterial activity over *S. aureus* since bacterial colonies were observed front and verse (Figure 2).

**Figure 2.** Antibacterial activity of CS polymer films with JR19 derivatives against S. aureus.



**F2** **F3** **F4** **F5**

Source: authors

## DISCUSSION

RF1 film was discarded due to strong electrostatic repulsion towards the agar medium, which deformed the film and hampered the analysis. The repulsion might be explained by a reaction between the culture medium and monomeric units of β-(1→4)-2-amino-2-deoxy-D-glucose and β-(1→4)-2-acetamido2-deoxy-D-glucose rt[10, 11, 12].

F2 showed no antimicrobial activity towards *S. aureus*, allowing greater bacterial growth than the other films. In this sense, JR19 and AgSD, included in the final composition of the film, might be the main agents of antimicrobial activity P[13, 14, 15]. Similarly, the F3 composition (CS associated with 8.6 mg of JR19) also lacked antimicrobial activity towards S. aureus, which may suggest that AgSD is the main agent of bacterial sensitivity[4, 6, 7].

In contrast, F4 presented high antimicrobial activity with no bacterial colony formation and showed an *S. aureus* inhibition halo. Therefore, F4 (1mg of AgSD) was the most promising

film for antibacterial activity. F4 antibacterial activity might be explained by the interaction with the peptidoglycan cell wall, which disrupted the bacterial wall. Also, the F4 bacteriostatic effect, represented by the *S. aureus* inhibition halo, might have contributed to the antibacterial activity.

Although AgSD and JR19 were added to the F5 film, no antibacterial activity was observed. F4 significant antimicrobial activity suggests specifically 8.6 mg of JR19 as an efficient concentration for this outcome. Combining AgSD and JR19 with CS as adjuvant therapies for wound healing is important for *in vitro* experiments[6, 7, 8].

JR19 has shown promising results for wound healing and is considered a privileged structure in medicinal chemistry due to its pharmaceutical relevance. JR19 shows antimicrobial activity towards various pathogens, which is crucial to prevent infections during wound healing[17, 18].

The combined activity of JR19 with AgSD in wound healing may be beneficial, considering their complementary properties. While JR19 is antimicrobial and anti-inflammatory, AgSD shows antimicrobial activity towards various bacteria frequently associated with cutaneous infections[10, 11].

Wanderley *et al*. (2020) developed CS films containing JR19 to create a therapeutic formulation. The authors analyzed the physicochemical properties, mechanics, and biocompatibility of the films. Results indicated JR19 in the films, with characteristics identified by differential exploratory calorimetry, thermogravimetry, and X-ray diffraction[17].

Besides the high antimicrobial activity, AgSD is safe and efficient in preventing secondary infections and promoting wound healing. By adding AgSD in films for wound healing, tissue regeneration is facilitated, inducing damaged tissue repair. Nevertheless, additional clinical studies are necessary to evaluate the safety and efficiency of AgSD as an alternate therapy for wound healing[19].

Thus, F4 film may inhibit bacterial growth due to structural and chemical differences from the other films tested. This potential inhibition might be related to the structural and chemical differences of the CS polymer with JR19 derivatives, which may interfere with bacterial cell wall adherence. Also, the antimicrobial activity of F4 compounds through diffusion might explain the *S. aureus* inhibition halo[18, 19].

## CONCLUSION

The synergy between JR19 and AgSD in the F4 film was beneficial. Combining these agents in cicatrization membranes can regenerate damaged tissue, stimulating wound healing. However, the safety and efficiency of this combination must be further tested in clinical trials to ensure its potential for wound healing.

Moreover, these results are specific for *in vitro* tests and may partially reflect the perfor-

mance of the film *in vivo*. Also, the efficiency of a membrane as a healing agent depends on factors, such as wound severity and individual response of the patient.

## CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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## AUTHOR CONTRIBUTIONS

**BBTO, MEAN e CABL:** conceptualization, investigation, methodology, and writing. **GGG:** methodology. **LRT e BPGLD e TKBO:** conceptualization, writing – original draft and writing – revision and editing. All authors approved the final version.

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# Posterior interosseous nerve syndrome: a case report and surgical treatment

## Síndrome do nervo interósseo posterior: um relato de caso e abordagem cirúrgica

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## Abstract

The posterior interosseus nerve compression syndrome (PINCS) is one of many compression neuropathies of the upper body and affects the extensor compartment of the forearm. Although conservative treatment is efficient in most cases, persistent situations can demand surgery for decompression. This study aimed to report a case of posterior interosseous nerve compression syndrome treated with surgical decompression due to the persistence of symptoms after the failure of the conservative treatment. Furthermore, the study highlighted the importance of following post-surgical orientations to achieve full recovery and minimize possible sequelae.

**Keywords**: Radial nerve; Radial neuropathy; Nerve compression syndromes; Surgery.

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## Resumo

A síndrome de compressão do nervo interósseo posterior (SCINP) é uma das muitas neuropatias compressivas da parte superior do corpo e afeta o compartimento extensor do antebraço. Embora o tratamento conservador seja eficiente na maioria dos casos, situações persistentes podem demandar cirurgia para descompressão. Este estudo teve como objetivo relatar um caso de síndrome de compressão do nervo interósseo posterior tratado com descompressão cirúrgica devido à persistência dos sintomas após a falha do tratamento conservador. Além disso, o estudo destacou a importância de seguir as orientações pós-cirúrgicas para obter recuperação completa e minimizar possíveis sequelas.

**Palavras-chaves**: Nervo radial; Neuropatia radial; Síndromes de compressão nervosa; Cirurgia.

## INTRODUCTION

Several compression neuropathies affect upper body limbs, and the anatomical and functional knowledge of each nerve is paramount to performing a correct diagnosis of compression[1]. The posterior interosseous nerve (PIN) is a branch of the profound radial nerve that originates in the brachial plexus[2].

The posterior interosseous nerve compression syndrome (PINCS) occurs when the nerve is compressed or irritated, causing pain, muscle weakness, and loss of function of the innervated muscles[3]. The radial nerve (RN) descends in the arm and divides into superficial and deep nerves in the proximal forearm. The deep branch of the posterior forearm emerges as the NIP, responsible mainly for the innervation of the extensor muscles of the forearm and the hand, providing motor innervation to the posterior forearm and extending up to the fourth dorsal compartment of the wrist[2].

The compression can occur in several points alongside the nerve trajectory: the arcade of Frohse (AF; i.e., a fibrous band in the supinator muscle where the nerve passes), the edge of the supinator, and fibrous bands surrounding the proximal radius[4]. Causes may include direct trauma or repetitive lesions (particularly of the forearm), tumors or ganglion cysts, and inflammation or cicatrization due to inflammatory or surgical conditions[4].

PINCS is considered the most common compressive syndrome, being the third most common regarding the main branches of the brachial plexus (after carpal tunnel and cubital tunnel syndromes). The incidence of nerve compression of RN was estimated at 2.97 for men and 1.42 for women (100,000 people/year). The proportion of surgeries was 0.5 and 0.8, respectively. The incidence may increase until middle age, followed by a decrease. Still, these data vary among studies, reporting the existence of 3.53 cases per 100,000 people/year [4,5].

The symptoms develop gradually and include weakness in thumb and finger extension; however, the wrist extension is preserved due to the innervation of the extensor carpi radialis longus[6]. Prolonged compression can lead to nervous ischemia, impairing neural function[4].

The treatment encompasses conservative and surgical treatments and requires direction and individualization. The first consists of reducing inflammation and swelling around the nervous structure using splints to reduce movements, non-steroidal anti-inflammatory medicaments, changes in lifestyle habits, local injections of corticosteroids, and physical therapy. Alternatively, surgery is an option when the conservative treatment shows no improvement after three to six months or when the patient presents pain after 12 weeks[4]. The type of procedure will depend on the site of injury and may include lesion resection, nerve release, supinator elongation, or synovectomy[3,4].

Thus, the present study aimed to report a case of PINCS treated by surgical decompression after symptoms persisted upon conservative treatment.

## CASE REPORT

A female patient, 35 years old, works as a lawyer with an emphasis on typing activities, sedentary, previously healthy, and with no prior injuries, reported the onset of paresthesia in the extension of fingers of her right hand one year ago. The symptoms aggravated when the patient was pregnant, presenting loss of motor function and paresthesia of the supinator, fingers, and little finger common extensor upon physical examination. Furthermore, the movement of the abductor pollicis longus, the extensor pollicis brevis and longus of the thumb, and the extensor indicis proprius was reduced. The physical examination also identified a positive Tinel sign at the level of the supinator muscle close to the cubital fossa.

Considering the clinical findings, electroneuromyography and ultrasound of the right forearm were requested; the former showed signs of radial nerve injury in the posterior interosseous branch, and the latter revealed signs of compression at the level of the AF with thickening of the PIN.

Although the initial treatment for PINCS was conservative (i.e., pain relief medication and motor physical therapy), the patient did not present any improvement and underwent surgery for decompression of the PIN. The surgery is reserved only for refractory cases for at least three months of the conservative treatment[3,4].

In this context, the surgical decompression was performed in the proximal section of the anterior side of the forearm, close to the medial edge of the brachioradialis muscle. A layered dissection was conducted, releasing the compression areas, including the superficial fibrous bands over the radiocapitellar joint, the fibrous edge of the extensor carpi radialis brevis, the AF, and the distal edge of the supinator[7].

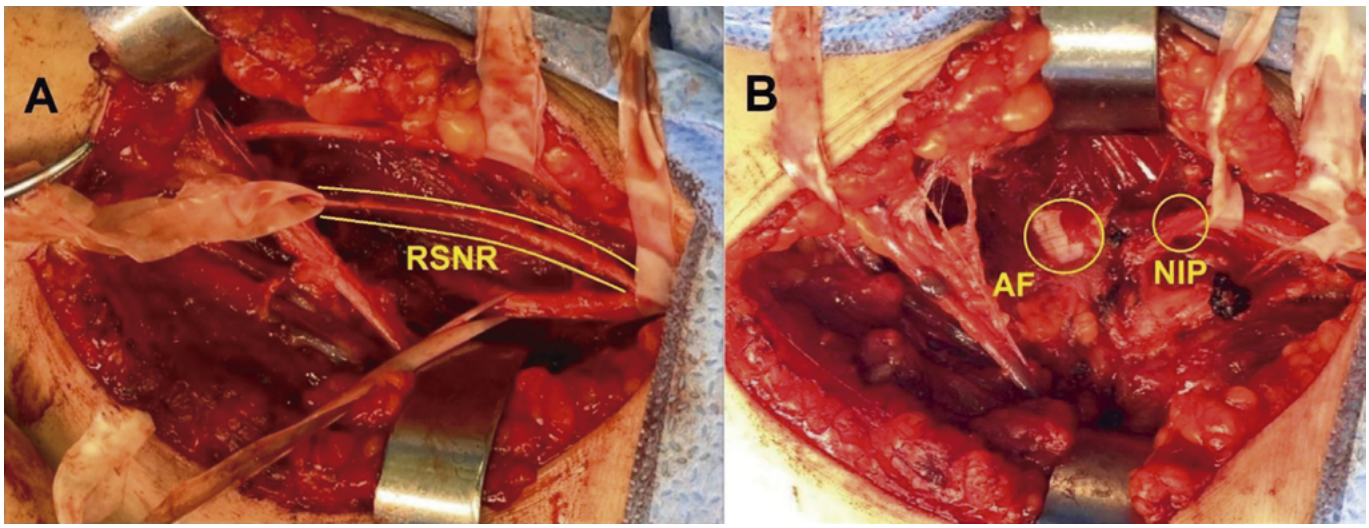


**Figure 1.** Proximal region of the anterior side of the forearms, close to the medial edge of the brachioradialis muscle. A: Superficial branch of the radial nerve (SBRN); B: arcade of Frohse (AF) and posterior interosseous nerve (PIN).

During the arcade opening, nerve thickening was observed, and the procedure provided complete decompression.

After two years and one month of the surgery, the patient did not present a satisfactory clinical improvement, with persistent pain and the inability to perform daily manual activities. The patient did not follow the recommended physical therapy rehabilitation protocol after surgery, which could have improved motor recovery.

## DISCUSSION

The RN is the main nerve that arises from the posterior fascia of the brachial plexus, innervating all the muscles in the posterior compartment of the arm and the forearm. This nerve travels from the posterior to the anterior compartment, wrapping around the radial groove of the humerus and passing through the intermuscular septum between the brachialis (medially) and the brachioradialis (laterally). Then, the RN continues distally, emerging between the brachioradialis and the extensor carpi radialis longus and dividing into the superficial branch of the RN and the PIN (i.e., the deep branch of the RN). The radial tunnel is a musculotendinous structure that extends from the lateral epicondyle of the humerus to the distal edge of the supinator muscle. Therefore, the proximal edge of the superficial head of the supinator can form the AF, a fibrous arch of variable thickness that has been described as the most common site of PIN compression[5].

The PIN compression can manifest as PINCS, leading to motor paralysis, or as radial tunnel syndrome, with impaired sensibility and pain in the lateral side of the elbow and forearm,

which can be confused with lateral epicondylitis. This condition worsens with repetitive pronation and supination of the forearm. On physical examination, the syndrome is marked by pain upon palpation of the PIN, especially in the AF, and may include discomfort with resisted middle finger or wrist extension (i.e., Milch and Maudsley signs), as well as increased pain during resisted pronation and supination[7,8].

The exact primary etiology is not fully understood, but it can occur by trauma or lesions that take space, such as rheumatoid arthritis, brachial neuritis, and spontaneous compression. Repetitive pronation and supination activities, such as typing (which is correlated to the case presented in this study), the frequent use of manual tools, and physical exercises that increase the stimulation of the forearm can also lead to PINCS. Some individuals present anatomical variations, including the narrowing of the channel where the nerve passes, that leave the posterior interosseous nerves more susceptible to compression. During pregnancy, hormonal alterations and increased liquid in the tissues may cause edema in the hand and wrists, increasing the risk of overload in the PIN, as observed in the presented case, since the patient reported worsened symptoms when pregnant and only sought the neurosurgical team after giving birth[5,7].

The diagnostic assessment involves a combination of medical history, physical examination, and complementary tests. A detailed medical history seeks to understand the symptoms and their duration, the triggering factors, and prior medical conditions to discard other causes. The physical examination focuses on the affected area, identifying pain, muscle weakness, and sensory changes. Specific tests may be conducted to evaluate nerve function, and complementary exams (e.g., nerve conduction study) are paramount to confirm the diagnosis by measuring the speed of electrical signals in the affected nerve. Electroneuromyography registers the electric activity on the muscle and the nerve response to electrical stimuli, identifying possible compressions or lesions. Image exams, such as ultrasound or magnetic resonance imaging, are requested to visualize anatomical structures of the forearm, including bones, muscles, and nerves, aiming to discover underlying causes of compression[6,8,9,10].

The PINCS treatment varies according to the intensity of the symptoms and the cause of the compression. Conservative treatments include rest, moderating physical activity, and ergonomic postures. The immobilization with wrist splints reduces the pressure on the nerve and helps to heal, especially in acute infections. Analgesic or non-steroidal anti-inflammatory drugs are used to treat pain and inflammation, and physical therapy is essential, including strengthening and flexibility exercises, as well as myofascial release techniques. Corticosteroid injections may be indicated to reduce inflammation in specific cases, usually guided by image exams. The surgery is considered in severe cases or cases unresponsive to conservative treatment, aiming at releasing nerve pressure, with the surgery being defined by the cause of the compression[6,9,10].

The surgery performs a lateral-anterior incision along the anterior side of the elbow joint,

five centimeters above the flexor crease, at the lateral edge of the biceps brachii muscle, and proceeds along this edge to the elbow joint, avoiding crossing the flexion crease at a 90º angle. Then, the incision curves medially following the medial edge of the brachioradialis muscle. During this stage, a careful dissection is performed between the brachioradialis and the extensor digitorum muscles, allowing visualization of the RN and its main branches: the PIN and the radial sensory nerve. The isolation of PIN is conducted with gentle dissection and the aid of a 2.5x magnifying surgical loupe, opening the AF to follow the nerve trajectory to its exit from the supinator muscle. This phase includes a compression test during the carpal flexion and forced pronation of the forearm, providing adequate nerve evaluation. The closing is performed in two plans with different sutures to close subcutaneous tissue and the skin [6,9,11].

PINCS prognosis depends on the cause of the compression, the severity of the nerve lesion, and the quality of the treatment. An early diagnosis and proper therapeutic resources generally ensure significant improvement and full recovery in most cases. An accurate diagnosis obtained through detailed clinical examination is paramount[6,11]. Although several patients experience a decrease in symptoms and the recovery of nerve function with time, severe cases or insufficient treatment may lead to permanent lesions, causing persistent symptoms or loss of function. The prognosis varies with the cause, the severity of the compression, the general health of the patient, and the adherence to treatment[4,6].

In summary, the prompt identification of PINCS and the proper intervention are fundamental to achieve positive results. An early diagnosis reduces symptoms, prevents complications, and facilitates nerve function recovery. Adherence to rigorous post-operative orientations is crucial to treatment success, favoring full recovery and minimizing sequela. This study also highlights the importance of multidisciplinary collaboration to achieve a better quality of life for individuals[4,6].

## CONFLICT OF INTEREST

Nothing to declare.

## AUTHOR CONTRIBUTIONS

**ECB** - Conceptualization, Writing – original manuscript and Writing – review and editing; **EPLR** - Conceptualization, Supervision, and Writing –review and editing; **HESJ** - Writing – original manuscript and Writing – review and editing; **ERM** - Writing – original manuscript and Writing – review and editing; **ALLP** - Writing – original manuscript and Writing – review and editing; **GG-CLGF** - Conceptualization, Writing – original manuscript and Writing – review and editing; **FAP** - Conceptualization, Data curation, investigation, Methods, Project management, Resources, Supervision, Writing – original manuscript and Writing – review and editing. All authors approved the final version.

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# Subcortical aphasia: a systematic review

## Afasia subcortical: uma revisão sistemática da literatura

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## Abstract

**Introduction:** Language is defined as the ability to communicate from several cognitive processes, while aphasia is an acquired disorder characterized by receptive and expressive problems in oral and written language. Subcortical structures may play an important role in speech production and processing, and recent studies have suggested that damage to these structures induces aphasia. Therefore, this study aimed to relate subcortical structures to language function and disorders. **Methods:** This systematic review of the literature was developed from March 2022 to May 2023 using questions from the PICO strategy and following the PRISMA guidelines. Blind and independent searches were conducted on PubMed, Cochrane Library, CAPES periodic, LILACS, Medline, and SciELO databases, considering studies published between 2018 and 2023. A manual search was performed to ensure the inclusion of ongoing or unpublished studies. **Results:** Of the 9,888 studies retrieved, 11 met the eligibility criteria and were included in the qualitative synthesis. **Conclusions:** A broad thalamocortical interaction was suggested for language functions and tasks, with special involvement of the left anterior thalamus.

**Keywords:** Aphasia; Basal ganglia; Thalamus; Language disorders; Systematic review.

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## Resumo

**Introdução:** A linguagem é definida como a capacidade de comunicação a partir de diversos processos cognitivos, enquanto a afasia é um distúrbio adquirido caracterizado por problemas receptivos e expressivos na linguagem oral e escrita. As estruturas subcorticais podem desempenhar um papel importante na produção e processamento da fala, e estudos recentes sugeriram que danos a essas estruturas induzem afasia. Portanto, este estudo teve como objetivo relacionar estruturas subcorticais com funções e distúrbios de linguagem. **Métodos:** Esta revisão sistemática da literatura foi desenvolvida de março de 2022 a maio de 2023 utilizando questões da estratégia PICO e seguindo as diretrizes PRISMA. Foram realizadas buscas cegas e independentes nas bases de dados PubMed, Cochrane Library, periódico CAPES, LILACS, Medline e SciELO, considerando estudos publicados entre 2018 e 2023. Foi realizada busca manual para garantir a inclusão de estudos em andamento ou não publicados. **Resultados:** Dos 9.888 estudos recuperados, 11 atenderam aos critérios de elegibilidade e foram incluídos na síntese qualitativa. **Conclusões:** Foi sugerida uma ampla interação tálamo-cortical para funções e tarefas de linguagem, com envolvimento especial do tálamo anterior esquerdo.

**Palavras-chave:** Afasia, Núcleos da base, Tálamo, Transtornos da linguagem, Revisão sistemática.

## INTRODUCTION

Language is defined as the ability to communicate from several cognitive processes, including visual perception, semantic processing, selection and recovery of phonological or orthographic representations, and motor output planning and execution. Also, naming is a key language process for effective communication that involves attaching a word or label to an object or concept, which is essential for speech. Difficulty with naming is reported in most types of aphasia[1].

Aphasia is a disorder characterized by receptive and expressive problems with oral and written language[2]. It typically arises from damage to the left frontotemporal cerebral cortex, which was associated with lesions in the basal ganglia, thalamus, lentiform nucleus, and caudate nucleus[3]. These structures play an important role in speech production and processing and contribute to naming and language correlation and modulation[1,3,4,6-13].

Studies have shown that thalamic hemorrhages often impair cognition, regardless of the damage location. However, different cognitive subdomains are affected depending on the location of the lesion within the thalamus. In this context, lesions in the lateral region of the thalamus may be associated with language, the posterior region to memory, and the anteromedial region to other cognitive subdomains[4]. . Common causes of language disorders include subcortical stroke and intracerebral hemorrhages, and individuals with thalamic aphasia present decreased comprehension[2]. In this sense, this systematic review aimed to relate subcortical structures to language

function and disorders, such as verbal fluency, listening comprehension, repetition, reading, and writing.

## METHODS

A systematic review was conducted between March 2022 and May 2023 using questions according to the PICO strategy (Population, Intervention, Control group, and Outcome). Chart 1 describes definitions and eligibility criteria.

**Chart 1.** Eligibility criteria for studies using the PICO strategy.

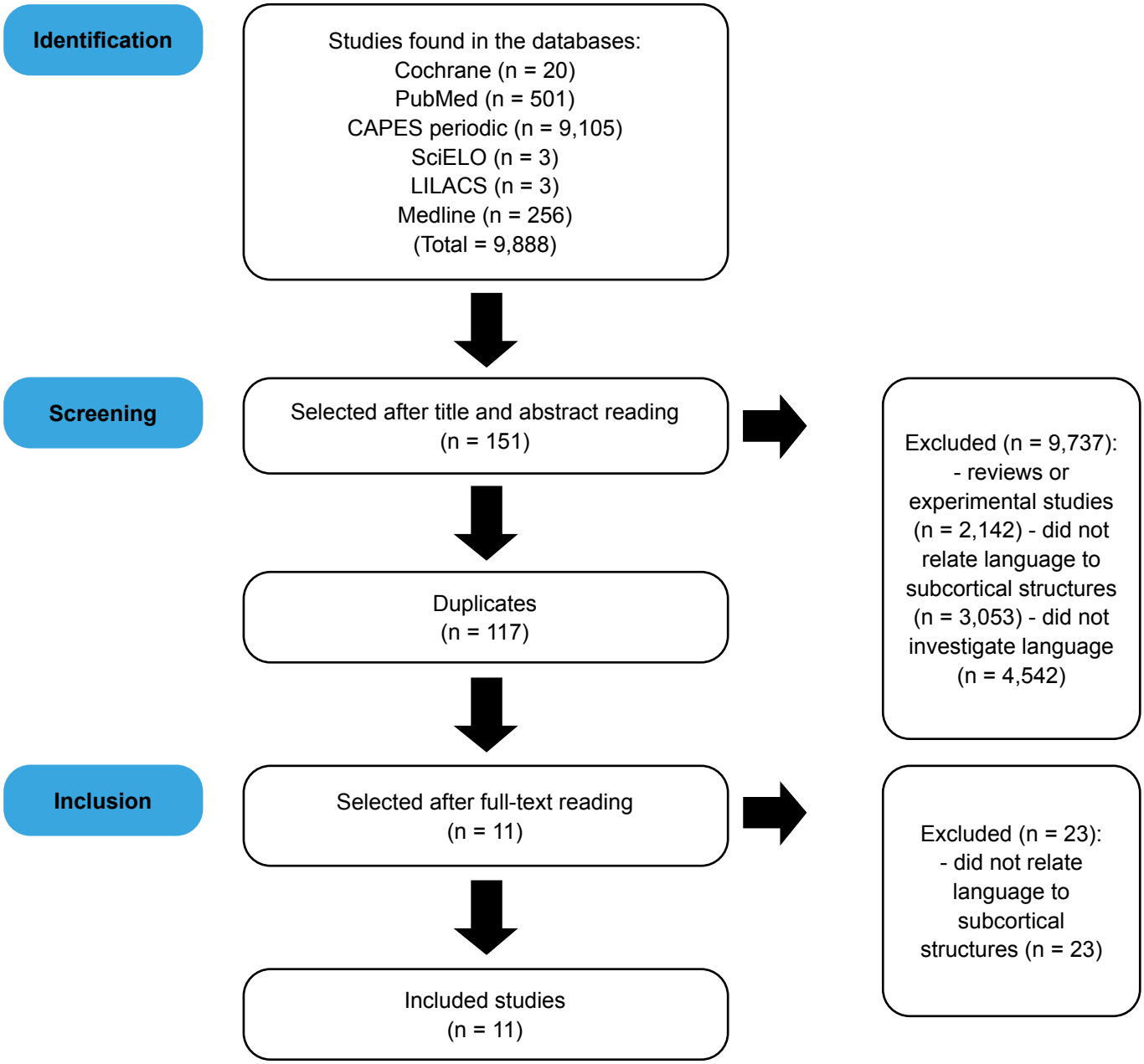
| **Guiding question: "what is the relationship between aphasia and cerebral subcortical structures?"** | | |
|---|---|---|
| Selection criteria | Inclusion criteria | Exclusion criteria |
| Population | Healthy or unhealthy humans, without age, sex, or color restriction | Experimental studies and animal models |
| Intervention | Not used as study criteria | Not used as study criteria |
| Control group | Not used as study criteria | Not used as study criteria |
| Outcomes | Study relating subcortical structures to language | Study not relating subcortical structures to language |
| Study type | Population-based studies. Descriptive or analytical studies in which the design investigated and related subcortical structures to language | Reviews, editorials, conference reports and scientific annals, events, theses, study cases, and studies that did not relate subcortical structures to language |

Source: the authors.

An independent and blind search of studies was conducted using PubMed, Cochrane Library, Coordination for the Improvement of Higher Education Personnel (CAPES) periodic, Latin American and Caribbean Health Sciences Literature (LILACS), Medical Literature Analysis and Retrieval System Online (Medline), and Scientific Electronic Library Online (SciELO) databases. Studies published in the last five years (2018 to 2023) were selected. A manual search was performed on websites and reference lists, and abstracts were reviewed to ensure the inclusion of relevant studies.

The first screening was performed on titles and abstracts without language restrictions. Literature reviews, experimental or irrelevant studies, and studies not correlating or investigating language and subcortical structures were excluded. Next, a full-text reading was performed to select the relevant studies for descriptive analysis (Figure 1).

**Figure 1.** Flowchart of the study selection.




Source: the authors.

The study selection was guided by the question: “what is the relationship between aphasia and cerebral subcortical structures?”. Four groups of descriptors from the Medical Subject Headings (MeSH) were used for the search strategy in Portuguese, English, and Spanish, and each group had two descriptors combined with the Boolean operator “AND”: “globus pallidus” AND “Language”; “corpus striatum” AND “Language”; “Caudate nucleus” AND “Language”; and “thalamus” AND “Language” (Chart 2).

**Chart 2.** Search strategy.

| Search strategy of databases with respective descriptors | | n |
|---|---|---|
| Medline | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 256 |
| Cochrane Library | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 20 |
| LILACS | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 3 |
| SciELO | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 3 |
| CAPES periodic | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 9,105 |
| PubMed | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 501 |

Source: the authors

Independent and blind researchers assessed each group of descriptors, and another researcher resolved any disagreements. The researchers followed a search protocol developed previously for this study, and all studies were included in a posterior consensus according to eligibility criteria and assessed critically for their methodology. The PRISMA[5] protocol was used to guide this systematic review.

## RESULTS

A total of 9,888 studies were retrieved from the searches. After analyzing titles and abstracts, 2,142 reviews or experimental studies, 3,053 studies without relationship between language and subcortical structures, and 4,542 studies not investigating language were excluded. Of the 151 remaining studies, 117 were duplicates. A total of 34 studies were selected for full-text reading; 23 were excluded for not addressing the relationship between language and subcortical structures. Therefore, 11 studies were included in the qualitative synthesis.

The included studies were from nine different countries (Canada, Germany, United States, Italy, Russia, Austria, China, Palestine, and Turkey). Nine studies were developed in universities[3,6-13] and two in medical or hospital centers[1,4]. All studies addressed the relationship between subcortical structures and language (Chart 3).

**Chart 3.** Analysis of the included studies.

| Author/ year | Study location | Number of individuals and characteristics | Studied structures | Assessed language function |
|---|---|---|---|---|
| Braun *et al*., 2019 | Austria | 23 healthy individuals | Hippocampus, globus pallidus, and caudate nucleus | Orthographic input in the long-term memory |
| Manes *et al*., 2018 | USA and Europe | 89 (77 individuals with Parkinson's disease and 12 healthy individuals) | Putamen, caudate nucleus, and external and internal globus pallidus | Speech |
| Cheema *et al*, 2018 | Canada | 33 (19 individuals with reading skills and 14 with difficulty in reading) | Caudate nucleus, putamen, and thalamus | Reading |
| Zhang *et al*., 2021 | China | 51 (25 individuals with subacute stroke and 26 healthy individuals) | Thalamus | Naming |
| Rangus *et al*., 2021 | Germany | 52 individuals with acute ischemic lesions isolated in the thalamus | Thalamus | Complex comprehension of speech and verbal fluency |
| Wang *et al*., 2021 | USA | 30 individuals with essential tremor (before and after DBS surgery) | Thalamus | Verbal abstraction |
| Lahiri *et al*., 2020 | India | 515 individuals after stroke (175 with an acute subcortical condition) | Putamen, striatocapsular region, thalamus, and white periventricular substance | Speech, comprehension, lexico-semantics functions, and work, reading, and naming memories |
| Campanella *et al*., 2020 | Italy | One individual with hemorrhagic stroke in the thalamus | Thalamus | Repetition, writing, and comprehension |
| Fritsch *et al*., 2019 | Germany | 1,064 individuals after stroke (52 with isolated thalamic lesion) | Thalamus | Integration of cortical information, lexical selection, and speech |
| Samara *et al*.,2020 | USA | One individual with glioblastoma multiforme | Thalamus | Speech and comprehension |
| Temel *et al*., 2021 | Turkey | 28 individuals with thalamic hemorrhage | Thalamus | Speech, comprehension, repetition, naming, reading, and writing |

Source: the autors.

A total of 1,887 individuals were analyzed; the sample size ranged from 23 to 1,064, and two case studies assessed only one individual. Several language functions were studied. Eight studies[3,4,6-9,11,12] investigated aspects related to speech or comprehension and their relationship with subcortical structures, and other functions, such as orthographic input in long-term memory,

reading, writing, naming, repetition, and work memory were also approached[1,4,7,10,12,13].

Among imaging tests, brain magnetic resonance imaging, especially functional magnetic resonance imaging (fMRI), was the main test analyzing brain structures[1,3,6-13]. Only one study[4] did not use magnetic resonance imaging but used clinical parameters and non-contrast head computerized tomography to assess these structures. Although these tests were also present in some studies, they were complementary to the fMRI.

The thalamus was the most studied subcortical structure related to subcortical aphasia: of the 11 selected studies, 9 assessed the thalamic function and its association with language functions[1,3,4,6-10,12]. Other structures were also studied, such as the putamen, caudate nucleus, globus pallidus, hippocampus, striatocapsular region, and white periventricular substance[10-13]. The involvement of a thalamic subregion, influence of the perfusion level, and functional connection with the temporal cortex was observed in the naming performance. Thus, the thalamus was considered a component of the lexico-semantic system[1].

Individuals with thalamic aphasia presented language dysfunctions, including complex comprehension of speech and verbal fluency, highlighting the involvement of the thalamus in domains of high-level language[6] It may occur due to the thalamus projection to all neocortex areas, including frontal and temporal regions associated with language, establishing reciprocal connections between the subregions of the Broca's area and subcortical structures[7]. Also, left anterior thalamus nuclei might play an important role in integrating left cortical information in the thalamocortical language networks[3]. Considering the lateralization and regionalization of the thalamic language function[8], these factors may explain thalamic aphasia, which is associated with lesions affecting exclusively the thalamus, usually on the left side[9].

The putamen was associated with the performance of reading words and non-words, reinforcing its fundamental role in executing highly familiar motor plans; however, this action is only possible when interacting with the thalamus[10]. Also, highly severe subcortical aphasia is related to the left region of the putamen compared with the thalamus, striatocapsular region, and white periventricular substance[12].

The caudate nucleus participated in tasks requiring information from sounds, such as phonemes and syllables, since individuals with dyslexia became slower when the activity in this nucleus increased[10]. Also, the caudate nucleus is involved in work memory and selection and inhibition of lexical candidates during silent reading, with involvement of the globus pallidus[13].

Activation of the hippocampus was associated with strong and weak memories of the perirhinal cortex and memories and familiarity of stimuli. This finding corroborated the hypothesis of the declarative and procedural model, which suggests that the hippocampus is part of a declarative memory system and involved in the storage of lexico-semantical information[13].

The association between language and the capsular striatum and periventricular white matter regions was not deeply studied. However, subcortical strokes in both structures were associated with aphasia[12].

## DISCUSSION

An adult fluent in any language has a daily active vocabulary ranging from 17,000 to 45,000 words. The efficacy, speed, and ease of the human brain in recognizing words are complex and intriguing. Also, the adequate processing of words requires activation, recovery, and reconstruction of orthographic information stored by memory[13].

Aphasia is an acquired disorder characterized by receptive and expressive problems with oral and written language[2]. It usually occurs due to lesions on the left frontotemporal cerebral cortex, which is part of a complex language network to comprehend the production and processing of speech[3]. However, research involving this adequate comprehension indicated that subcortical structures, such as the thalamus, should be recognized as part of the complex language networks and investigated as potential aphasia foci[3].

In the mid-19th century, aphasia was recognized as a possible derivation from subcortical pathologic processes, and the traditional classification of aphasia by Wernicke included subcortical aphasia among the subtypes. However, some authors rejected this idea at the beginning of the 20th century since subcortical disorders involving base nuclei and other structures would result in dysarthria instead. The idea of subcortical aphasia was abandoned when Dejerine et al. investigated the language zones, corresponding to the perisylvian region of the left hemisphere. Recently, lesions in subcortical structures were constantly associated with aphasia due to the development of precise imaging tests (e.g., computerized tomography), restarting the discussion on the topic[12].

Although literature have described the striatocapsular region and thalamus as the two structures most affected by subcortical aphasia, recent studies indicated other subcortical structures related to dysarthria (mostly initiated by mutism), hypophonic, slow, and melodic speech, and aphasia[12]. A study in individuals with subcortical disorders identified several language components associated with these structures, including sentence length, grammatical form, ease of initiating speaking, articulation, voice volume, and comprehension[12]. Manes et al.[11] investigated the involvement of subcortical structures in language disorders of individuals with Parkinson's disease and suggested that these disorders were associated with changes in connections of cortical structures with the putamen and left internal globus pallidus.

The fMRI is one of the main methods used to analyze anatomical structures related to language function and has been used in many studies[1,6,10,11]. The structures related to language may be approached by assessing cerebral hemodynamic activity during language comprehension and

statistical analysis. Also, three regions subjacent to language comprehension are consistently found in fMRI of adults: the left inferior frontal, left middle temporal, and left superior temporal gyrus[14].

Zhang et al.[11] developed a study on the importance of thalamocortical connections for the naming skill in the context of cerebral perfusion. The naming process consists of the assignment of a lexical label to an object or concept, which is essential for efficient communication. It also comprehends distinct cognitive executions, including visual perception, semantic processing, lexical selection, recovery of phonologic or orthographic representations, and planning and execution of speech motor output. The difficulty in naming is commonly observed in aphasia, and its complexity may justify the liability to a series of pathologies, including vascular events and chronic neurodegenerative processes[1].

The naming process usually occurs in specific networks of the left perisylvian cortex, including the Broca area, posterior temporal gyrus, motor cortex, middle frontal gyrus, bilateral fusiform regions, and anterior temporal lobes. Recent studies reported that different types of errors in naming depend on the specific location of the cerebral damage. Also, subcortical structures (particularly the thalamus) and cortical-subcortical connections were recognized as having a relevant impact on this process[1].

Basal ganglia and its complex network are related to motor skills and naming. For example, language lateralization (characterized by anomie and impaired repetition or listening comprehension) was identified in up to 64% of left thalamic lesions. This might result from the thalamic influence on the temporal and frontal cortex through connectivity with the thalamic middle pulvinar nuclei[1].

## CONCLUSION

The results supported the notion of language lateralization in the thalamus and suggested a predominant involvement of the left anterior nuclei. However, the mechanism of how a left anterior thalamic lesion leads to aphasic symptoms needs further investigation. In general, a wide thalamocortical interaction in language functions and involvement of the thalamus in the information integration needed for language tasks were suggested. Thus, this study evidenced a possible specific left anterior thalamus involvement in the language function.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTIONS

**ABA**: conceptualization, data curation and analysis, methodology and project administration, research, and writing, review, and edition of the manuscript; **IFGG**: methodology administration, data analysis, and writing, review, and edition of the manuscript; **GSSGM**: data analysis and research; **WHSB**: data analysis and research; **KFSV**: data analysis and research; **DECB**: data analysis and research; and **LCAA**: conceptualization, supervision, project administration, data and experiment validation, and review and edition of the manuscript. All authors approved the final version to be published.

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# Effectiveness of ECMO treatment for acute respiratory distress syndrome of patients with covid-19: a literature review

## Eficácia do tratamento com ECMO para síndrome do desconforto respiratório agudo em pacientes com covid-19: uma revisão da literatura

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## Abstract

**Introduction**: The highly virulent SARS-CoV-2 virus spread worldwide between 2020 and 2022, causing the covid-19 pandemic. The characteristics of easy transmission, difficulty to control, and severe respiratory conditions led to social isolation and the use of FFP2 masks, with hospitalizations and high mortality. Treatments such as medications, patient pronation, and invasive treatments, such as mechanical ventilation, were used to prevent the irreversibility. However, extracorporeal membrane oxygenation (ECMO) was a viable alternative for eligible patients who were unresponsive to conventional treatments. **Objective**: This study aimed to discuss the effectiveness of the ECMO treatment during the covid-19 pandemic. **Methodology**: Among the studies published between 2019 and 2023 and retrieved from databases (Google Scholar, SciELO, and PubMed), 21 met the inclusion criteria. **Final considerations**: The ECMO treatment demonstrated potential to contribute to the recovery of patients with severe respiratory failure despite its risks and the need for a trained multidisciplinary team combined with 24-hour care and monitoring, being an alternative to inefficient conventional treatments.

**Keywords**: Covid-19; Extracorporeal membrane oxygenation; ECMO; Respiratory failure; Therapeutic support.

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## Resumo

**Introdução**: O vírus SARS-CoV-2, altamente virulento, se espalhou pelo mundo entre 2020 e 2022, causando a pandemia de covid-19. As características de fácil transmissão, dificuldade de controle e quadros respiratórios graves levaram ao isolamento social e ao uso de máscaras PFF2, com internações e alta mortalidade. Tratamentos como medicamentos, pronação do paciente e tratamentos invasivos, a exemplo de ventilação mecânica, foram utilizados para prevenir a irreversibilidade. No entanto, a oxigenação por membrana extracorpórea (ECMO) foi uma alternativa viável para pacientes elegíveis que não responderam aos tratamentos convencionais. **Objetivo**: Discutir a eficácia do tratamento com ECMO durante a pandemia de covid-19. **Metodologia**: Entre os estudos publicados entre 2019 e 2023 e recuperados de bases de dados (Google Acadêmico, SciELO e PubMed), 21 atenderam aos critérios de inclusão. **Considerações finais**: O tratamento com ECMO demonstrou potencial para contribuir na recuperação de pacientes com insuficiência respiratória grave, apesar dos riscos e da necessidade de equipe multidisciplinar treinada, aliada a cuidados e monitoramento 24 horas, sendo uma alternativa aos tratamentos convencionais ineficientes.

**Palavras-chave**: Covid-19; Oxigenação por membrana extracorpórea; ECMO; Falência respiratória; Suporte terapêutico.

## INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the coronavirus disease 2019 (covid-19) that emerged in China in December 2019. The SARS-CoV-2 spreads via aerosols, coughs, sneezes, and droplets from the respiratory tract containing viral load. The transmission mostly occurs by asymptomatic patients, and family environments and healthcare services are the focal points of contamination[1].

The SARS-CoV-2 is a variation of the *Coronaviridae* family and expresses a single-stranded positive-sense RNA (RNA+)[2,3] that encodes approximately 29 proteins. Relevant proteins include the S protein (Spike), which promotes the viral cell infection; the N protein from the viral nucleocapsid, regulating replication; and the ORF7 protein, essential to viral release, triggers apoptosis in host cells and is associated with damage in alveolar cells[3].

During transmission, the virus attaches to the mucosa of respiratory epithelium, binding the surface protein Spike with the angiotensin-converting enzyme 2 (ACE2) tissue receptor, highly expressed in pulmonary cells. Once bonded, the virus is endocytosed, and viral replication starts. The new particles are released by budding in the vascularized pulmonary parenchymal tissue, progressing to haematogenous spread and infection of other cells and tissues expressing ACE2 [4,1].

The viral tropism for cells of the respiratory system leads to classic symptoms, such as

fever and cough. However, the ACE2 receptor is expressed in other organs (e.g., kidneys, intestines, and heart), and its activation is associated with different clinical symptoms[4].

Patients infected with the SARS-CoV-2 virus present a high chance of developing flu-like symptoms, except for asymptomatic cases. This acute respiratory condition includes fever, cough, sore throat, runny nose, or dyspnea due to the lack of a peak production of angiotensin[5,6].

The pre-existing comorbidities considered as risk factors for severe progression of covid-19 include diabetes, high-risk pregnancies, immunosuppressive conditions, and respiratory, cardiovascular, liver, and chronic kidney diseases[5]. However, the presence of one or more symptoms is related to the interaction between host cells and SARS-CoV-2 since the immune response of the patient is crucial to disease evolution[4]. According to the Ministry of Health of Brazil (2020), 80% of cases were mild, whereas severe cases ranged from 5% to 10%[7].

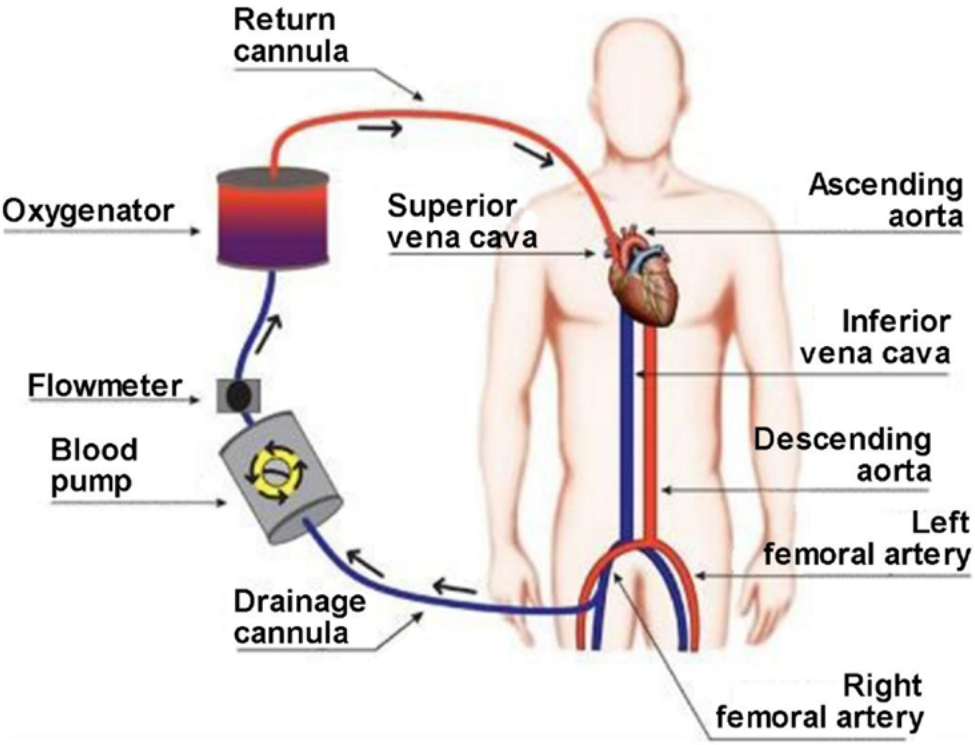
The high virulence of SARS-CoV-2 is responsible for the progression to acute respiratory distress syndrome (ARDS), especially in patients with old age or with pre-existing conditions[7]. Consequently, patients over 60 years old (physiologically immunocompromised due to aging) or with hypertension, diabetes, respiratory diseases, or heart conditions have increased risk factors, and one or more factors increase three to four-fold the odds of hospitalization[8,9].

Patients with covid-19 have symptoms related to cellular distress due to hypoxia (oxygen saturation below 95%), hypotension, respiratory distress, and increased respiratory rate. Additionally, underlying diseases may present worse clinical evolution, such as chronic obstructive pulmonary disease[7]. This requires intensive and continuous care by a multidisciplinary team with mechanical ventilation, pronation, neuromuscular blocking agents, pulmonary vasodilators, high positive end-expiratory pressure, and recruitment maneuvers[10].

The last therapeutic resource is the extracorporeal membrane oxygenation (ECMO), the main device for extracorporeal life support for pulmonary or cardiac failure. The two classic configurations are the venovenous ECMO (ECMO-VV) or venoarterial ECMO (ECMO-VA), which require a cannula for drainage and the other for return of oxygenated blood[11].

The ECMO-VV is used for respiratory failure with preserved cardiac function. In this procedure, blood is drained from the right femoral vein, flows via an oxygenator, and is infused in the right internal jugular vein, the first option for vascular access. The oxygenated blood perfuses the lungs to assist the impaired pulmonary tissue (Figure 1)[10,11].

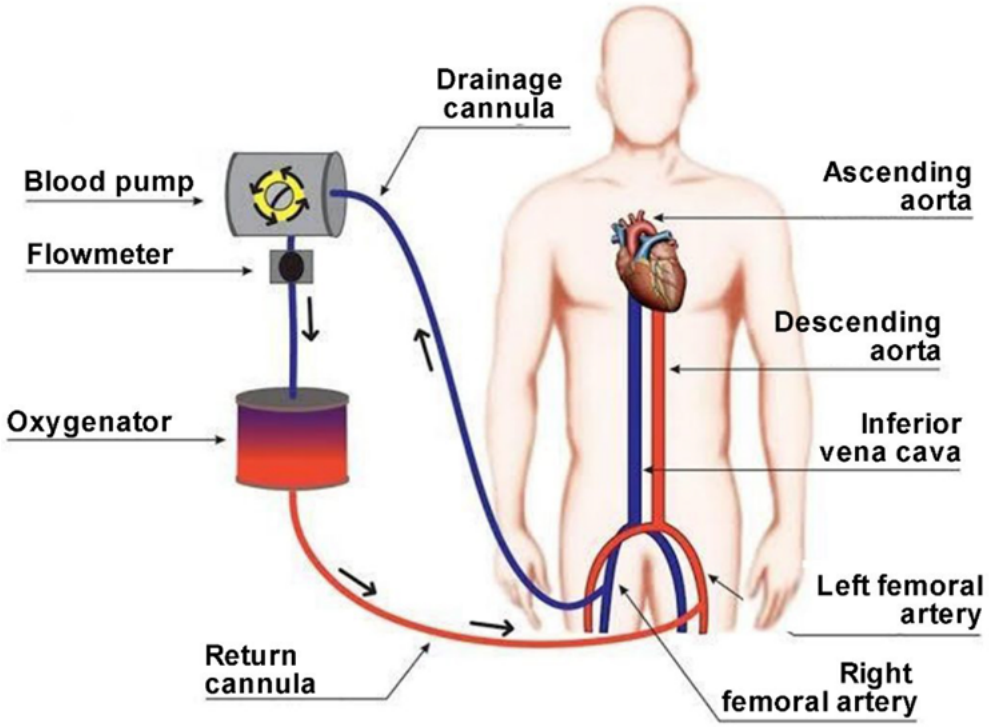
**Figure 1.** Venovenous ECMO




Source: Chaves (2019)[11].

The ECMO-VA is indicated for cardiac support with or without preserved pulmonary function with central (i.e., after post-thoracotomy) or peripheral implantation. In central ECMO-VA, blood is drained from the right atrium and is infused in the ascending aorta. Meanwhile, in peripheral ECMO-VA, blood is drained from the femoral or jugular vein and is infused via the axillary, femoral, or carotid arteries (Figure 2)[10,11].

**Figure 2.** Venoarterial ECMO.




Source: Chaves (2019)[11].

The ECMO treatment was performed in the Middle East during the respiratory syndrome coronavirus (MERS-CoV) outbreaks in 2012 and the H1N1 influenza pandemic in 2009. Due to its effectiveness in the treatment of severe cases, ECMO was considered an option for covid-19[10] because of the alarming epidemiological data reported by the Ministry of Health of Brazil[12].

Thus, this study aimed to discuss the effectiveness of ECMO as a therapeutic alternative for the treatment of severe ARDS in hospitalized patients with covid-19, supporting its clinical relevance.

## METHODS

This study is an integrative review conducted using articles indexed in databases such as Google Scholar, the Scientific Electronic Library Online (SciELO), and Medline (PubMed). The inclusion criteria were studies published in Latin America between 2019 and 2023 in Portuguese, English, and Spanish.

Keywords were used combined and individually in Portuguese (*oxigenação por membrana extracorpórea*, *ECMO*, *falência respiratoria,* and *suporte terapêutico),* English (extracorporeal membrane oxygenation, intensive care, and ARDS), or Spanish (*terapia*, *recuperación*, and *oxigenación por membrana extracorpórea*).

Original articles, case reports, systematic reviews and meta-analyses, and randomized and non-randomized clinical trials were included. Studies that were duplicated and did not meet the theme were excluded. A total of 68 articles were found, and 21 met the criteria (Table 1).

**Table 1.** Characteristics of the included studies and the analysis of clinical aspects of infection in patients with covid-19 and the use of ECMO-VV.

| Title | Author (Year) | Objective | Main considerations |
|---|---|---|---|
| Description of covid-19 cluster: isolation and testing in asymptomatic individuals as strategies to prevent local dissemination in Mato Grosso state, Brazil, 2020 | Silva *et al.* (2020)[1]. | To describe a covid-19 cluster and the strategies used to contain the virus in a municipality in the countryside of the state of Mato Grosso, Brazil. | The covid-19 cases should not be dismissed, even with negative molecular test results. The inclusion of complementary serological tests was proposed as a beneficial approach to clarify these cases and identify asymptomatic patients. This approach may support strategies for controlling and preventing covid-19. |
| SARS-CoV-2 as the causative agent of covid-19: Epidemiology, genetic characteristics, clinical manifestations, diagnosis and possible treatments | Bezerra *et al.* (2020)[2]. | To conduct an integrative review of the main characteristics of SARS-CoV-2 and the epidemiological, clinical, and diagnostic aspects of covid-19 and possible treatments. | The high rate of viral spread and the lack of effective vaccines or treatments available highlighted the need for further studies. |
| Coronavirus SARS-CoV-2 and Covid-19 | Uzunian *et al.* (2020)[3]. | To explain the structure and function of the agent responsible for covid-19 in ARDS. | A prophylactic immunization against this virus was unknown. In severe hospitalized patients, intubation combined with oxygenation was performed to ensure adequate ventilation of the alveoli. |
| Immunopathological mechanisms involved in SARS-CoV-2 infection | Brito *et al.* (2020)[4]. | To gather evidence regarding the main mechanisms of transmission and immunopathology of SARS-CoV-2 infection. | The immune response of the host plays a crucial role in the pathogenesis of covid-19. In vitro studies are essential to elucidate the pathogenic mechanisms of SARS-CoV-2 and to the development of vaccines and therapeutic targets. |
| Suspected covid-19 case definition: a narrative review of the most frequent signs and symptoms among confirmed cases | Iser *et al.* (2020)[5]. | To describe the most frequent signs and symptoms of SARS-CoV-2. | Considering the lack of diagnostic tests and a wide spectrum of symptoms, health services should employ a sensitive case definition for appropriate surveillance, prevention, and treatment. |

| | | | |
|---|---|---|---|
| Does angiotensin II peak in response to SARS-CoV-2? | Xavier *et al*. (2020)[6]. | To address the covid-19 severity and to analyze the relationship between symptoms and angiotensin-converting enzyme 2, providing an accurate understanding of the prognostic of the disease. | The ARDS plays a critical role in the early response to SARS-CoV-2 infection, affecting the prognosis of covid-19. |
| Comorbidities and deaths by covid-19 in Brazil | Souza *et al*. (2021)[8]. | To describe the cases of patients who died due to covid-19 in Brazil, highlighting age, sex, and comorbidities. | The presence of one or more comorbidities, particularly heart diseases, was associated with a poor prognosis of covid-19. Additionally, the age of the patient was a relevant aspect. |
| Covid-19 and hospitalizations for SARI in Brazil: a comparison up to the 12th epidemiological week of 2020 | Bastos *et al*. (2020)[9]. | To investigate the pattern of hospitalizations due to SARI in Brazil since the outbreak of SARS-CoV-2, comparing the temporal and age profiles and laboratory results from 2010 to 2019. | The increase in hospitalizations due to SARI, the lack of specific information regarding the etiological agent, and the predominance of cases among older adults during the rise of covid-19 cases suggest that severe cases were identified via SARI surveillance, overloading the healthcare system. The inclusion of tests for SARS-CoV-2 in the SARI surveillance protocol and its effective implementation is crucial for monitoring the progression of severe covid-19 cases in Brazil. |
| Evidence on the effectiveness of ECMO in adults hospitalized with covid-19 | Carvalho *et al*. (2021)[10]. | To inform on the anesthetic, surgical, and intensive care during the start and management of ECMO in patients with respiratory failure, disseminating knowledge on its efficacy. | The ECMO should be the last resource after the failure of other ventilatory support strategies, including prone positioning, use of high positive end-expiratory pressure, alveolar recruitment maneuvers, pulmonary vasodilators, and neuromuscular blocking agents. |
| Extracorporeal membrane oxygenation: a literature review | Chaves *et al*. (2019)[11]. | To present the theoretical and practical concepts on the use of ECMO for refractory respiratory or cardiac failure in conventional clinical management and critical patients. | The ECMO is one of the main devices of extracorporeal life support currently used and requires a multidisciplinary team with expertise for this support. |

| | | | |
|---|---|---|---|
| Brazilian Guidelines for the pharmacological treatment of patients hospitalized with covid-19 | Falavigna *et al*. (2022)[13]. | To elaborate recommendations to support decisions regarding the pharmacological treatment of patients hospitalized with covid-19 in Brazil. | Few therapies were efficient in the treatment of hospitalized patients with covid-19, being recommended corticosteroids and prophylaxis for thromboembolism. |
| The use of ventilators in the covid-19 pandemic | Barbosa *et al*. (2020)[14]. | To present challenges in the use of ventilators during the pandemic in different countries. | Challenges, such as difficulty in social distancing, increased infection rates, and reduced availability of ventilators, potentially overwhelmed healthcare systems worldwide, especially in Brazil. Thus, alternatives emerged to address the demand for this resource. |
| Clinical characteristics and predictors of mechanical ventilation in patients with covid-19 hospitalized in Southern Brazil | Bastos *et al.* (2020)[15]. | To describe the clinical characteristics and predictors of mechanical ventilation in adult patients hospitalized with covid-19. | Advanced age was the main predictor of respiratory insufficiency, with a need for mechanical ventilation in the Brazilian population. The presence of comorbidities, especially systemic arterial hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, malignancies, and obesity, was associated with worse prognosis and death. |
| Use of conscious pronation in the respiratory management of patients with covid 19: a literature review | Campos *et al*. (2022)[16]. | To evaluate the indications and advantages of the use of conscious pronation in the management of non-intubated patients with respiratory impairment due to covid-19. | Conscious pronation is a simple and easy intervention that patients may perform with proper guidance and minimal assistance. Furthermore, conscious pronation does not require institutional resources or have associated costs. |
| Pronation in ARDS due to covid-19: more pros than cons | Battaglini *et al*. (2022)[17]. | To identify the factors that contribute to improve oxygenation and mortality after pronation in patients with covid-19 using mechanical ventilation. | The use of a prone position in covid-19 patients with severe hypoxemic respiratory failure was important. This technique should be maneuvered early and regardless of the oxygenation response. However, results still need validation in comprehensive randomized controlled trials. |

| | | | |
|---|---|---|---|
| Join Society of Critical Care Medicine- Extracorporeal Life Support Organization task force position paper on the role of the intensivist in the initiation and management of Extracorporeal Membrane Oxygenation | Della-Volpe *et al.* (2020)[18]. | To define the role of the intensivist in the initiation and management of patients on ECMO. | The role of the intensivist in the care of patients on ECMO is in development, especially regarding patient selection, cannulation, and management of ECMO. |
| ECMO use in covid-19: Case report of a venovenous ECMO in an adult patient with covid-19 | Mássimo *et al*. (2021)[19]. | To report a clinical case of an adult patient diagnosed with covid-19 submitted to ECMO in a private hospital in the metropolitan area of Belo Horizonte, Minas Gerais. | The ECMO treatment was designed to restore vital function and reduce adverse outcomes. Additionally, the ECMO supports vital organ systems during the recovery of the patient since it is not a direct treatment. |
| In search of the ideal monitoring of heparin in mechanical circulatory support | La Guerra et al. (2020)[20]. | To analyze the correlation between rTTPa and anti-Xa to describe the therapeutic range in the anticoagulation with UFH in patients under short-term mechanical support and to describe the complications and hematological disorders after this period. | The study observed a limited correlation between rTTPa and anti-Xa, with a more solid trend with anti-Xa. The use of anti-Xa monitoring may be safer and reduce hemorrhagic complications despite the quick laboratory results for rTTa. Therefore, the team and service should provide training and standardized management of the quality of care. |
| Extracorporeal respiratory support in patients | Oliveira *et al.* (2020)[21]. | To address aspects associated with ECMO in patients and describe clinical involvement. | The decision not to offer ECMO is equivalent to denying conventional ventilation since ECMO is used during diagnosis and in the search process for effective therapeutic strategies. Thus providing the opportunity to improve cardiorespiratory conditions and increase chances of recovery. |
| Effectiveness of extracorporeal membrane oxygenation (ECMO) therapy in critically patients with covid-19 | Lavezzo *et al*. (2022)[22] | To conduct an integrative review of the literature on the investigation of ECMO therapy efficacy in critically ill patients with covid-19. | The ECMO might improve outcomes for patients with severe covid-19, mainly in cases of patients aged under 71 years and with fewer comorbidities. However, evidence associates ECMO with an increased risk of thrombosis. |

ARDS: acute respiratory distress syndrome, SARI: severe acute respiratory illness, ECMO: extracorporeal membrane oxygenation, rTTPa: activated partial thromboplastin time-ratio, anti-Xa: activated anti-factor X, UFH: unfractionated heparin.

# DEVELOPMENT

## Epidemiology

According to the Ministry of Health of Brazil (2023)[12], 660 million cases of covid-19 and more than six million deaths were reported worldwide until December 2022. The incidence and mortality rate in Brazil was 17,153.2 cases and 327.7 deaths per 100,000 inhabitants, respectively. From February 2020 to December 2022, Espírito Santo recorded the highest incidence rate (32,262 cases per 100,000 inhabitants), with a mortality rate of 368,2 deaths per 100,000 inhabitants. However, Rio de Janeiro had an incidence rate of 15,555.4 cases per 100,000 inhabitants, with the highest mortality rate in Brazil (440.6 deaths per 100,000 inhabitants) (Table 2)[12].

## Therapeutic resources

The recommendation for mild cases of covid-19 is rest, a balanced diet, hydration, medication when needed (e.g., analgesics and antipyretics), and social distancing for five days from the onset of symptoms[7]. Moreover, for hospitalized patients on oxygen therapy, dexamethasone (a steroidal anti-inflammatory drug) was prescribed for ten days due to the inflammatory process associated with increased cytokine production to reduce pulmonary edema[13].

Severe forms of covid-19 potentially evolve into acute respiratory failure, requiring mechanical to replace totally or partially the involuntary ventilatory activity, which reduces respiratory work and enhances gas exchange efficiency. Mechanical ventilation presents as non-invasive with an external interface or invasive using intubation or tracheostomy. The maximum period of mechanical ventilation is 29.5 days[14,15].

Pronation (i.e., the patient placed in a prone position) is indicated in cases of progression to ARDS with refractory hypoxemia to mechanical ventilation, reducing hypoxemia and improving the ventilation/perfusion ratio[16,17]. In Latin America, 72% of hospitalized patients required pronation before receiving ECMO[23].

**Table 2.** Distribution of new covid-19 cases and deaths recorded in epidemiological week 52 (EW 52), total cases, incidence, and mortality coefficients (per 100,000 inhabitants) by Region/State, Brazil, 2022[12]

| Region/State | Confirmed cases | | | | Confirmed deaths | | | |
|---|---|---|---|---|---|---|---|---|
| | New | Total | Cumulative Incidence | Incidence in EW 52 | New | Total | Deaths | Deaths in EW 52 |
| **North** | **8.593** | **2.839.575** | **15.207,20** | **46.0** | **22** | **51.363** | **275.1** | **0.1** |
| AC | 889 | 158.669 | 17.738,90 | 99.4 | 4 | 2.040 | 228.1 | 0.4 |
| AM | 138 | 624.864 | 14.850,40 | 3.3 | 3 | 342.7 | 14.418 | 0.1 |
| AP | 28 | 182.516 | 21.179,10 | 3.2 | 0 | 2.165 | 251.2 | 0.0 |
| PA | 823 | 861.041 | 9.907,60 | 9.5 | 8 | 18.953 | 218.1 | 0.1 |
| RO | 4.008 | 471.673 | 26.255,70 | 223.1 | 7 | 7.399 | 411.9 | 0.4 |
| RR | 180 | 181.245 | 28.715,20 | 28.5 | 0 | 2.180 | 345.4 | 0.0 |
| TO | 2.527 | 359.567 | 22.610,80 | 158.9 | 0 | 4.208 | 264.6 | 0.0 |
| **Northeast** | **24.354** | **7.206.999** | **12.561,40** | **42.4** | **240** | **133.829** | **233.3** | **0.4** |
| AL | 1.323 | 335.176 | 10.000,60 | 39.5 | 11 | 7.196 | 214.7 | 0.3 |
| BA | 6.116 | 1.769.063 | 11.848,50 | 41.0 | 82 | 31.230 | 209.2 | 0.5 |
| CE | 2.786 | 1.437.171 | 15.643,40 | 30.3 | 11 | 28.067 | 305.5 | 0.1 |
| MA | 759 | 488.093 | 6.860,40 | 10.7 | 6 | 11.034 | 155.1 | 0.1 |
| PB | 3.131 | 700.127 | 17.333,00 | 77.5 | 15 | 10.525 | 260.6 | 0.4 |
| PE | 5.926 | 1.122.935 | 11.677,00 | 61.6 | 22 | 22.579 | 234.8 | 0.2 |
| PI | 2.127 | 413.535 | 12.602,10 | 64.8 | 21 | 8.027 | 244.6 | 0.6 |
| RN | 1.395 | 582.618 | 16.485,30 | 39.5 | 71 | 8.689 | 245.9 | 2.0 |
| SE | 791 | 358.281 | 15.451,00 | 34.1 | 1 | 6.482 | 279.5 | 0.0 |
| **Southeast** | **95.414** | **14.407.277** | **16.185,70** | **107.2** | **623** | **333.330** | **374.5** | **0.7** |
| ES | 6.561 | 1.311.144 | 32.262,00 | 161.4 | 28 | 14.964 | 368.2 | 0.7 |
| MG | 52.536 | 4.079.422 | 19.158,80 | 246.7 | 189 | 64.447 | 302.7 | 0.9 |
| RJ | 10.121 | 2.701.378 | 15.555,40 | 58.3 | 167 | 76.508 | 440.6 | 1.0 |
| SP | 26.196 | 6.315.333 | 13.643,20 | 56.6 | 239 | 177.411 | 383.3 | 0.5 |
| **South** | **55.012** | **7.712.937** | **25.546,00** | **182.2** | **144** | **109.809** | **363.7** | **0.5** |
| PR | 14.773 | 2.861.213 | 24.843,70 | 128.3 | 47 | 45.718 | 397 | 0.4 |
| RS | 32.435 | 2.895.571 | 25.348,70 | 283.9 | 72 | 41.508 | 363.4 | 0.6 |
| SC | 7.804 | 1.956.153 | 26.972,10 | 107.6 | 25 | 22.583 | 311.4 | 0.3 |
| **Central-west** | **23.571** | **4.164.493** | **25.232,80** | **142.8** | **81** | **65.522** | **397** | **0.5** |
| DF | 4.114 | 888.063 | 29.067,70 | 134.7 | 0 | 11.838 | 387.5 | 0.0 |
| GO | 11.695 | 1.823.980 | 25.641,00 | 164.4 | 51 | 27.766 | 390.3 | 0.7 |
| MS | 2.549 | 593.209 | 21.115,20 | 90.7 | 17 | 10.903 | 388.1 | 0.6 |
| MT | 5.213 | 859.241 | 24.367,20 | 147.8 | 13 | 15.015 | 425.8 | 0.4 |
| **Brazil** | **206.944** | **36.331.281** | **17.157,20** | **97.7** | **1.110** | **693.853** | **327.7** | **0.5** |

Source: adapted from the Brazilian Ministry of Health[12]

## Indications for ECMO

Hospitalized patients on mechanical ventilation and in intensive care with worsening progression should be evaluated by a multidisciplinary team considering advanced support treatments. Patients with ARDS at high risk of death ($PaO_2/FiO_2$ below 100) are indicated for ECMO[18,24], and a trained team may immediately start ECMO at a specialized center when its benefits are evidenced[19,24].

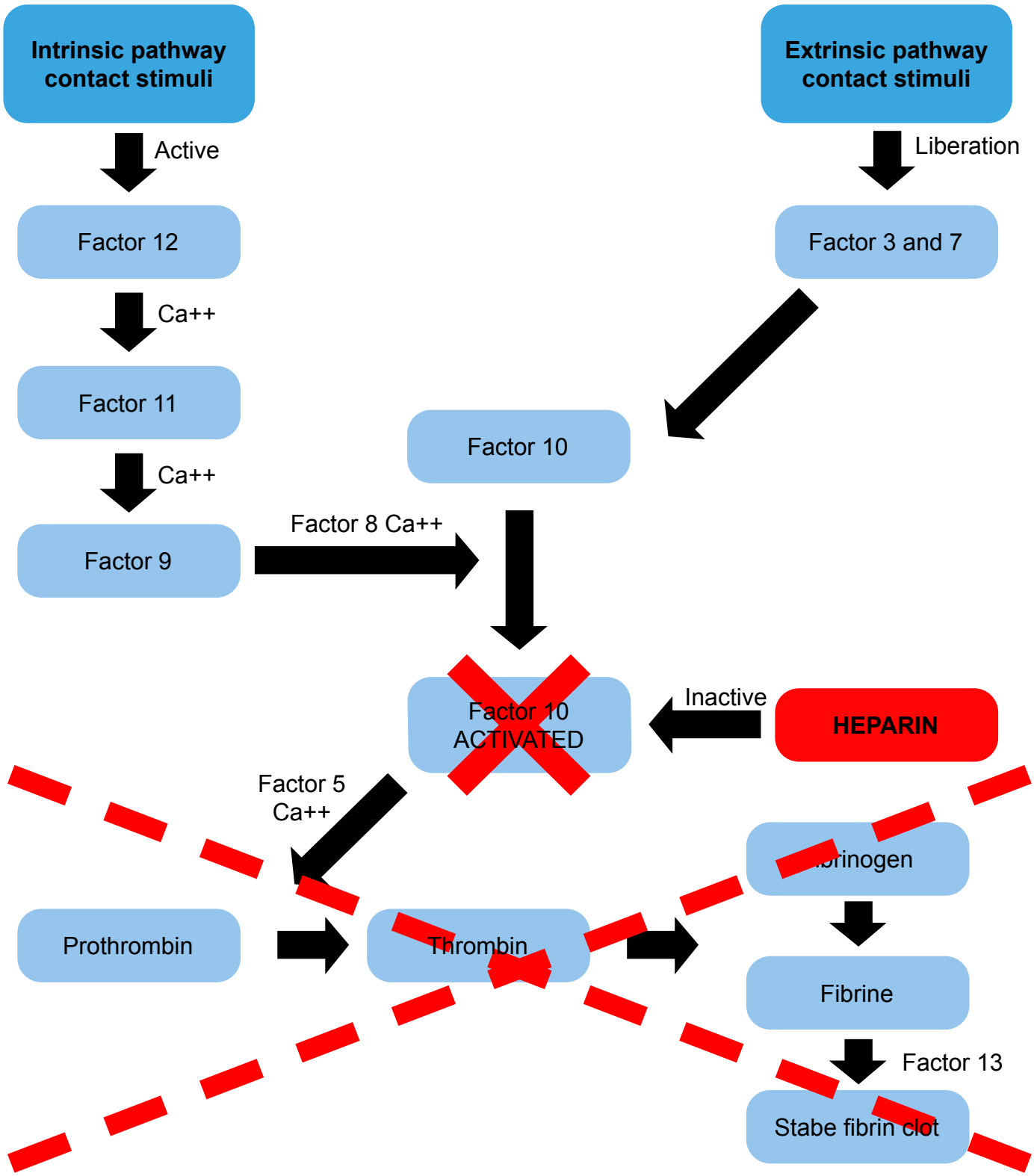
Despite ECMO treatment being an option, contraindication occurs on terminal illness, severe damage to the central nervous system, and do-not-resuscitate order[24]. The Extracorporeal Life Support Organization (ELSO) regulates and determines the exclusion criteria for ECMO treatment for patients with covid-19. Patients with comorbidities may be excluded due to a worse prognosis. The prognosis worsens with advanced age; however, this is a relevant factor when the potential for favorable outcomes and availability of resources are balanced. Thus, patients on mechanical ventilation for more than seven days must be evaluated for indication of ECMO treatment[19,24].

## Patient care in ECMO

A multidisciplinary team constantly monitors patients on ECMO since complications are frequent due to the use of vasopressors and anticoagulants (e.g., heparin) drugs[11]. Although most lines are coated with anticoagulant-like molecules, patients on ECMO receive anticoagulants to prevent clot formation in the circuit and vascular thrombosis at the cannula insertion sites[25]. Heparin acts by inactivating factor 10a in the coagulation cascade (Figure 3), preventing clot formation[20].

Anticoagulation is monitored using the activated coagulation time (ACT) or the activated partial thromboplastin time (aPTT) tests, performed every four to six hours[25]. Reference values are from 180 to 220 and 40 to 55 seconds for ACT and aPTT, respectively.

**Figure 3.** Heparin action in the coagulation cascade.




Source: authors.

## Complications of ECMO

Complications regarding ECMO are frequent and categorized as clinical or mechanical. Mechanical complications are triggered by issues in the extracorporeal circuit, such as failure of the oxygenation membrane, rupture of the system, and coagulation. Moreover, clinical complications include intracranial, intrathoracic, and retroperitoneal hemorrhages, acute kidney injuries, infections due to invasive devices, and thromboembolism[11,21-22].

## Weaning from ECMO

Weaning from ECMO should only start when the patient autonomously performs gas exchanges to supply the needs generated by their body surface (peak pressure ≤ 30 $cmH_2O$, positive end-expiratory pressure ≤ 15 $cmH_2O$, tidal volume ≤ 6mL /Kg of predicted body weight, respiratory rate ≤ 35 breath per minute e $FiO_2$ ≤ 60%)[23]. Additionally, radiography findings and pulmonary compliance should be improved.

After, an autonomy test for weaning from ECMO-VV is performed, suspending the fresh gas flow in the system. Arterial blood gas tests are evaluated in patients stable for six hours. Blood pH and $PaO_2$ levels within the expected parameters are considered to ECMO weaning after 12 hours of sustained stability without ventilatory support from the membrane and with stable hemodynamic parameters[11].

## DISCUSSION

Hospitalized patients with covid-19 often need intensive treatments, including ECMO. In Brazil, the average length of ECMO treatment is ten days, and the survival rate is 57%, similar to the global rate reported by ELSO[26].

The ECMO is an intensive treatment with benefits and risks, preventing multiple organ failure, worse respiratory insufficiency outcomes, and the disease progression to ARDS[25]. However, ECMO may be associated with a high risk of thromboembolism[19].

During ECMO treatment, temporary support of pulmonary and cardiac function provided by the oxygenating membrane leads to changes in the body and respiratory system. This membrane provides gas diffusion between fresh gas flow and the venous blood, supplying oxygen-rich blood and exuding carbon dioxide[11]. However, ECMO can be recognized as a foreign body, resulting in severe conditions such as a systemic inflammatory response syndrome[11,21]. Despite risks, ECMO may enhance the chances of recovery for patients with ARDS or refractory cardiocirculatory impairment[10,19].

Comorbidities are risk factors that affect ECMO treatment. In 2020, 31% of patients in Latin America had hypertension, and 48% were overweight and/or obese, which is contraindicated for

advanced therapeutic intervention, according to ELSO[23]. During the covid-19 pandemic, although used as a last resource, the ECMO treatment provided an important treatment for hospitalized patients with ARDS[10].

## FINAL CONSIDERATIONS

The ECMO is one of the main treatments to save patients with severe respiratory failure, providing temporary support in conventional treatments of pulmonary or refractory cardiac function. Furthermore, the ECMO decreases the load on these organs and contributes to the recurrence of the condition and recovery of the patient.

The treatment followed ELSO recommendations and was supported by a trained multidisciplinary team during the pandemic. In this way, the treatment elicited positive results, improving the condition of 57% of patients with severe covid-19.

The ECMO treatment offers a high-efficacy alternative to treat severe patients of new pandemic diseases that cause severe respiratory failures. Thus, the potential described in case reports and others studies during the covid-19 pandemic was corroborated in the present study.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## FUNDING

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## AUTHOR CONTRIBUTIONS

**LSR e MPV:** Conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft. **RCC:** Formal analysis, resources, supervision, validation, visualization, writing – review & editing. All authors read and approved the published version of the manuscript.

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# Implementation of plant extracts in healing materials: an advanced method to promote healing

## Implantação de extratos fitoterápicos em materiais cicatrizantes: uma abordagem avançada da promoção da cicatrização

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## Abstract

**Objective:** To analyze the effects of plant extracts on wound healing materials, focusing on their physicochemical properties and effectiveness in healing. **Methods:** This integrative review was conducted in PubMed and Lilacs databases using the descriptors “plant medicine” and “wounds” combined with the Boolean operator AND; the publication date encompassed studies from 2018 to 2023. Twelve studies were analyzed. **Results:** Selected studies were characterized by the following information: author, year of publication, population and intervention, objectives, and conclusion. Plant extracts were widely used alone or combined with other healing materials; most studies presented promising results. **Conclusion:** The analyzed studies corroborate the importance of using plant extracts in wound healing associated (or not) with other existing measures, demonstrating their effective therapeutic potential. Despite the progress made, the healing potential of plant extracts still needs further research.

**Keywords:** Plant extracts; Phytotherapy; Healing; Wounds and injuries.

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## Resumo

**Objetivo:** Analisar os efeitos dos extratos fitoterápicos em materiais cicatrizantes de feridas, com foco nas suas propriedades físico-químicas e sua eficácia na cicatrização. **Metodologia:** Tratou-se de uma revisão integrativa realizada nas bases de dados PubMed e Lilacs utilizando os descritores fitoterápico e feridas combinados com o operador booleano AND, considerando artigos incluídos no período de 2018 a 2023. Foram analisadas 12 publicações. **Resultados:** Foi realizada a identificação dos trabalhos selecionados, elencando-se os dados relacionados a autor, ano de publicação, população e intervenção, objetivos e a conclusão do estudo. Foi observada a ampla utilização de fitoterápicos, atuando isoladamente e em conjunto com outros materiais cicatrizantes. Os resultados foram promissores na maioria dos estudos. **Conclusão:** Os estudos analisados corroboram a importância do uso de fitoterápicos no processo de cicatrização de feridas, podendo associar a outras medidas já existentes, evidenciando o eficaz potencial terapêutico. Apesar dos avanços, temos muito a evoluir quanto à utilização e validação do potencial cicatrizante dos fitoterápicos.

**Palavras-chave**: Extrato vegetal; Fitoterapia; Cicatrização; Ferimentos e lesões.

## INTRODUCTION

A wound is a deformity or continuity solution that can reach from the epidermis to deeper structures[1]. Skin diseases, injuries, and burns affect more than 600 million people each year and cost more than $1 billion to health systems worldwide. In Brazil, wounds caused more than 700,000 hospitalizations in 2020, costing about R$850 million to the Unified Health System (SUS), according to the Department of Informatics of the Unified Health System[2]. Several conditions at the wound location must be controlled to ensure efficient healing, such as oxygenation, temperature, and the use of appropriate bandages.

Bandages or coverings are therapeutic means of cleaning and applying material to protect, absorb, and drain a wound, helping in its resolution[4]. Several bandages are commercially available, and the most commonly used are zine, cerium nitrate, hydrocolloid, hydrogel, non-adherent gases, synthetic biological membranes, and dermal regeneration matrix. The choice of bandage should be based on the characteristics of the wound, prioritizing those that cause less pain, are more comfortable for the patient, and are more economically viable[5].

An alternative to wound treatment would be the use of plant extracts. The National Health Surveillance Agency (ANVISA) considers plant extracts those obtained exclusively from raw materials of plant origin with constant and reproducible quality and whose risk and efficacy can be characterized in ethnopharmacological surveys, scientific-technical documentation, publications,

or clinical trials[6].

The use of plant extracts to treat, cure, and prevent diseases is an ancient practice that continues to the present day[7]. Therefore, this integrative review aimed to analyze the effects of plant extracts on wound healing materials, focusing on their physicochemical properties and effectiveness in promoting healing.

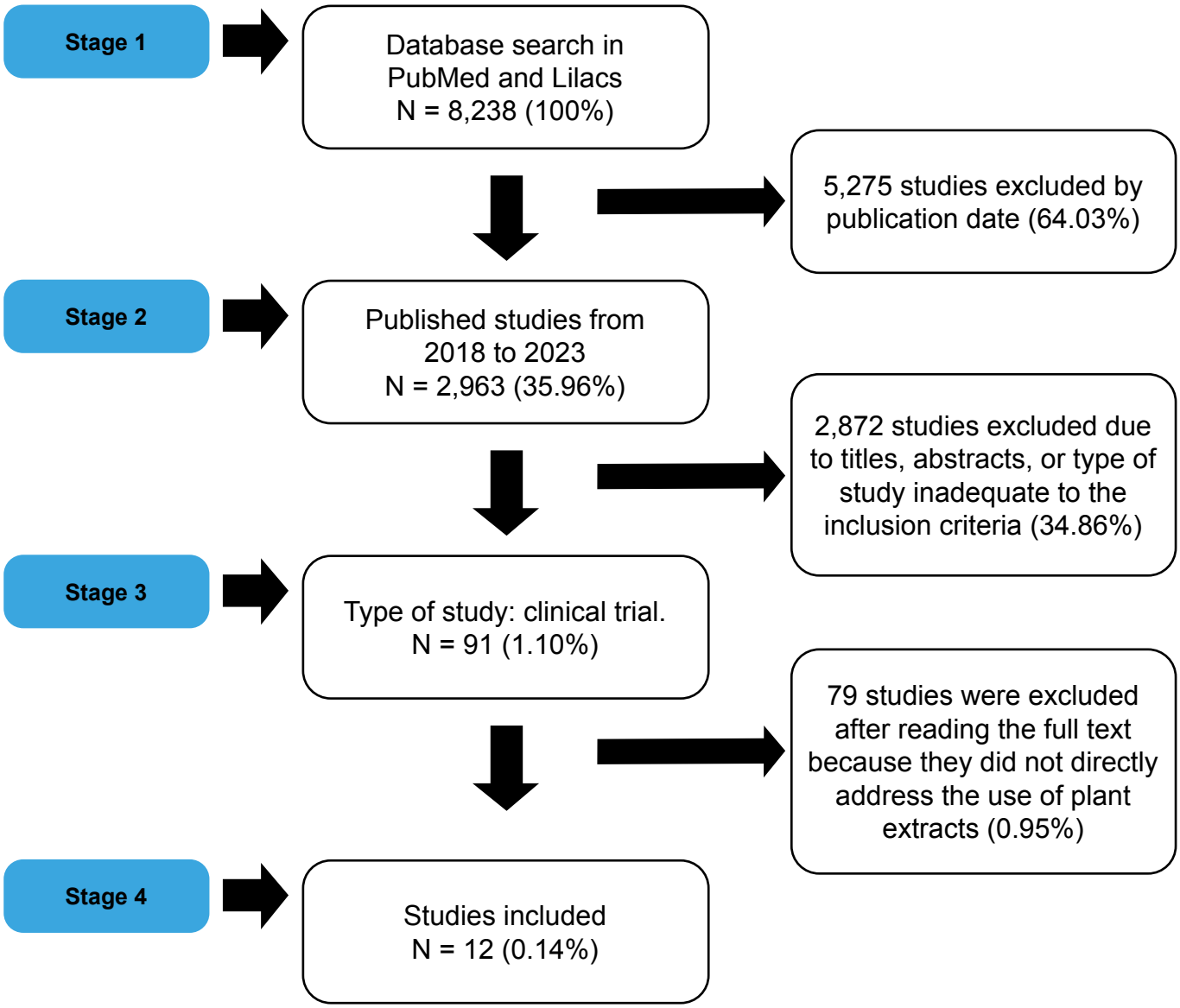
## MATERIAL AND METHODS

This integrative literature review analyzed and combined studies with several methodologies, comparing the use of plant extracts as wound healing materials. The study was based on the question: “What are the main plant extracts that are effective in wound healing, and what are their main physicochemical properties?”. The integrative review used a qualitative methodology to collect and summarize the scientific knowledge produced on the theme. The integrative review method adapts the synthesis of knowledge and the applicability of the results, ensuring a care practice based on scientific evidence. This method is considered a unique tool in the health field, as it synthesizes the available research on a theme and guides the practice based on scientific knowledge[8].

The search occurred in October and November 2023 in the PubMed and Lilacs databases, using the terms “plant medicines” and “wounds”; the search terms were combined with the Boolean operator “AND”, and studies published in the last five years were considered. In the initial phase, the titles and abstracts were read, considering the selection criteria. Then, the independent reviewers performed a previous reading of all the selected studies. The results are summarized in the flowchart of Figure 1.

The review had the following inclusion criteria: a) studies; b) available in full text free of charge (original type, clinical trial); c) studies addressing specific themes of plant extracts used in wound healing; d) published from 2018 to 2023; e) availability in Portuguese and English. Reviewers excluded studies that did not address the guiding question of the review.

**Figure 1.** Flowchart referring to search results.




Source: authors

## RESULTS

The integrative review included 12 studies. They were identified based on data related to the title, author, year of publication, population, and study objective (Chart 1).

**Chart 1.** Summary of studies included (n = 12).

| Authors and Year | Population and intervention | Objective | Conclusion |
|---|---|---|---|
| Giostri *et al*., 2021. | Patients with acute hand wounds. *Calendula officinalis L.* Extract. | Photoplanimetry was used to analyze the progression of the healing by second intention in acute hand wounds using the standardized extract of *C. officinalis.* | The *C. officinalis* extract led to faster epithelialization of the hand wounds. |
| Surakunprapha *et al*., 2020. | Patients with post-sternotomy scarring. Plant extracts in silicone gel. | To determine whether adding plant extracts to the silicone gel would enhance the healing effect on post-sternotomy scarring. | Post-sternotomy scars tend to show better vascularity and pigmentation when treated with silicone gel combined with plant extracts. |
| Rambe *et al*., 2022. | *In vivo* – rats. Rosella leaf extract gel (*Hibiscus sabdariffa L.).* | To evaluate the effect of rosella leaf extract on wound healing in rats. | The experimental groups presented no differences in wound healing and epithelial thickness compared with the control group. |
| Hadizadeh-Tal *et al*., 2022. | Primiparous with episiotomy. Rosemary cream. | To determine the effect of rosemary cream on the healing of episiotomy wounds in primiparous women. | Rosemary cream may be effective in healing episiotomy wounds in primiparous women. However, further studies are suggested to confirm the findings. |
| Faraji *et al*., 2021. | Episiotomized primiparous women. *Commiphora myrrha* (Nees) Engl. and *Boswellia carterii Birds*. | To investigate the efficacy and safety of myrrh and frankincense sitz baths in the healing of episiotomy wounds in primiparous women. | Myrrh was more efficient than frankincense and betadine in healing the episiotomy wound and can be recommended as a safe natural therapy. |
| Sabando *et al*., 2020. | *In vivo* – rats. Hydrocolloid film based on pectin, starch, *Gunnera tinctoria, and Ugni molinae* plant extracts. | Prepare pectin or starch cross-linked blend-based hydrocolloid films loaded with bioactive extracts of *G. tinctoria* and *U. molinae* leaves with controlled release of bioactive compounds and healing properties. | Licorice root hydroalcoholic extract can accelerate the healing process of second-degree burns. |
| Garbuio *et al*., 2022. | Breast cancer patients Chitosan-coated chamomile microparticles. | To evaluate the effect of a topical formulation containing microparticles of *Chamomilla recutita (L.) rauschert* coated with chitosan in relation to the incidence, degree, and days of onset of radiodermatitis in women with breast cancer. | Although chamomile presented did not reduce any degree of radiodermatitis, the extract was effective in reducing grade 2 or toxicity, improving skin recovery, and decreasing high-intensity local symptoms. |
| Liu *et al*., 2020. | Patients with diabetic foot ulcers. Topical composite fluid of the *Phellodendron amurense* cortex. | To analyze the clinical application of the composite fluid of the *P. amurense* cortex in the treatment of diabetic foot ulcers. | The treatment with *P. amurense* cortex can promote ulcer healing and increase the concentration of growth factors, in addition to being safe and reliable. |

| | | | |
|---|---|---|---|
| Soltani *et al*., 2020. | Head and neck cancer patients who had radiation-induced oral mucositis. *Plantago major L* syrup. | To evaluate the efficacy of *P. major* on the symptoms of radiation-induced mucositis in cancer patients. | *P. majo*r syrup effectively reduced the symptoms of radiation-induced mucositis in patients with head and neck cancer. |
| Mohaghegh *et al*., 2022. | The study involved women who underwent episiotomy during childbirth. *Malva Sylvestris* lotion. | To investigate the effect of *M. sylvestris* lotion on episiotomy pain and healing. | Although *M. sylvestris* presented positive results in wound healing in animal and *in vitro* studies, this extract did not show positive results on wound healing and pain relief from episiotomy. |
| Zabihi *et al*., 2023. | Patients with burns. Licorice root hydroalcoholic extract. | To investigate the healing effect of licorice root hydroalcoholic extract on the healing process of second-degree burns wounds. | Licorice root hydroalcoholic extract may accelerate the healing process of second-degree burns. |
| Abbasi *et al*., 2023. | Patients with Aphthous stomatitis Sage (Salvizan gel). | Compare the effects of topical application of sage gels (Salvizan) and triamcinolone acetonide on recurrent aphthous stomatitis. | This study showed that Salvizan gel was very effective for treating recurrent aphthous stomatitis, presenting significantly better outcomes than triamcinolone acetonide in pain recovery and wound healing. |

Source: authors

## DISCUSSION

The studies showed that plant extracts can benefit wound healing. However, each author developed the intervention based on their clinical experiences, using several plant extracts and different methodologies.

The results evidenced the importance of the diversity of plant extracts used in the healing process of the most varied types of wounds. The association of extracts with other pre-existing formulations presented effective therapeutic potential. Wounds after sternotomy treated with the association of silicone gel with plant extracts obtained better healing than those treated with only silicone gel[9]. Moreover, licorice hydrogel healed wounds related to burns[10].

In another study, a hydrocolloid film composed of pectin, starch, *Gunnera tinctoria,* and extracts from *Ugni molinae* plants was used to treat wounds in rats. This film presented properties suitable for adopting plant extracts with healing properties[11].

The plant extract based on the cortex of *Phellodendri* was also evaluated, considering its efficacy for treating diabetic foot ulcers in 720 patients; 540 from the experimental group were treated with the compound and presented a significantly higher healing rate than the control group[12]. Similarly, the healing and anti-inflammatory activity of *Calendula officinalis* in acute hand wounds decreased exudate and hyperemia. Thus, patients treated with *C. officinalis* had a clear reduction in the inflammatory process and accelerated healing compared with the placebo group[13].

For the healing of recurrent aphthous stomatitis, researchers compared the action of Salvizan gel with triamcinolone acetonide; the former presented better results than the latter (1.5 vs 2.5 days for pain recovery). In addition, Salvizan gel reduced wound healing time by 2.7 days[14]. In contrast, Roselle leaf extract gel (*Hibiscus sabdariffa L.*) used in rats did not provide differences in healing and epithelial thickness between groups. However, this extract presented greater healing properties based on clinical and histological evaluation when used at a concentration of 15%. Thus, further studies must investigate the healing effects of the Roselle leaf[15].

Plant extracts can reduce the severity of side effects of radiation in cancer treatment. For example, *Plantago major L.* syrup was used to treat oral mucositis; the intervention group had significantly less severe mucositis and experienced less pain during radiotherapy than the placebo group[16].

These results corroborate the use of chitosan-coated chamomile microparticle formulation to prevent radiodermatitis in the breast. The study observed that the formulation was effective in reducing grade 2 (or higher) toxicity, improving skin recovery, and preventing radiodermatitis in patients with breast cancer undergoing radiotherapy[17].

Currently, obstetrics also recognize the use of plant extracts due to the healing effects of the body in several ways, providing antibacterial, anti-inflammatory, analgesic, anti-allergic, astringent, and healing effects due to these properties. Plant extracts can be used post-episiotomy, a procedure performed at the time of delivery to expand the passage of the vaginal canal preventing perineal lesions, facilitating and speeding up the expulsion of the baby. The delayed healing of episiotomy wounds may lead to infection, triggering perineal pain and discomfort; thus, improving the healing of the wound resulting from episiotomy is one of the main concerns in the postpartum period[18].

The extracts of *Commiphora myrrha*, *Boswellia carteri,* and *Baccharis dracunculifolia* showed good results in the post-episiotomy healing process[19,20]. In contrast, *Malva sylvestris* failed to demonstrate a positive effect on wound healing and pain relief from episiotomy despite demonstrating efficiency in animal and *in vitro* studies[21].

## CONCLUSION

The specific chemical properties of each plant extract contribute to efficiency in tissue repair, offering a less expensive and integrated intervention to health care. The reviewed studies demonstrated that plant extracts can be effectively incorporated into wound treatments, highlighting the importance of continuing to explore and scientifically validate their mechanisms of action and therapeutic benefits. Despite the advances, the healing potential of plant extracts still needs further research.

Therefore, research should be conducted carefully regarding the characterization of the

plant extract used and its mechanism of action to develop plant products of proven quality, serving as an incentive to conduct further studies on the theme.

## CONFLICT OF INTEREST

Nothing to declare.

## CONTRIBUTIONS OF THE AUTHORS

**SMLTC**: Conceptualization, data curation, data analysis, research, methodology, project administration, supervision, data and experiment validation, data presentation design, writing – original manuscript and writing - review and editing; **GSPB**: Conceptualization, data curation, data analysis, research, methodology, development, data and experiment validation, writing - original manuscript and writing - review and editing; **LFMN and MVFF**: Research; **TKBO**: Conceptualization, data curation, data analysis, research, methodology, project administration, supervision, data and experiment validation, data presentation design and writing - original manuscript and writing - review and editing. All authors approved the final version to be published.

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# The use of scintigraphy for diagnosing and evaluating paraganglioma: an integrative review

## Uso da cintilografia para diagnóstico e avaliação do paraganglioma: uma revisão integrativa

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## Abstract

Paraganglioma is a tumor of the endocrine system with a significant hereditary characteristic that affects younger people, causing headaches, palpitations, and diaphoresis. This tumor may be present in the head and neck region as a carotid body tumor and has a low incidence of metastasis. Although several tests can be used, such as computed tomography and magnetic resonance imaging, scintigraphy is useful for diagnosing and assessing paraganglioma. Online databases, such as Scielo, Oxford Academic, PubMed, and The Journal of Nuclear Medicine, were used to compare the relationship between scintigraphy and paraganglioma. Data were analyzed based on the germline classifications of the paraganglioma and the Shamblin classification for prognosis and surgical risk. The imaging exam and the new drugs used in the exams increased the life expectancy and quality of life of affected patients. Also, these approaches have been a major advance in nuclear medicine.

**Keywords:** Paraganglioma; Scintigraphy; Carotid body; Tumor

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## Resumo

O paraganglioma é um tumor do sistema endócrino com característica hereditária significativa que afeta pessoas mais jovens, causando dores de cabeça, palpitações e diaforese. Esse tumor pode estar presente na região da cabeça e pescoço como um tumor do corpo carotídeo e tem baixa incidência de metástase. Embora vários exames possam ser utilizados, como tomografia computadorizada e ressonância magnética, a cintilografia é útil para o diagnóstico e avaliação do paraganglioma. Bancos de dados online, como Scielo, Oxford Academic, PubMed e The Journal of Nuclear Medicine, foram utilizados para comparar a relação entre cintilografia e paraganglioma. Os dados foram analisados com base nas classificações da linha germinativa do paraganglioma e na classificação de Shamblin para prognóstico e risco cirúrgico. O exame de imagem e os novos medicamentos utilizados nos exames aumentaram a expectativa de vida e a qualidade de vida dos pacientes afetados. Além disso, essas abordagens têm sido um grande avanço na medicina nuclear.

**Palavras-chave:** Cintilografia; Corpo carotídeo; Paraganglioma; Tumor

## INTRODUCTION

Paraganglioma is an endocrine tumor closely linked to genetic anomalies, with some genes recorded as endothelial PAS domain protein 1, dihydrolipoamide S-succinyltransferase, and succinate dehydrogenase complex flavoprotein subunit A. Similar to pheochromocytoma, this tumor secretes catecholamines, and it is more likely to be inherited than other tumors[1]. The clinical presentation usually appears between 11 and 13 years and includes episodic symptoms of palpitations, headaches, and diaphoresis[2,3]. Metastasis is usually absent, and malignancy is not associated with poor prognosis[4]. Around 70% to 80% of head and neck paragangliomas are symptomless[5] and can be presented as carotid body tumors, which are irrigated by their vasa vasorum and the arterial branches of the external carotid artery. The carotid body is anatomically described as a structure measuring about 3.5 cm that can be found at the bifurcation of the common carotid artery at the level of its adventitial layer[6,7].

Biochemical tests, one of the evaluation tests, are used to detect the excess of catecholamines or metanephrines. Then, imaging exams (e.g., computed tomography or magnetic resonance imaging) are conducted. However, imaging tests to assess the functional aspect are recommended to exclude the hypothesis of metastasis and assess regional extension or a suspected paraganglioma; the scintigraphy with I-123 metaiodobenzylguanidine can be conducted in this context[2,8]. Some drugs help to detect this tumor because they interact with specific paraganglioma receptors, such as 6-18F-fluoro-l-3,4-dihydroxyphenylalanine, 18F-FDG, and 68 analogs of Ga-DOTA-somatostatin. Thus, scintigraphy is important for managing and treating paraganglioma[9,10].

## METHODOLOGY

This literature review was performed in the Scielo, Oxford Academic, and PubMed databases, using the descriptors Radionuclide Imaging and Paraganglioma for the MeSH search and Scintigraphy and Paraganglioma for the DeCS search; descriptors were combined using the boolean operator “AND”. The inclusion criteria were congruence with the theme, relevance to the research, publication date between 2018 and 2023, and studies published in English, French, or Portuguese. Exclusion criteria were non-conformity with the topic, irrelevance to the research, articles published in other languages not included in the inclusion criteria, and more than five years since publication. A total of 1,015 articles were found in the search, and 10 were included in the review.

## RESULTS AND DISCUSSION

A detailed analysis showed that a specialized evaluation of pheochromocytoma or paraganglioma is needed to clarify the clinical management and the expected prognosis. A biochemical interpretation was also conducted to provide individualized follow-up. Three clusters were formed based on the underlying germline or somatic mutations of the pheochromocytomas and paragangliomas: clusters 1A and 1B related to pseudohypoxia (cluster 1); cluster 2 associated with kinase signaling; and cluster 3 linked to Wnt 3 signaling. These clusters are also clinical, biochemical, and imaging signatures that can guide clinical therapy, specifying the individual intervention for each one. However, the inoperable or metastatic disease cluster does not yet have a proper intervention in clinical practice, suggesting the need for personalized genetic treatment as a routine procedure in these cases[1].

The analysis also evidenced the importance of imaging for evaluating and managing pheochromocytomas and paragangliomas, which often even guides treatment. In the study, the discovery of susceptibility genes associated with these tumors improved the understanding of clinical phenotypes and imaging. Thus, imaging is essential as it can detect the subtypes of pheochromocytoma and paraganglioma. Several radiopharmaceuticals were created to target specific receptors and metabolic processes of pheochromocytomas and paragangliomas, including 131 I/ 123 I-metaiodobenzylguanidine, 6-18 F-fluoro-l-3,4-dihydroxyphenylalanine, 18 F-FDG, and 68 Ga-DOTA-somatostatin analogs[10].

One investigation of demographic, clinical-pathological, and radiological data included 104 patients (33 men and 71 women, mean age 54.6 ± 13 years) with cervical paraganglioma in the carotid bifurcation between 2003 and 2017. The radiological analysis showed that ten patients had bilateral tumors; thus, 114 patients received treatment during this period, and all underwent surgery. After the procedure, seven patients had hoarseness, two had facial paralysis, one had dysphagia, and one had Horner’s syndrome[5].

The 114 patients underwent the Shamblin classification to stratify surgical risk and potential vascular complications. The highest percentage found was Shamblin II (n = 66; 57.9%). The Shamblin classification is shown in Table 1[5].

**Table 1.** The Shamblin classification according to Basel & Bozan[5].

| Type | Description | Prevalence of paraganglioma according to Basel & Bozan[5] n = 114 (100%) |
|---|---|---|
| I | Localized tumors that do not extend beyond the carotid body (< 6 cm) | 15 (13.2%) |
| II | Tumors that partially extend beyond the carotid vessels (Up to 6 cm) | 66 (57.9%) |
| III | Large tumors that completely bypass the carotid vessels (> 6 cm) | 33 (28.9%) |

Source: Basel & Bozan, 2021[5].

Each patient can undergo a different type of surgery, depending on what is most appropriate for each case. Those with tumors larger than five centimeters can be treated with spring embolization and surgical resection. Patients with Shamblin III can undergo surgical resection with a polytetrafluoroethylene graft. Although these surgeries can present complications, recent studies showed that patients did not have a lasting sequelae[5].

Paraganglioma is considered a neuroendocrine tumor that can be named pheochromocytomas or extra-adrenal paragangliomas when they appear in the adrenal glands or outside the adrenal glands, respectively. Most pheochromocytomas and paragangliomas are benign, with a few spreading to other sites. When the biochemical results are positive, imaging tests can be performed to confirm the diagnosis, in which the location, course, and best surgical treatment are defined. PET-CT with Ga-DOTA-SSA is the best diagnostic option. Scintigraphy can be very effective as it is a safe, non-invasive, and efficient method for locating pheochromocytomas and paragangliomas outside the adrenal glands, providing functional and anatomical data. Metaiodobenzylguanidine scintigraphy is indicated to evaluate the whole body since it shows the correct topography of the tumor. Tomography or magnetic resonance imaging is used to show anatomically where they meet and with whom they converge[10].

## CONCLUSION

The use of metaiodobenzylguanidine is a great ally for diagnosing paraganglioma. Oth-

er substances can also be used, such as 131 I/ 123 I-metaiodobenzylguanidine, 6-18 F-fluoro-l-3,4-dihydroxyphenylalanine, 18 F-FDG, and Ga-DOTA-somatostatin analogs, which have proved to be more effective. These drugs are an achievement in nuclear medicine that directly impacts the life expectancy and quality of life of affected patients. Paraganglioma is a rare disease, and most studies are scarce and generally retrospective. In addition, the pharmaceutical industry lacks investment in research into new drugs. Thus, surgery is considered the definitive choice of treatment and should be encouraged since the percentage of patients with sequelae and complications is relatively low. However, considering the topography of the tumor, very close to large vessels and neural structures, the surgery can still be considered a challenge for inexperienced surgeons. When evaluating a patient with paraganglioma, physicians must decide whether the surgery will be conducted, considering the risks or benefits and life expectancy. Moreover, preoperative embolization can also be chosen for large tumors, which increases the success rate of the surgery.

## CONFLICT OF INTEREST

Nothing to declare

## AUTHOR CONTRIBUTIONS

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# Meeting of medicine, art, and humanization in health: an experience report

## Encontro de medicina, arte e humanização em saúde: um relato de experiência

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## Abstract

**Objective**: This study aimed to describe an event regarding the relationship between medicine, art, and humanization in health. **Methods**: This experience report with a critical-reflexive methodology was based on the perspective of students from the *Liga Acadêmica de Medicina de Família e Comunidade*. **Results**: Participants were receptive to the event mediated by artists and health professionals, suggesting that art associated with medicine is a therapeutic tool that can be used in health promotion and disease prevention. **Conclusions**: The workshops and discussions were relevant to empower participants regarding humanized care and the need for comprehensive and interdisciplinary work.

**Keywords**: Medicine; Art; Humanization; Health promotion; Comprehensive health.

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## Resumo

**Objetivo**: Descrever a experiência de um evento que tratou da relação entre Medicina, Arte e Humanização na Saúde. **Métodos**: Tratou-se de um relato de experiência, com abordagem crítica e reflexiva sob o olhar dos estudantes da Liga Acadêmica de Medicina de Família e Comunidade. **Resultados**: Nas mediações realizadas por artistas e profissionais da saúde, ficou evidente a receptividade dos participantes em relação ao tema, que trouxe a importante compreensão de que, em interseção com Medicina, a Arte é uma ferramenta terapêutica que pode ser utilizada na promoção da saúde e na prevenção de doenças. **Conclusões**: As oficinas e rodas de conversas foram importantes para a emancipação dos participantes sobre o cuidado humanizado e a necessidade do trabalho integral e interdisciplinar.

**Palavras-chave**: Medicina; Arte; Humanização; Promoção da saúde; Integralidade em saúde.

## INTRODUCTION

For a long time, the biomedical model was the standard of care followed in the health field, characterized by the one-cause explanation of disease, biologicalism, fragmentation, mechanistic, and technicality of care. Although achieving solutions, this model is limited since it does not consider the individual, emotional, and collective aspects of the health-disease process[1]. This methodology results in the hospital-centric view observed during medical school, in which humanistic, social, and dialectical care is neglected, hindering the development of communication skills and empathy needed for medical practice[2, 3].

In contrast, humanistic healthcare practices place the patient at the center of care, seeking to develop citizenship-oriented attitudes and values. This vision, more centered on the patient and less on pathology, gives the needed attention to the social, cultural, and emotional aspects of patients. The National Humanization Policy considers humanization in health as a way to improve the quality of care, strengthening the commitment of healthcare professionals and users of the health system using welcoming, ambiance, and extended and shared clinics[5].

Historically, Hippocrates (460-377 B.C.) already propagated the idea of valuing the different forms of the health production process. In one of his quotes, the philosopher affirms the need for full assistance to the sick, correlating it with love for men or the art of love for caring[6]. In this sense, the complex art of medicine is the ability of the healthcare professional to understand the patient as another vulnerable being, considering the life context. This art requires a balance between empathy, serenity, and projection to counterbalance the understanding of the pathology. The incorporation of art and the focus on humanization redefine medical practice and the experience of the patient, revealing the profound interconnection between healing and the authentic expression of humanity[7].

Considering the etymology, medicine and art are Latin words that means the art of healing and the technique of being and acting, respectively. In this sense, these activities are inseparable since medicine is one of the ways of exercising art. Their separation results in what is often observed in health care. Therefore, the reconnection of medicine with art is about reaching people and overcoming curative medicine[8].

The Brazilian medical practices reflect how art and medicine combined produce significant results that cause pride and bring to reality an optimistic perspective, which only existed in idealization. Dr. Nise da Silveira brought an enriching example when she highlighted the therapeutic power of art therapy in medicine. Although much of what she did was linked to an art form, other areas still need to be explored[9].

The medical course, following the 2014 National Curriculum Guidelines, seeks to promote a critical, broad, and reflective education that provides an ethical and humanistic understanding of the doctor-patient interaction during care[10]. However, medical education institutions are still resistant to adopting means that encourage skills improvement that better understand the individuality of each patient[11].

Considering the need to provide spaces for dialogue on person-centered care, a group of students promoted the First Meeting of Medicine, Art, and Humanization in Health (MMAHH) to create an environment of holistic and transdisciplinary integration. This vision goes beyond the exact sciences, promoting dialog and reconciliation between the human sciences, art, literature, poetry, and spiritual experience[12]. The concept of understanding the multidimensional human being can be associated with the work of the Brazilian educator and philosopher Paulo Freire, who highlighted education as a collective and interdisciplinary work with objectives aimed at the uniqueness of each patient[13].

Therefore, addressing the patient fully and listening to their wishes, tastes, and ideas strengthens the doctor-patient relationship and helps with the health disease process and well-being. This relationship can be achieved with therapeutic activities that awaken the imagination and self-esteem, such as writing, music therapy, and play therapy. In this way, art and medical-humanistic content are stimulated so that they can be disclosed and reproduced. Thus, the present study aimed to report on the experiences and lessons learned from promoting an event involving medicine, art, and humanization in health. Practical activities were performed by students from the *Liga Acadêmica de Medicina de Família e Comunidade* (LAMFC) of *Faculdade de Medicina de Olinda*.

## EXPERIENCE REPORT

This experience report described a two-day event performed in the Renildo Calheiros auditorium at the *Faculdade de Medicina de Olinda*. The event was conceived and organized by

LAMFC students and covered internal and external participants of the institution, including participants from outside the health field. The 1st MMAHH focused on artistic practices as therapeutic tools for humanizing health care.

The theme was chosen considering the lack of use of art as a care tool, as well as the need to apply an integrative and holistic vision in the health field. The event was aligned with the National Humanization Policy (*HumanizaSUS)*; the activities followed the principles of welcoming and valuing the subjective, collective, and social dimension of patients and their autonomy and protagonism, as well as the integrality of care[2]. Another pillar that permeated the 1st MMAHH was the dialogue advocated by Paulo Freire in his book Pedagogy of Autonomy, a source of problematization and critical reflection of the individual in the face of society[11]. At the event, discussions and the various manifestations of art led to debates and questions about hospital-centered methods of care, which segment the patient into parts and diseases and exclude their complexity and totality. The mediators were invited by several means of communication, including personal invitations and social networks, with the aim of broadening thinking about art therapy. They were different areas of activity, such as psychiatrists who use different artistic manifestations in their professional and personal practices, popular education, art education, and music, with the aim of promoting an event with a better grounding in the theme. In addition, LAMFC students were distributed among the workshops and were trained to act as monitors and assist in the artistic activities.

The event was divided into workshops involving the public in the construction of discussions, allowing their immersion in the universe of care through art and its use as a therapeutic tool in individual and collective spheres. The workshops included activities to integrate and synchronize the participants; mandala workshops; exchanges of experiences with popular educators, painters, musicians, psychiatrists, academic educators, and students; clowning; and painting.

On the first day, the workshops encompassed reciting poems led by a medical student to remind us that art is found every day in small details, followed by an origami workshop with a popular educator who taught the importance of valuing popular knowledge for health promotion (Figure 1).

**Figure 1.** Materials produced in the origami and popular education workshop.


Image authorized by event participants.

After this workshop, a round table discussion with a psychiatrist discussed the importance of the cinematic arts as a way of expressing feelings, which are often difficult to put into words. The need for a unique, subjective, and personalized approach for each human being was evidenced, given their many specificities (Figure 2). At the end of the first day of the meeting, a mandala workshop was held, given by the LAMFC supervisor professor, in which emotions and intentions were expressed using this art, and experiences and creations were shared with the other participants.

**Figure 2.** Conversation round held on the first day of the meeting on valuing popular knowledge for health promotion.

Image authorized by event participants.

The second day was opened by a medical student who shared some of his experiences with music as a therapeutic tool in the hospitals where he did the internship.

Then, a workshop with a psychiatrist and painter proposed the creation of a self-portrait, entering into the universe of colors, strokes, and meanings behind each representation. A workshop was also provided by a clown therapist and psychologist, who performed a dynamic to emphasize the importance of the connection between the caregiver and the patient. At the closing ceremony, a doctor and musician shared his experiences with the liberating power of music.

Last, all participants could use the space to hear and be heard, express themselves, and feel the transformative power of the various artistic manifestations.

## RESULTS

The significant results of the 1st MMAHH evidenced the importance and relevance of addressing the theme of art and humanization, especially in medical school. The event provided a favorable environment for integration between different areas of knowledge, congregating students, professionals, and members of the community in an interdisciplinary dialogue. The presence of participants from outside the health field enriched the discussions and promoted a broader and more inclusive view of issues related to health and humanization.

In addition, participants had the opportunity to improve their communication and empathy skills in the workshops and conversation circles. The safe environment provided allowed them to express their experiences, feelings, and perspectives, promoting a greater understanding of the needs and experiences of others.

The dialogs inspired by the Pedagogy of Autonomy (Paulo Freire) encouraged participants to take a leading role and be autonomous, as well as to be active agents in the moments they experienced[12]. Moreover, the painting, music, and clowning activities provided moments of relaxation, creativity, and self-expression. These practices contributed to promoting the mental health and emotional well-being of the participants, offering a revitalizing break from academic and professional routines.

The 1st MMAHH proved to be a valuable and impactful initiative in the academic and human formation of medical students. By providing a space for reflection, dialog, and artistic expression, the event strengthened the values of empathy, integration, and patient-centered care, preparing participants for a more compassionate, holistic, and effective medical practice.

## FINAL CONSIDERATIONS

The 1st MMAHH promoted the well-being and health of the guests, participants, and LAMFC members and was a revolutionary experience in the traditional academic environment. The

event allowed critical thinking about these areas, given the prejudices and stigmas about the union between medicine and art. Despite being seen as sectors that do not work together, their union is a perfect match for therapy, as it promotes the transformation of ideas and feelings.

Thus, welcoming spaces, such as the 1st MMAHH, are suitable for building bonds, debating, and deconstructing concepts, which are essential for the human, social, academic, and professional training of health students. These spaces act as tools for perceiving oneself and others as human beings who need comprehensive care.

## CONFLICT OF INTEREST

Nothing to declare

## AUTHOR CONTRIBUTIONS

All the authors participated equally in the construction of this experience report and approved the final version.

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# Intervention in a basic health unit for preventing and controlling overweight and obesity: results from a multidisciplinary and participatory intervention

## Intervenção em uma unidade básica de saúde para prevenção e controle do sobrepeso e da obesidade: resultados de uma abordagem multidisciplinar e participativa

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## Abstract

This experience report describes the practice of health education to prevent overweight and obesity. The intervention was conducted by medical students in collaboration with the Family Health Team professionals, targeting the population assigned to a basic health unit in Olinda, Pernambuco, Brazil.

**Keywords:** Primary health attention; Health education; Obesity; Overweight; Primary prevention.

## Resumo

Este relato de experiência descreve uma prática de educação em saúde voltada para a prevenção do sobrepeso e da obesidade. A intervenção foi conduzida por estudantes de medicina em colaboração com a Equipe de Saúde da Família, com foco na população adscrita a uma Unidade Básica de Saúde situada no município de Olinda, Pernambuco, Brasil.

**Palavras-chave:** Atenção primária à saúde; Educação em saúde; Obesidade; Prevenção primária; Sobrepeso.

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## INTRODUCTION

Global health has been impacted by the increasing prevalence of overweight and obesity, raising concerns about the associated health risks[1]. In Brazil, overweight and obesity cases increased by 132% and 231% (respectively) between 2013 and 2022, suggesting that over half of the Brazilian population is experiencing issues related to excess weight[2].

High intake of critical nutrients (salt, sugar, oils, and fats) and low consumption of grains, fruits, and vegetables are considered inadequate diets and the primary risk factors for chronic non-communicable diseases (NCDs) in Latin America[3].

Over the past four decades, dietary patterns have changed worldwide. An increased intake of foods high in free sugars, sodium, saturated fats, and trans fats, combined with a minor intake of foods with high nutritional value, is associated with several NCDs[4]. For all regions and socioeconomic levels, the overall dietary quality of Brazilian adolescents is inadequate, characterized by low consumption of fruits, vegetables, legumes, and dairy products and by high intake of fats[5]."

Regarding health services, food surveillance acts by anthropometric assessment and monitoring dietary consumption. These data, available in the Food and Nutritional Surveillance System (SISVAN)[6], enhance the understanding of the health issues affecting the population, fostering the development of public policies and establishment of priorities[7]. The Surveillance System for Risk and Protective Factors for Chronic Diseases through Telephone Surveys and the Family Budget Survey also contribute to this effort[6].

Monitoring body mass index allows the observation of tendencies in overweight and obesity across various geographic areas and the identification of critical factors associated with these conditions. This information is crucial to support public policies aimed at obesity prevention, promoting healthy lifestyles, and encouraging regular physical activity since childhood[8, 9].

A high number of basic health unit (BHU) users present NCDs (e.g., obesity), a risk factor for other complications, such as diabetes mellitus, hypertension, cardiovascular diseases, and cancer.

In 2018, the Unified Health System spent over 3.45 billion reais on hypertension, diabetes mellitus, and obesity[3]. About 370 million reais (11% of direct costs) were attributed to obesity, recognized as a major public health issue. Since obesity directly impacts the quality and duration of life, prevention and early diagnosis are essential to promote health and reduce morbidity and mortality[3].

The epidemiological profile shows that the NCD cases are increasing in Pernambuco, Brazil; this tendency is also observed in other Brazilian cities. As for the nutritional status of the population, SISVAN data reveals an increasing number of overweight and obesity cases in the municipality of Olinda, Pernambuco, including at the BHU in this report[6]. The increased number

of cases and their associated morbidity and mortality highlights the need for interventions that can change this context.

Thus, this study reports a successful experience in health education aimed at raising awareness among the population served by a BHU in Olinda, Pernambuco, Brazil, about the benefits of making lifestyle changes to prevent overweight and obesity.

## EXPERIENCE REPORT

The Maguerez Arc problematization methodology was used to explore the content of the study, emphasizing that learning originates from direct contact with the topic and the interpretation of reality. During the practical activities of the Curricular Unit Integration of Academia, Service, and Community, a group of medical students interacted with the population served by a BHU in Olinda.

This experience and the observation of SISVAN data evidenced a high prevalence of overweight and obesity among individuals registered at the BHU, along with a predominance of detrimental habits (inadequate nutrition, sedentarism, and alcohol consumption). These findings highlighted the need for an educational and preventive intervention, focusing on critical aspects of health promotion.

The study was thoroughly explored during the theorization phase. As a result, the students observed that overweight and obesity presented high prevalence and low control rates, represented some of the main modifiable risk factors, and were important public health concerns[1, 2].

After the theorization that clarified the community profile, the Family Health Team (FHT) professionals from the BHU helped with the hypothesis elaboration for solutions to the main problem. Among them, the conduct of a health education activity using a horizontal dialogue was considered, including anthropometric assessment and follow-up care.

On the day of the activity, an introductory dynamic was conducted in the waiting room with the present audience, encompassing the individuals previously invited by the community health agents and those who had appointments on that day. Then, the topic was discussed, covering the prevalence of overweight and obesity, the conceptual distinction between these conditions, and how to identify them. This step aimed to evaluate the prior knowledge of the population on the topic.

Subsequently, the audience was instructed on the importance of preventing and controlling overweight and obesity, considering the reality of community, access to physical activities, and healthy eating. Topics, such as sedentarism, healthy eating habits, and instructions for a balanced lifestyle, were discussed and aligned with the socioeconomic and cultural context of the population. Individuals were also informed about the importance of reducing smoking and alcohol consumption and practicing regular physical activity, emphasizing their benefits in the prevention

of obesity-related diseases and the management of existing health conditions.

Besides the instructions on the benefits of lifestyle changes, a poster with tips for physical activities and dietary guidance was elaborated based on the possibilities and daily life of the community. During the intervention, the proximity to the shore was emphasized, which is an accessible location for the practice of physical activity. As a final activity, a nutritive snack made from fruits and healthy ingredients was provided to consolidate the concepts of a balanced diet and healthy habits. This activity also aimed to demonstrate that maintaining a healthy diet is achievable, even with limited access and resources. Moreover, the fruits used in this activity (bananas, grapes, and apples) were bought from the local market, considering the affordability for the community and seasonality of the harvests. The initiative aimed to promote an experience of healthy food choices, offering a snack aligned with the principles of a balanced and nutrient-rich diet.

During the meeting, the population underwent an anthropometric assessment (body mass index) and abdominal circumference. Additionally, the personal data of the individuals (name and Unified Health System card number) was collected to facilitate follow-up care by the FHT and doctor at the BHU.

After evaluation, individuals received additional guidance on the importance of a physical activity plan and healthy eating. To continue individualized care, each individual had appointments scheduled over the following three months, enabling the FHT to closely monitor their progress and provide ongoing support for maintaining a healthier lifestyle.

The reported action innovates by combining an educational intervention adjusted for the socioeconomic and cultural context of the population with practical activities, such as guidance, provision of nutritive snacks, anthropometric assessment, and the creation of visual materials. This strategy aimed to teach and allow individuals to practice the principles of healthy habits. Furthermore, the initiative by professionals to document and follow up with the group over three months demonstrates commitment and engagement, further strengthening the intervention proposal. The close interdisciplinary collaboration among students, FHT, and the community fostered an atmosphere of trust and a constant feedback flow, optimizing the effectiveness of the intervention.

## RESULTS

After the intervention, the students were satisfied with the results achieved by the active and engaged participation of the community, characterized by constant interaction, expressions of interest, and gratitude for the attention provided by the students.

Given the success and engagement of the population, strategies for obesity prevention must extend beyond guidance alone. Multifactorial interventions are widely recommended for the effective prevention and control of obesity, as they integrate nutrition, physical activity, and

behavioral change, including personalized counseling and continuous monitoring of diet or physical activity (or both)[10]. In this context, the population sought information about healthy eating and regular physical activity practices associated with continuous and individualized support.

One of the pillars for control and prevention of overweight and obesity is adequate and healthy nutrition. However, according to the National Policy on Food and Nutritional Security and the National Policy on Food and Nutrition, the problem is not only nutritional but also cultural, social, and economic[11]. This concept guided the intervention adopted by the students and the FHT, promoting awareness of the importance of a healthy lifestyle.

Moreover, guidance on the regular practice of physical activity proved to be a crucial intervention. Besides its association with weight reduction, studies indicate that physical activity decreases the risk of NCDs, reduces mortality from all causes, and promotes quality of life[12]. Thus, the intervention adopted by the students aligns with current recommendations, emphasizing the importance of global measures against obesity.

Adopting intersectoral policies to reverse the obesogenic environment in which individuals live, in addition to providing educational and behavioral support, is essential for the prevention and control of obesity[13].

## FINAL CONSIDERATIONS

In the short term, the effective interaction among the FHT professionals, students, and community of Olinda reinforced the positive aspect of this educational intervention in promoting healthy lifestyles. This synergy, combined with the active engagement of the community, reveals the power of health education adapted to local realities.

In the medium term, the commitment to medical follow-up will be crucial for the consolidation and expansion of the benefits already achieved. Continuous guidance to the community regarding the importance of healthy food choices and physical activities into daily routines is essential to positively change the health of the population.

However, additional measures must be implemented for sustainable long-term results, including extensive public policies, continuous awareness campaigns, and health support infrastructures. Thus, this experience report serves as a starting point and a reference model. Similar initiatives are encouraged to be replicated and adapted according to the needs of different communities, always striving for a healthier and more resilient future for all.

## CONFLICT OF INTERESTS

Nothing to declare

## AUTHOR CONTRIBUTIONS

**FAP**: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review and editing; **AAT**: Writing – review and editing; **DCA**: Writing – review and editing; **JKLM**: Writing – review and editing; **JCBC**: Writing – review and editing; **LGLT**: Writing – review and editing; **CYSVM**: Supervision, Writing – review and editing. All authors approved the final version of the manuscript.

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# Practices of obstetric semiology in a medical skills laboratory: an experience report

## Práticas de semiologia obstétrica em um laboratório de habilidades médicas: um relato de experiência

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## Abstract

General practitioners are responsible for prenatal consults and other healthcare services for pregnant women. Thus, they need to have an efficient academic background in Obstetrics. This experience report aimed to describe practices in obstetric semiology occurring between March and November 2023 in a medical skills laboratory of a higher education institution in Pernambuco. The students practiced semiology techniques used in Obstetrics and the care of pregnant women with pathologies. The activities supplied the demands of the health of women and validated the urgency of a medical formation centered on direct knowledge application, improving its efficiency and giving students a leading role.

**Keywords:** Prenatal care, Prenatal education, Pregnancy complications, Clinical practice guide.

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## Resumo

É papel do médico generalista realizar rotinas de pré-natal e outros atendimentos a gestantes. Para isso, é necessária uma formação acadêmica eficaz em obstetrícia. Este relato de experiência objetivou descrever práticas em semiologia obstétrica que aconteceram entre março e novembro de 2023 em um Laboratório de Habilidades Médicas. Tratou-se de um estudo descritivo desenvolvido com base em atividades realizadas em uma instituição de ensino pernambucana. Os alunos praticaram técnicas utilizadas na semiologia obstétrica e no atendimento a gestantes em contextos patológicos. Tais atividades atendem às demandas da saúde da mulher e ratificam a urgência de uma formação médica centrada na aplicação direta do conhecimento, tornando-a mais eficiente e dando protagonismo aos estudantes.

**Palavras-chave:** Cuidado pré-natal, Educação pré-natal, Complicações na gravidez, Guia de prática clínica.

## INTRODUCTION

The Unified Health System (SUS) was established by the 1988 Constitution[1] and brought new health policies to Brazil. The National Politics of Integral Attention to Women's Health[2], implemented in 2004, was developed to ensure integral and longitudinal attention to women, and it is the foundation for actions in the area. Among the guiding policies, the promotion of health and the need for consolidation of obstetric advances are highlighted[3]. Thus, prenatal care in primary health care (PHC) is one of the key points for the health prevention and promotion of Brazilian women[2, 3, 4].

Prenatal care aims to monitor the pregnant woman to secure maternal health and fetal development, perform timely diagnoses, and reduce maternal-fetal mortality, providing safety to mother and child. To achieve this, the Ministry of Health recommends a minimum of six prenatal visits in PHC, with follow-ups alternating between a general practitioner and nursing staff[5].

In the PHC, pregnancy monitoring generally begins with routine-risk prenatal care, followed by regular follow-ups and screenings to ensure good pre- and postnatal conditions. According to the Prenatal Care Technical Manual[6], a pregnancy is considered high-risk only in specific situations, such as pregnancy-induced hypertension and gestational diabetes mellitus; when these situations occur, the pregnant woman should be referred to a specialist. Thus, these guidelines are essential to organize the care in prenatal follow-up, leading to optimal maternal-fetal outcomes.

In this context, the general practitioner working in the PHC should provide efficient care to pregnant women, conducting prenatal routines, timely diagnoses, and direct high-risk prenatal care when needed[5, 6]. Therefore, they need solid academic training in Obstetrics using practical activities that prepare the students for real clinical situations[7]. To ensure adequate training, the

Ministry of Education encourages medical courses to provide laboratories equipped for student development. In turn, the institutions adopt various technologies, such as mannequins, anatomical models, and simulated clinics, to enhance the learning process[7, 8, 9].

Therefore, this experience report described the practical activities in obstetrics semiology performed between March and November 2023 in a medical skills laboratory (MSL) at a higher education institution in the Pernambuco state.

## METHODS

This experience report was developed based on the obstetric semiology practices of the Academy Obstetrics League (AOL) conducted in an MSL.

The practical activities occurred between March and November 2023 and aimed to revisit the knowledge of obstetric anamnesis and physiological and pathological obstetric exams.

A literature search was conducted to support the practices and to solidify the importance of the activities conducted by the AOL. Thus, the following descriptors were selected in the Medical Subject Headings (MeSH) platform: prenatal care, prenatal education, pregnancy complications, and clinical practice guide.

Searches were performed using the descriptors in Portuguese, English, and Spanish in the SciELO, LILACS, and Virtual Library on Health databases. Studies published from January 2017 to November 2023 were selected, as well as the Prenatal Care Manual, developed by the Brazilian Federation of Gynecology and Obstetrics Association[6], and the antenatal card from the Brazilian Ministry of Health[5].

## RESULTS

The practical activities of the AOL occurred from March to November 2023 in a MSL of a higher education institute in Pernambuco and covered crucial topics for Obstetrics in general medicine.

During each workshop, the students performed the main techniques of obstetric semiology. Throughout 12 classes, the students were divided into three groups to discuss and practice several themes, such as prenatal and antenatal cards, medical history and obstetric physical exams, and the evaluation of postpartum bleeding and emergency measures.

In the workshop regarding the prenatal consult and the antenatal card, the students learned the importance of this instrument to follow up the pregnancy and verify the identity, social issues, obstetric history, results of exams and screenings, follow-ups, and other procedures. The antenatal card facilitates continuity of care since it encompasses all healthcare services, promoting more effective communication between healthcare professionals and the services involved, as well as the generation of data for epidemiological research[10].

In the workshop about obstetric physical exams, the students practiced Leopold maneuvers, the use of an ultrasound device to listen to fetal heartbeats, the measurement of fundal height, and the evaluation using vaginal touch (Figure 1). These practices provide essential abilities to assess the state of the pregnancy and the well-being of the baby[11].

**Figure 1.** Student of the Academic Obstetrics League measuring the fundal height in the obstetric semiology practice in the medical skills laboratory.

Source: personal archive.

In the third workshop, a simulation of the first prenatal consult with a pregnant patient was conducted, combining the medical history with an obstetric physical exam. Simulation, also known as role-playing, is an active teaching method based on performing arts and improvisation. This activity involves simulating consults and other procedures in which students interact with fictitious patients[12].

The fourth workshop was about postpartum bleeding and emergency measures, exercising the assessment and the handling of possible complications during postpartum (Figure 2).

**Figure 2.** Use of mannequins in the postpartum bleeding and emergency measures practice in the medical skill laboratory.


Source: personal archive.

According to the Pan-American Health Organization, postpartum bleeding is one of the main obstetric complications and a relevant cause of maternal death in Brazil[13]. This practice highlighted the importance of effective communication within the healthcare team during obstetric emergencies, which is also crucial for ensuring better maternal outcomes[14]. Moreover, general practitioners must recognize abnormal bleeding and intervene immediately to control hemorrhage. This scenario reinforces the importance of incorporating practices that support learning and prepare future professionals to handle emergency, high-stress, and critical obstetric situations[9,15].

## CONCLUSION

The practical activities promoted by the AOL addressed the current demands in the health of women and also highlighted the importance of medical education focused on the direct application of knowledge. Training with more practical activities, as demonstrated in this study, improves care and gives students a leading role in their education.

Furthermore, case simulations, evidence-based discussions, and the practice of clinical maneuvers were key elements in preparing general practitioners to manage various situations in maternal care. This study also confirmed the need for academic training other than theoretical knowledge and empowered students as active agents in improving maternal-fetal outcomes, preparing them for real-world challenges. The importance of a more humanized and effective medical practice was also emphasized.

## CONFLICT OF INTEREST

Nothing to declare

## AUTHORS CONTRIBUTIONS

All authors participated in the manuscript production and approved the final version.

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## Critical Review

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**LEE, Peter; GOLDBERG, Carey; KOHANE, Isaac. A Revolução da Inteligência Artificial na Medicina: GPT-4 e Além. São Paulo: Editora Ciência Moderna, 2023.**

The book The AI Revolution in Medicine: GPT-4 and Beyond, by Peter Lee, Carey Goldberg, and Isaac Kohane was published in 2023 and explores the impacts of artificial intelligence (AI) in medicine, focusing on the GPT-4 model, developed by OpenAI. The work presents a detailed overview of transformations in the field of diagnoses, treatments, and medical data management, taking a critical look at ethical and safety challenges. The narrative stands out for the association of practical examples with theoretical reflections, ensuring a fluid and engaging reading.

The authors begin the book by describing the first interaction of Peter Lee with the Davinci3 AI system, the precursor of GPT-4. The report sets a tone of fascination and caution, reflecting the mixed reactions that are common to cutting-edge technologies. The most impressive ability of GPT-4 is to conduct natural conversations, providing detailed and contextually accurate responses. However, Lee mentions limitations and challenges, such as the tendency of the AI to “hallucinate” information, which is a critical point for safety in medical contexts.

The book addresses the integration of AI into healthcare systems, promoting greater accuracy and speed in analyzing exams and screening patients. The book presents compelling data on the reduction of human errors using AI and also highlight sthe importance of ongoing supervi-

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sion by healthcare professionals. The automation of medical records, which saves time and minimizes errors, is highlighted as one of the main benefits of AI, especially in medical research and the development of new treatments.

The authors highlight the difference between correlation and causality in medical data, emphasizing that the AI fails to understand causal relationships. In this sense, human supervision remains essential to ensure patient safety. Furthermore, continuous verification of responses generated by AI is crucial to ensure the reliability of medical decisions.

One of the most futuristic aspects discussed in the book is the potential of wearable devices, which monitor the health of the patient in real-time, providing personalized recommendations. However, the authors address the ethical challenges, such as the privacy of health data. The need for regulation and clear standards for the collection and analysis of this data is discussed in depth.

Last, the authors present a comprehensive vision of the future of medicine alongside AI, proposing that technology can complement human capabilities as long as it is used ethically and transparently. Furthermore, healthcare professionals need to be continuously trained to ensure the correct interpretation of AI recommendations, highlighting the need for a careful and gradual transition of these technologies.

In summary, The AI Revolution in Medicine: GPT-4 and Beyond is an essential reading for healthcare professionals and researchers and offers a balanced analysis of the promises and challenges of AI. The book highlights the transformative potential of this technology in the medical field, as well as the importance of ethics, safety, and human supervision in this implementation.