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Original Article

Temporal analysis of mortality from preventable causes in a municipality in the midwest of Santa Catarina

Análise temporal da mortalidade por causas evitáveis no período de 2013 a 2022, em um município do meio oeste catarinense

Análisis temporal de la mortalidad por causas prevenibles en un municipio del centro oeste de Santa Catarina

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ABSTRACT

Background and Objectives: Preventable deaths are those that could have been avoided by effective health service actions during the period in which they occurred. Describing preventable mortality provides valuable indicators of health services, enabling the assessment of quality and effectiveness based on the data obtained. The objective was to analyze mortality trends from preventable causes and outline the profile of preventable deaths in the municipality of Caçador, Santa Catarina, from 2013 to 2022. **Methods:** An ecological time-series study with secondary data from the DATASUS Mortality Information System. The analysis was bivariate, and Joinpoint regression was used for temporal trend analysis, employing the Empirical Quantile method and the Weighted Bayesian Information Criteria. **Results:** 67.3% of deaths were classified as preventable. Time trend analysis identified two distinct phases: an average annual reduction of 13.09% between 2013 and 2015, followed by an increase of 2.44% per year from 2015 to 2022. Stratification by sex revealed significant trends for males, with a 15.62% annual decrease in the initial period and a subsequent 2.9% annual increase, particularly associated with cardiovascular diseases, which accounted for 10.0% of preventable deaths among men. Among females, an average downward trend of 0.23% per year was observed, without statistical significance. **Conclusion:** A higher rate of preventable mortality was observed in males, and of these, NCDs had a higher rate during the period. Analyzing mortality data is a practice as a tool for managing, planning, and evaluating public policies.

Keywords: *Mortality. Cause of Death. Mortality Rate. Morbidity and Mortality Indicators.*

RESUMO

Justificativa e Objetivos: Óbitos evitáveis são aqueles que poderiam ter sido evitados por ações efetivas dos serviços de saúde no período de ocorrência. Descrever mortalidade evitável fornece valiosos indicadores de serviços de saúde, sendo possível avaliar a qualidade e resolutividade a partir dos dados obtidos. O objetivo foi analisar as tendências de mortalidade por causas evitáveis e delinear o perfil dos óbitos evitáveis no município de Caçador, Santa Catarina no período de 2013 a 2022. **Métodos:** Estudo ecológico de série temporal, com dados secundários do Sistema de Informação sobre Mortalidade DATASUS. A análise foi bivariada e para análise de tendência temporal utilizou a regressão *Joinpoint*, empregando o método *Empirical Quantile* e o critério *Weighted Bayesian Information Criteria*. **Resultados:** Foram classificados como evitáveis 67,3% óbitos. A análise de tendência temporal, identificou duas fases distintas: uma redução anual média de 13,09% entre 2013 e 2015, seguida por um aumento de 2,44% ao ano de 2015 a 2022 A estratificação por sexo demonstrou tendências significativas para o sexo masculino, com queda de 15,62% ao ano no período inicial e subsequente aumento de 2,9% ao ano, especialmente associado a doenças cardiovasculares, que representaram 10,0% dos óbitos evitáveis entre os homens. No sexo feminino, observou-se uma tendência de queda média de 0,23% ao ano, sem significância estatística. **Conclusão:** Observou-se uma maior taxa da mortalidade evitável no sexo masculino, e dessas as DCNT tiveram uma maior taxa no período. Analisar dados de mortalidade é uma prática como instrumento de gestão, planejamento e avaliação de políticas públicas.

Descritores: *Mortalidade. Causa de Óbito. Taxa de Mortalidade. Indicadores de Morbimortalidade.*

RESUMEN

Justificación y Objetivos: Las muertes prevenibles son aquellas que podrían haberse evitado mediante acciones efectivas de los servicios de salud durante el período en que ocurrieron. Describir la mortalidad prevenible proporciona indicadores valiosos de los servicios de salud, lo que permite la evaluación de la calidad y la efectividad con base en los datos obtenidos. El objetivo fue analizar las tendencias de mortalidad por causas prevenibles y delinear el perfil de muertes prevenibles en el municipio de Caçador, Santa Catarina, de 2013 a 2022. **Método:** Un estudio ecológico de series de tiempo con datos secundarios del Sistema de Información de Mortalidad DATASUS. El análisis fue bivariado y se utilizó la regresión Joinpoint para el análisis de tendencias temporales, empleando el método de cuantiles empíricos y los criterios de información bayesianos ponderados. **Resultados:** El 67,3% de las muertes se clasificaron como prevenibles. El análisis de tendencias temporales identificó dos fases distintas: una reducción anual promedio del 13,09% entre 2013 y 2015, seguida de un aumento del 2,44% anual entre 2015 y 2022. La estratificación por sexo reveló tendencias significativas para los hombres, con una disminución anual del 15,62% en el período inicial y un aumento anual posterior del 2,9%, particularmente asociado con las enfermedades cardiovasculares, que representaron el 10,0% de las muertes prevenibles en hombres. Entre las mujeres, se observó una tendencia descendente promedio del 0,23% anual, sin significancia estadística. **Conclusión:** Se observó una mayor tasa de mortalidad prevenible en los hombres, y de estos, las ENT tuvieron una tasa más alta durante el período. El análisis de datos de mortalidad es una práctica como herramienta para la gestión, planificación y evaluación de políticas públicas.

Palabras Clave: *Mortalidad. Causa de muerte. Tasa de mortalidade. Indicadores de morbilidad y mortalidade.*

INTRODUCTION

Since the implementation of the Unified Health System (SUS) in 1990, the promotion, prevention, and access to health have been enshrined as fundamental rights guaranteed by the Federal Constitution, establishing shared responsibility between the State and individuals throughout the life cycle, encompassing all instances and levels of care in a universal manner.[1] The evaluation of population health involves, among other approaches, the analysis of the effectiveness of health services offered in different regions, with health indicators playing a central role in converting data into useful information for the formulation and implementation of public health policies. These indicators allow the identification of trends over time, assisting in disease monitoring and the evaluation of existing programs.[2]

Among the main indicators used, mortality stands out, providing geographical, demographic, and etiological information about the determinants of deaths, allowing for more effective health interventions and policies.[3] These indicators are crucial for monitoring and analyzing the performance of the health system, enabling the formulation of evidence-based actions to benefit all users of the SUS.[4]

The mortality indicator reveals a significant evolution in the last thirty years in Brazil, reflecting reductions in death rates in parallel with demographic and epidemiological transformations driven by the consolidation of the SUS.[5] However, this transition is not homogeneous in all regions of the country; areas with less socioeconomic development show a slower reduction in mortality from infectious diseases and external causes.[6] The authors emphasize that, although Brazil is experiencing a transition in mortality and morbidity patterns, significant disparities persist attributed to social inequalities and difficulties in accessing health services.[1]

Avoidable mortality as a concept emerges as an essential tool for monitoring trends and evaluating the quality of health care. This approach allows the identification of discrepancies between observed and expected deaths, reflecting the impact of medical interventions, technological advances, and health practices.[7] The analysis of mortality from preventable causes contributes to understanding death profiles, providing support for the development of public policies that respond to regional demands, and for local planning, allowing primary care to direct its efforts to the most vulnerable groups.[8]

The Brazilian List of Preventable Causes of Death by health system interventions, developed after the implementation of the SUS (Brazilian Unified Health System), defines situations in which deaths could be prevented by appropriate health care actions and preventive measures.[9]

In this context, preventable mortality in Brazil shows significant progress in recent decades, but also reveals persistent inequalities that challenge the health system. Data from the 2019 Global Burden of Disease (GBD) study show that, although mortality rates from preventable causes decreased significantly between 1990 and 2019, with a reduction from 343.9 to 155.8 deaths per 100,000 inhabitants, the decline was more pronounced for infectious causes, maternal and neonatal conditions, while non-communicable chronic diseases (NCDs) and external causes remained as structural challenges to public health.[8] The proportional decrease in mortality from NCDs contrasts with their continued status as the main cause of death, highlighting the limitations of strategies for controlling and preventing these diseases amidst population aging and the Brazilian epidemiological transition.[1,8]

Furthermore, the weight of external causes among young adults, especially men, as pointed out by Malta et al, reaffirms the complexity of preventable mortality, influenced by social determinants, violence, and weaknesses in the healthcare network.[8] The negative correlation between preventable mortality and the Sociodemographic Index (SDI) ($R = –0.74$; $p < 0.000001$) reinforces the role of territorial and socioeconomic inequalities in determining health.[1]

In this scenario, it becomes urgent to rethink intersectoral public policies and health surveillance strategies that not only expand access but also promote social justice and equity in the distribution of resources and healthcare. To this end, the continuous promotion of scientific production and rigorous epidemiological analysis is fundamental, as it provides essential technical and ethical support for the formulation of effective, sustainable public policies centered on health equity.

Considering these premises, this study aimed to analyze mortality trends from preventable causes and to outline the profile of preventable deaths in Caçador city, in Santa Catarina, from 2013 to 2022.

METHODS

This study is characterized as descriptive, ecological and time-series, encompassing the analysis of a ten-year historical series, between 2013 and 2022. The research was conducted in Caçador, located in the mid-west of the state of Santa Catarina, in the Alto Vale do Rio do Peixe region, with a total population of 73,720 inhabitants, according to the 2022 Census. Its economy is diversified, with emphasis on the timber, metallurgical, agricultural, and service sectors. Caçador has a healthcare network composed of basic health units, specialized outpatient and hospital services, being

a regional reference in some specialties, considering access and coverage of services as determining aspects of the preventability of deaths. The city presents a demographic and epidemiological profile compatible with regions in transition, with a significant presence of preventable causes of mortality between 5 and 74 years old.[10]

The data used were obtained from the Mortality Information System (SIM), made available by the Department of Informatics of the Unified Health System (DATASUS) platform. Inclusion criteria considered deaths referring to the resident population, occurring in the analyzed period and classified according to the Brazilian List of Avoidable Causes of Death by interventions in the SUS from 5 to 74 years old. The use of this age group is justified by allowing the comparability of data, temporal monitoring, and analysis of the effectiveness of public health policies, based on causes of death that can be prevented by already consolidated interventions, such as immunization, screening, adequate treatment, and health promotion. Additionally, the age range between 5 and 74 years excludes causes mostly attributed to perinatal conditions and extreme senility, focusing on potentially preventable deaths in groups with greater exposure to effective SUS interventions.[9]

The variables analyzed included sex, age group from 5 to 74 years, color/race, place of occurrence, educational level, year of occurrence, and cause of death, according to the chapters of preventable causes defined by the International Statistical Classification of Diseases and Related Health Problems (ICD-10), highlighting the three main subgroups. Deaths of children under 1 year to 4 years were excluded. Annual crude mortality rates were calculated for Brazil and for Caçador, as well as the total rate for the analyzed period.

Initially, bivariate analyses were performed to describe the prevalence of deaths from preventable causes among men and women, according to demographic characteristics such as age, color/race, marital status, and education level. Pearson's chi-square test was applied to verify associations, considering those with a p-value < 0.05 as significant.

For the analysis of the association between sex and sociodemographic characteristics in relation to mortality from preventable causes, descriptive statistics with absolute and relative frequencies were used. The comparison between proportions was performed using Pearson's chi-square test, considering a significance level of 5% ($p < 0.05$).

In situations where the assumptions of the chi-square test were not met, specifically when at least one cell in the table contained an expected frequency less than 5, Fisher's Exact Test was applied. This procedure was necessary for categories with a smaller number of observations, such as the "Yellow" and "Indigenous" categories of the race variable, in order to ensure the statistical validity of the results.

For the temporal analysis of preventable deaths, a descriptive approach was used, based on historical series, with the aim of identifying trends, patterns, and variations throughout the studied period. The temporal analysis was performed using annual rates or moving averages, allowing for the assessment of trends of increase, decrease, or stability over time. The mortality rate from preventable causes was obtained by dividing the number of deaths by the total estimated population for the year of occurrence, and multiplying the result by 100,000 inhabitants. Age standardization was performed using the direct method, using the Brazilian population from the 2022 Census as the standard and stratifying the results by sex.

The temporal trend analysis used Joinpoint regression, employing the Empirical Quantile method and the Weighted Bayesian Information Criteria (BIC). This method, developed by the American Cancer Research Center, allows the identification of changes in mortality trends by detecting inflection points, dividing the data into distinct segments. The Annual Percent Change (APC) was calculated with 95% confidence intervals (95% CI), with APCs with $p<0.05$ considered significant. The analyses were conducted in Joinpoint software version 5.2.0, with a maximum of one inflection point.

The study followed the ethical principles established by Resolutions No. 466/2012 - 510/2016 - 580/2018 of the Ministry of Health, and was approved by the Research Ethics Committee of the University of Alto Vale do Rio do Peixe, under CAAE 83317624.3.0000.0259 and opinion No. 7.111.996 in September 2024.

RESULTS

Between 2013 and 2022, a total of 3,137 deaths were recorded in the city of Caçador (SC). Of these, 67.3% (n = 2,112) were classified as preventable, 29.0% (n = 909) as resulting from causes not clearly preventable (garbage category), and 3.7% (n = 116) had poorly defined causes. Bivariate analysis of deaths from preventable causes showed a higher prevalence in males compared to females. In the age group analysis, the 15-19 year old group stood out among males, with 86.7% of deaths classified as preventable. Among women, the highest prevalence was observed in the 5-9 year old age group (60.0%). The variable color/race did not show a statistically significant association with the preventability of deaths. For categories with a small number of observations, such as 'Yellow' and 'Indigenous', Fisher's Exact Test was applied. In both cases, the p-values (0.304 and 1.000, respectively) indicated the absence of a statistically significant

association between sex and mortality from preventable causes, considering these racial categories.

Regarding marital status, a higher frequency of preventable deaths was observed among single men (73.6%) and widowed women (65.0%). In relation to education level, the prevalence was higher among men with 8 to 11 years of schooling (65.6%) and women without formal education (56,3%) (Table 1).

Table 1. Proportion of avoidable mortality from preventable causes standardized by sex according to sociodemographic characteristics in Caçador between 2013 and 2022.

	Female N (%)	Male N (%)	p-value*
Age range			<0,001
5 a 9	6 (60,0)	4 (40,0)	
10 a 14	8 (42, 1)	11 (57,9)	
15 a 19	6 (13,3)	39 (86,7)	
20 a 24	15 (24,2)	47(75,8)	
25 a 29	19 (27,5)	50 (72,5)	
30 a 34	21 (30,0)	49 (70,0)	
35 a 39	32 (43,8)	41 (56,2)	
40 a 44	47 (41,6)	66 (58,4)	
45 a 49	42 (30,7)	95 (69,3)	
50 a 54	74 (33,6)	146 (66,4)	
55 a 59	102 (40,2)	152 (59,8)	
60 a 64	144 (44,0)	183 (56,0)	
65 a 69	150 (45,3)	181 (54,7)	
70 a 74	157(41,1)	225 (58,9)	
Race			0,173
White	701 (39,7)	1064 (60,3)	
Black	16 (51,6)	15 (48,4)	
Yellow	0 (0,0)	4 (100,0)	
Brown	98 (34,3)	188 (65,7)	
Indigenous	1 (100,0)	1 (50,0)	
Marital Status			<0,001
Single	130 (26,4)	363 (73,6)	
Married	298 (38,9)	468 (61,1)	
Widowed	147 (65,0)	79 (35,0)	
Separated	72 (42,6)	97 (57,4)	
Other	77 (37,0)	131 (63,0)	
Unknown	99 (39,6)	151(60,4)	
Education			<0,001
None	80 (56,3)	62(43,6)	
1 to 3	216 (40,3)	320 (59,7)	
4 to 7	232 (36,7)	401 (63,3)	
8 to 11	111 (34,4)	212 (65,6)	
12 or more	38 (40,0)	57 (60,0)	
Unknown	146 (38,1)	237 (61,9)	

Legend: * Pearson's chi-squared test; * Fisher's exact test.

External causes accounted for 21.0% of preventable deaths, with a predominance of transport accidents (35.7%) and assaults (19.0%). A peak in mortality from external causes was observed in 2021, with 69 deaths (15.6% of the total preventable deaths in the period) (Figure 1).

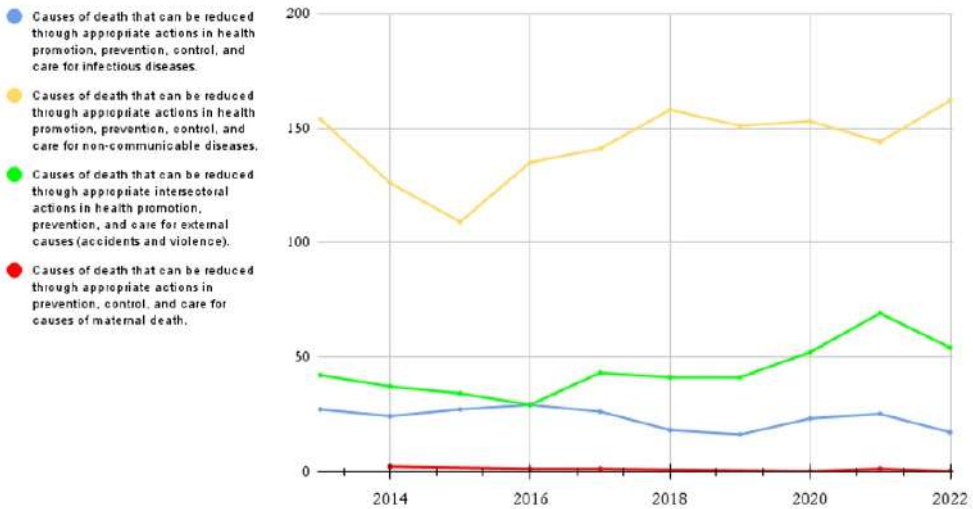

Figure 1. Temporal trends by groups of preventable causes between 2013 and 2022 in the city of Caçador.

Infectious diseases maintained a linear trend (11.0% of the total), with a cumulative reduction of 4.3% during the studied period. Among these, respiratory infections – especially pneumonia and influenza – accounted for 52.0% of cases. Maternal deaths corresponded to 0.24% of the total number of deaths, all attributed to obstetric complications. The estimated Maternal Mortality Ratio (MMR) was 43 per 100,000 live births. No deaths from vaccine-preventable diseases were recorded during the analyzed period.

The temporal trend analysis, performed using the Joinpoint model, identified two distinct phases: an average annual reduction of 13.09% (not statistically significant) between 2013 and 2015, followed by an increase of 2.44% per year from 2015 to 2022 (Table 2; Figure 2). Stratification by sex showed significant trends for males, with a decrease of 15.62% per year in the initial period and a subsequent increase of 2.9% per year, especially associated with cardiovascular diseases (CVD), which represented 10.0% of preventable deaths among men. In females, an average decreasing trend of 0.23% per year was observed, without statistical significance (Table 2; Figure 2).

Table 2. Annual Percentage Change (APC) and 95% Confidence Intervals (95% CI) of age-standardized mortality rates from preventable causes, stratified by sex, in Caçador between 2013 and 2022.

Sex	Period	APC (CI95%)
Both	2013-2015	-13,09 (-20,5; 0,30)
Both	2015-2022	2,44 (-0,67; 13,52)
Male	2013-2015	-15,62 (-23,40; -1,81)*
Male	2015-2022	2,90 (0,06; 13,13)*
Female	2013-2022	-0,23 (-3,09; 2,82)

Legend: *p<0,05

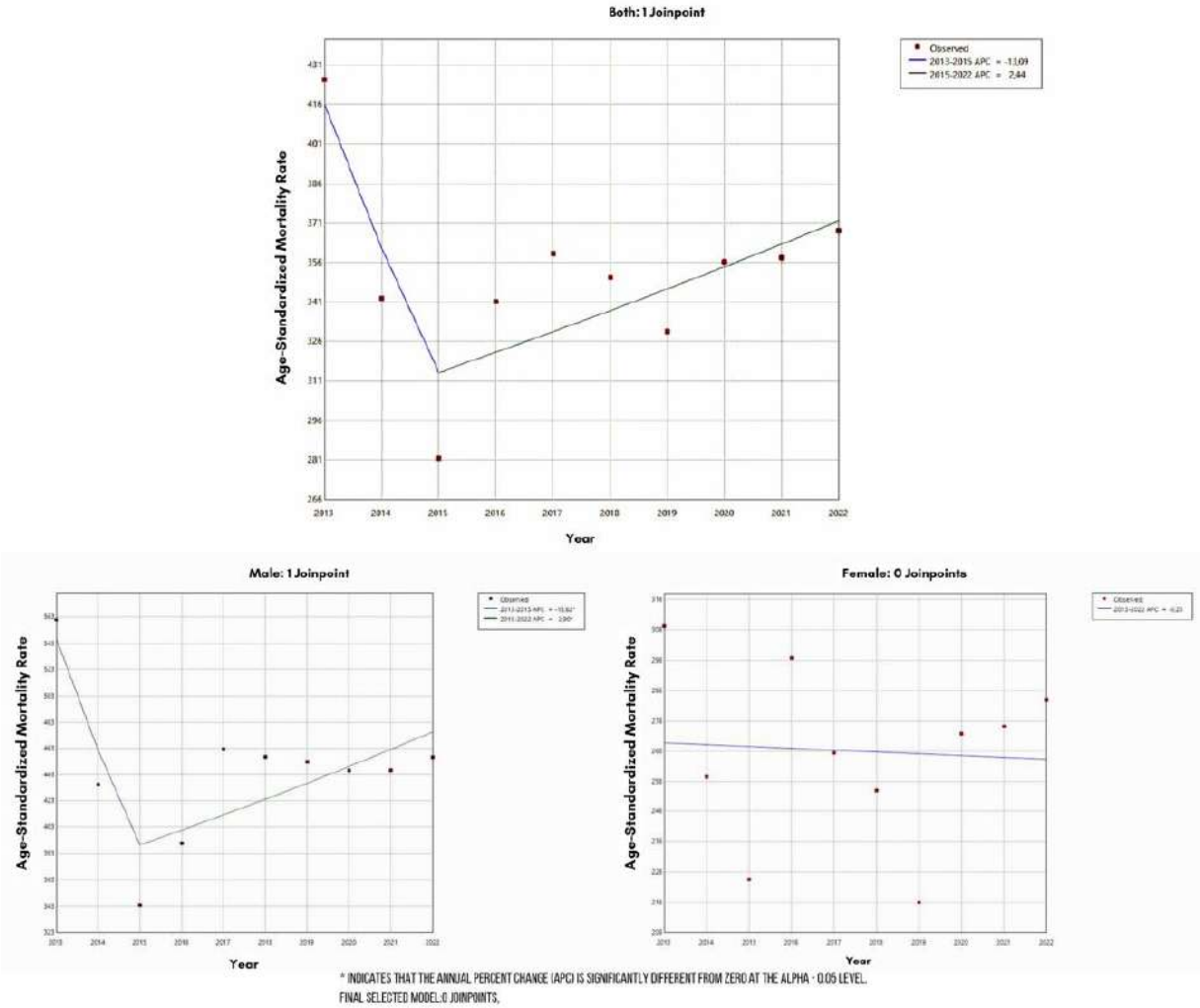

Figura 2. Joinpoint regression model of the standardized mortality rate for all preventable causes (A), for males (B) and for females (C) in Caçador between 2013 and 2022.

DISCUSSION

The results of this study reinforce previous findings on disparities in mortality by sex, with a higher proportion of preventable deaths among men. This difference is often attributed to lower male adherence to health services and factors related to male lifestyle and social contexts in which they are embedded.[11,12] In addition, men tend to seek medical attention only in situations of clinical worsening, which compromises the effectiveness of preventive actions and can contribute to more serious outcomes.[13] Another relevant issue concerns the organization of operating hours of health services, especially those linked to the Unified Health System (SUS). The predominantly daytime hours of

operation can constitute a significant barrier to access for men who are working during this period, hindering the provision of preventive care and continuous health monitoring.

The predominance of deaths among white individuals in Caçador reflects the demographic profile of the state of Santa Catarina, which, according to the 2022 Demographic Census, has the second highest percentage of white population in the country (76.3%).[10] This data, therefore, does not reveal a specific racial inequality, but follows the local population composition. Regarding marital status, the literature suggests that marital union is associated with healthier lifestyles and greater social support, which may explain the higher mortality observed among single men.[14] In the case of women, the higher mortality rate among widows may be related to female longevity and greater exposure to chronic conditions at advanced ages.[15] In this regard, the authors highlight the greater propensity of women to practice self-care and adhere to health prevention actions.[13]

Throughout the analyzed period, it was observed that non-communicable chronic diseases (NCDs) represented the main cause of preventable deaths, accounting for 68.0% of these deaths. Among them, cerebrovascular diseases (15.0%), ischemic heart diseases (14.0%), and diabetes mellitus (13.0%) stand out. The temporal analysis revealed a slight decrease between 2013 and 2015, followed by stabilization until 2020 and a gradual increase in 2021 and 2022. These findings align with authors who attribute the growth of NCDs to population aging, but also reveal structural weaknesses in the health system's capacity to carry out effective actions for the prevention, control, and continuous care of NCDs, especially in territories marked by social vulnerabilities.[1,8,16] The Global Burden of Disease (GBD) study indicates that, although standardized mortality rates for NCDs have decreased in recent decades, the absolute number of deaths remains high, especially in the North and Northeast regions, where primary care coverage is often insufficient and social determinants of health, such as low income, limited education, and food insecurity, strongly influence illness.[8] The World Health Organization (WHO) recognizes that genetic, behavioral, and environmental factors contribute to the development of these diseases.[17] NCDs are aggravating factors for mortality rates; therefore, primary care plays a fundamental role in the diagnosis and management of these diseases, thus preventing future complications, with expanded diagnostic capacity, provision of longitudinal and multidisciplinary care, health education programs focused on self-care and behavioral changes, in addition to integration with intersectoral actions that promote healthy environments and equitable access to social determinants of health.[18]

Regarding external causes, which accounted for 21.0% of preventable deaths, their prevalence among young people stands out, representing a significant impact on premature mortality. Similarly, studies corroborate the data and show an increase in mortality from external causes in recent years, mainly mortality related to traffic accidents.[19] The recommendations of the Ministry of Health for the consolidation of intersectoral actions in education, prevention, and strengthening of the emergency network to reduce morbidity and mortality from external causes are highlighted.[20]

Among deaths from infectious causes, respiratory infections – mainly pneumonia and influenza – were responsible for more than half of the cases (52.0%). The global reduction in infant mortality from pneumonia is directly associated with the introduction of the pneumococcal vaccine. However, this progress is still uneven, especially in regions with less access to vaccination.[21]

Maternal deaths, which represented 0.24% of the total deaths, showed a Maternal Mortality Ratio (MMR) of 43 per 100,000 live births, a value close to the state average (41/100,000) and lower than the national average (77/100,000).[22] Despite advances since the 1990s, maternal mortality still requires continuous efforts, especially through the strengthening of Maternal Death Investigation Committees and the qualification of obstetric care.[23]

The fact that no deaths from vaccine-preventable diseases were registered during the analyzed period is an indication of the effectiveness of immunization policies, especially the National Immunization Program (NIP), whose coverage has historically been high in the city.[24]

This result highlights the importance of maintaining high vaccination rates and epidemiological surveillance as essential strategies for the prevention of vaccine-preventable diseases. This study has important limitations, among which the use of secondary data from death records stands out. These records are subject to underreporting, inconsistencies in filling out death certificates, and inaccurate classification of causes of death – especially in cases categorized as garbage codes (poorly defined). Such limitations may compromise the accuracy of the estimates, especially in specific cause analyses. To mitigate these effects, rigorous classification criteria were adopted according to the Brazilian list of preventable causes, and a stratified analysis was performed by demographic variables, in addition to the use of statistical trend techniques that increase the robustness of the findings. For future studies, the incorporation of qualitative methods and triangulation of sources is suggested for a deeper understanding of the determinants of preventable mortality in the local context.

The findings of this study reiterate the urgency of an integrated, intersectoral, and territorialized approach to health, centered on equity, the prevention of diseases, and the reduction of structural inequalities that permeate the Brazilian health system. The persistent and high proportion of preventable deaths, particularly among men of working age and due to NCDs, reflects failures in guaranteeing timely access, continuity of care, and the effectiveness of Primary Health Care (PHC) actions.[1,8] Furthermore, social vulnerability determined by factors such as low education, food insecurity, precarious housing, and unemployment exacerbates the risk of illness and premature death, disproportionately impacting peripheral, Black, Indigenous populations, and those residing in regions with a low Sociodemographic Index (SDI).[8]

Considering this perspective, strengthening PHC with well-distributed multidisciplinary teams, updated care protocols for chronic diseases and external causes, expanding health promotion actions in school, community, and work contexts, as well as investing in epidemiological surveillance sensitive to the local reality and improving the quality of death records, becomes strategic. The continuous and qualified analysis of mortality data should be valued as a management and monitoring tool, capable of supporting evidence-based public policies aimed at overcoming health inequities, especially through actions focused on the most underserved territories. In this way, the promotion of life and the prevention of avoidable deaths become central ethical and operational commitments in the consolidation of a truly universal and equitable health system.

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AUTHORS' CONTRIBUTIONS

Valéria Delazzari Valer contributed to the bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, table preparation, conclusions, review, and statistics. **Paula Brustolin Xavier** contributed to project administration, bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, conclusions, review, and statistics. **Maiton Bernardelli** contributed to the writing of the abstract, methodology, interpretation of the results, conclusions, review, and statistics. **Heloisa Marquardt Leite** contributed to the review and statistics. **Bruno Vitiritti** contributed to the review and final adjustments.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Original Article

Reports of sexual violence and alcohol use in Minas Gerais from 2018 to 2022

Notificações de violência sexual e uso de álcool em Minas Gerais entre 2018 e 2022
Notificaciones de violencia sexual y consumo de alcohol en Minas Gerais entre 2018 y 2022

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ABSTRACT

Background and Objectives: Sexual violence is a serious public health issue. Alcohol intoxication acts as a risk factor for its occurrence as it affects both the victim's ability to defend themselves and the aggressors' inhibitions, who tend to misinterpret social cues and act more aggressively. This study aimed to describe the epidemiological characteristics of reports of sexual violence suspected to be associated with alcohol consumption in the state of Minas Gerais from 2018 to 2022. **Methods:** This is a descriptive study, with data analysis based on the epidemiological profile, obtained from reports of sexual violence with suspected alcohol use in Minas Gerais, using secondary data from SINAN, collected by SES/MG through Tabnet. **Results:** Most reports of sexual violence involved women (92.71%), with the highest incidence in the 20–29 age group (24.30%). Regarding education level, a significant portion of the records was incomplete or left blank (25%). Rape was the most prevalent type of violence (74.60%). Most victims did not receive adequate care, with blood collection being the most frequently performed procedure (40.89%). Aggressors were predominantly male (95.66%), acting alone in most cases (74.56%), with most being friends or acquaintances of the victim (31.41%). **Conclusion:** The study reinforces the urgency of public policies aimed at preventing excessive alcohol consumption and supporting victims of sexual violence, in addition to the need to train professionals to improve the completion of reports and strengthen preventive actions.

Keywords: *Sexual violence. Alcohol abuse. Health information systems.*

RESUMO

Justificativa e Objetivos: A violência sexual é um grave problema de saúde pública. A intoxicação pelo álcool age como fator de risco para sua ocorrência, pois afeta tanto a capacidade das vítimas de se defenderem quanto as inibições dos agressores, que tendem a mal interpretar sinais sociais e agir com maior agressividade. Este estudo objetivou descrever as características epidemiológicas das notificações de violência sexual com suspeita de associação ao consumo de álcool, no estado de Minas Gerais, entre os anos de 2018 e 2022. **Métodos:** Caracteriza-se por um estudo descritivo, com análise dos dados a partir do perfil epidemiológico coletados por meio das notificações de violência sexual com suspeita de uso de álcool, em Minas Gerais, com base em dados secundários do SINAN coletados pela SES/MG por meio do Tabnet. **Resultados:** A maioria das notificações de violência sexual envolveu mulheres (92,71%), com maior incidência na faixa etária de 20 a 29 anos (24,30%). Em relação à escolaridade, uma parcela significativa dos registros estava incompleta ou em branco (25%). O estupro foi o tipo de violência mais prevalente (74,60%). A maioria das vítimas não recebeu atendimento adequado, sendo a coleta de sangue o procedimento mais realizado (40,89%). Os agressores eram predominantemente homens (95,66%), agindo sozinhos na maioria dos casos (74,56%), com a maior parte sendo amigos ou conhecidos da vítima (31,41%). **Conclusão:** O estudo reforça a urgência de políticas públicas que previnam o consumo excessivo de álcool e apoiem vítimas de violência sexual, além da necessidade de capacitar profissionais para melhorar o preenchimento de notificações e fortalecer as ações preventivas.

Descritores: *Violência sexual. Abuso de álcool. Sistemas de informação em saúde.*

RESUMEN

Justificación y Objetivos: La violencia sexual es un grave problema de salud pública. La intoxicación por alcohol actúa como un factor de riesgo para su ocurrencia, ya que afecta tanto la capacidad de defensa de las víctimas como las inhibiciones de los agresores, quienes tienden a malinterpretar señales sociales y a actuar con mayor agresividad. Este estudio tuvo como objetivo describir las características epidemiológicas de las notificaciones de violencia sexual con sospecha de asociación al consumo de alcohol en el estado de Minas Gerais entre 2018 y 2022. **Métodos:** Se trata de un estudio descriptivo, con análisis de datos a partir del perfil epidemiológico, recolectados a partir de notificaciones de violencia sexual con sospecha de consumo de alcohol en Minas Gerais, utilizando datos secundarios del SINAN, recolectados por la SES/MG a través del Tabnet. **Resultados:** La mayoría de las notificaciones de violencia sexual involucraron a mujeres (92,71%), con mayor incidencia en el grupo de edad de 20 a 29 años (24,30%). En cuanto al nivel educativo, una parte significativa de los registros estaba incompleta o en blanco (25%). La violación fue el tipo de violencia más prevalente (74,60%). La mayoría de las víctimas no recibió atención adecuada, y la recolección de sangre fue el procedimiento más realizado (40,89%). Los agresores eran predominantemente hombres (95,66%), actuaban solos en la mayoría de los casos (74,56%), y en su mayoría eran amigos o conocidos de la víctima (31,41%). **Conclusión:** El estudio refuerza la urgencia de políticas públicas que prevengan el consumo excesivo de alcohol y apoyen a las víctimas de violencia sexual, además de la necesidad de capacitar a los profesionales para mejorar el llenado de notificaciones y fortalecer las acciones preventivas.

Palabras Clave: *Violencia sexual. Abuso de alcohol. Sistemas de información en salud.*

INTRODUCTION

Sexual violence, which includes non-consensual sexual interactions such as sexual assault and rape, is recognized as a major challenge to global public health.[1] This type of violence not only compromises human dignity, but also constitutes a serious violation of the victims' human rights. Its roots are linked to social disparities, reflecting gender inequalities and power dynamics related to economic status, the use of physical force, and the presence of weapons.[2]

The Pan American Health Organization defines sexual violence as any behavior of a sexual nature, attempt to perform a sexual act, or other action directed at someone's sexuality through coercion by another person, regardless of their relationship with the victim or the context involved.[3]

During their lifetime, approximately one in three women, which is equivalent to around 736 million women, experience physical or sexual violence, and around 20% of these women reported having suffered sexual assault during childhood. It is worth noting that in most cases where these situations occur, the main perpetrators are partners, and therefore these cases are not reported or victims are coerced into silence.[4]

In parallel with this, since 2011, reporting domestic violence, sexual violence, and other forms of violence has become mandatory for all health services, whether public or private, throughout Brazil. In 2014, the list of diseases and conditions subject to mandatory reporting was updated, requiring cases of sexual assault to be reported to municipal health departments within 24 hours.[5]

Studies have established links between risky behaviors and sexual activities in leisure contexts.[6] Alcohol is often used to increase the chances of sexual encounters or to influence people's behavior and desire, making them more receptive to sex. Its consumption emerges as the main risk factor for non-consensual sexual relations, forced touching, and additional risks. However, its effects differ between men and women: in women, the ability to react to warning signs is diminished, compromising protective behavioral strategies, while in men, impulses are uninhibited, and aggression is intensified.[6]

Regarding the behavior of sexual offenders and alcohol use, studies indicate that alcohol can exacerbate aggression and lower inhibitions, facilitating violent behaviors. The pharmacological mechanisms of alcohol reduce cognitive functioning, while the psychological mechanisms involve the interaction between perpetrators' beliefs about the effects of alcohol and its actual repercussions. When intoxicated, aggressors tend to misinterpret social cues, focusing more on immediate cues such as sexual arousal and frustration, and less on long-term consequences and empathy for the victim. This increases the propensity to commit sexual assault.[7]

This study is relevant because it addresses the critical intersection between alcohol consumption and sexual violence, an area of great impact on public health and human rights. Considering the issues outlined above, this study aims to describe the epidemiological characteristics of reports of sexual violence suspected to be associated with alcohol consumption in the state of Minas Gerais.

METHODS

This is a descriptive study of the epidemiological profile of reports of sexual violence involving suspected alcohol use. The data were collected from secondary sources of the Notifiable Diseases Information System (SINAN) managed by the Minas Gerais State Health Department (SES/MG).

The SINAN data were collected using the Health Information Tabulator tool (Tabnet) tool on the SES/MG website and exported to Microsoft Excel 365 software between December 2023 and February 2024. They comprise reports registered by health services in Minas Gerais between 2018 and 2022 related to the place of residence. The variables analyzed were: characterization of victims of sexual violence; data on victims of sexual violence; type of sexual violence; procedure performed; data on the probable perpetrator of the violence; and the relationship between sexual violence and alcohol use. Data analysis was performed using simple descriptive statistics with absolute and relative values and presented in tabular format.

The study was conducted using publicly available data published on the SES/MG website (vigilancia.saude.mg.gov.br), without the possibility of identification, and thus does not require review by the Research Ethics Committee, as provided for in Resolution No. 510, dated April 7, 2016.

RESULTS

From the data collected, it was possible to verify that between 2018 and 2022, 62,763 cases of violence related to alcohol use were reported. Of this total, 5,213 refer to cases of sexual violence related to the use of this substance in the same period. The data show that 949, 1,050, 980, 938, and 1,288 cases were reported in 2018, 2019, 2020, 2021, and 2022, respectively.

The results were grouped into five tables for the presentation of the data shown below. Sociodemographic data and characteristics of individuals who were victims of alcohol-related sexual violence during the study period are presented. Among

the victims, females (92.71%) were predominant in the reports (Table 1).

A higher proportion of notifications was found in the 20-29 age group (24.30%). Brown race/color was attributed in most cases of notifications (47.29%), followed by white (30.08%). Among reports with valid education data, a high proportion was attributed to the field being unknown or blank (25%), followed by individuals who had not completed 5th to 8th grade of elementary school (16.98%). In the sexual orientation field, there was a predominance of victims who declared themselves to be heterosexual (56.09%). Regarding gender identity, the field was most often described as not applicable (70.08%), followed by being left blank or described as unknown (28.20%).

Table 1. Distribution of victim characterization notifications by gender, according to age group, race/color, education level, sexual orientation, and gender identity, MG, Brazil, 2018–2022.

	N (%)
Total	5213 (100.00)
Gender	
Male	380 (7.29)
Female	4.833 (92.71)
Age group	
< 1	44 (0.84)
1 to 4	249 (0.23)
5 to 9	441 (4.78)
10 to 14	897 (17.21)
15 to 19	878 (16.84)
20 to 29	1.267 (24.30)
30 to 39	676 (12.97)
40 to 49	452 (8.67)
50 to 59	199 (8.46)
60 to 69	63 (3.82)
70 to 79	35 (1.21)
> 80	12 (0.67)
Race/color	
Ignored/Blank	358 (0.77)
White	1.568 (30.08)
Black	763 (6.87)
Yellow	40 (0.36)
Brown	2.465 (47.29)
Indigenous	19 (14.64)
Education	
Incomplete elementary education (1st to 4th grade)	344 (6.60)
Elementary education (4th grade)	216 (4.14)
Incomplete elementary education (5th to 8th grade)	885 (16.98)
Illiterate	56 (1.07)
Completed higher education	180 (3.45)
Incomplete higher education	260 (4.99)
Complete elementary education	368 (7.06)
Complete secondary education	664 (12.74)
Incomplete secondary education	467 (8.96)
Ignored/Blank	1303 (25.00)
Not applicable	470 (9.02)
Sexual orientation	
Bisexual	116 (2.23)
Straight	2924 (56.09)
Homosexual (gay/lesbian)	177 (3.40)
Ignored/Blank	818 (15.69)
Not applicable	1178 (22.60)
Gender identity	
Ignored/Blank	1470 (28.20)
Not applicable	3655 (70.11)
Transgender Man	15 (0.29)
Transgender Woman	68 (1.30)
Transvestite	5 (0.10)

Still regarding the victim, in terms of the type of violence that occurred, there was a higher prevalence of rape (74.60%), followed by sexual harassment (33.68%). It is worth noting that the same victim may have suffered more than one type of sexual violence, meaning that there is a chance that more than one field was marked on the notification form (Table 2).

Table 2. Distribution of reports of sexual violence by suspected alcohol use, MG, Brazil, 2018–2022.

	Yes N (%)	No N (%)
Type of violence		
Sexual harassment	1757 (33.68)	3456 (66.32)
Rape	3888 (74.60)	1325 (25.40)
Child pornography	101 (1.94)	5112 (98.06)
Sexual exploitation	177 (3.40)	5036 (96.60)
Other forms of violence		
Ignored/Blank	9 (0.17)	5204 (99.83)
Yes	8 (0.15)	5205 (99.85)
No	184 (3.53)	5029 (96.47)

When analyzing the data on procedures performed on victims of sexual violence with suspected alcohol use, it is noted that most were not performed; however, when performed, most were for blood collection (40.89%), followed by prophylaxis for sexually transmitted diseases (STDs) (Table 3).

Table 3. Distribution of notifications of procedures performed in cases of sexual violence based on suspected alcohol use, MG, Brazil, 2018–2022.

	Yes N (%)	No N (%)
Procedure performed		
STD prophylaxis	1984 (38.05)	3229 (61.95)
HIV prophylaxis	1769 (33.94)	3444 (66.06)
Hepatitis B prophylaxis	1250 (23.97)	3963 (76.03)
Blood collection	2132 (40.89)	3081 (59.11)
Semen collection	378 (7.25)	4835 (92.75)
Vaginal secretions collection	982 (18.83)	4231 (81.17)
Emergency contraception pill	1207 (23.15)	4006 (76.85)
Abortion permitted by law	116 (2.23)	5097 (97.77)

Abbreviations: STD: Sexually Transmitted Diseases; HIV: Human Immunodeficiency Virus.

Regarding data on the probable perpetrator, it can be observed that, in most of the cases recorded, sexual violence was committed by one individual (74.56%) and that most perpetrators were male (95.66%) (Table 4).

Table 4. Distribution of notifications of data from the probable perpetrator, MG, Brazil, 2018–2022.

	N (%)
Total	5213 (100.00)
Number of people involved	
Ignored/Blank	213 (4.09)
One	3.887 (74.56)
Two or more	1.113 (21.35)
Gender of the probable perpetrator	
Ignored	66 (1.27)
Male	4.987 (95.66)
Female	75 (1.44)
Both genders	85 (1.63)

In parallel with this, in cases where the degree of kinship of the probable perpetrator was recorded, most were committed by friends/acquaintances (31.41%), followed by someone unknown (26.09%) to the victim (Table 5).

Table 5. Distribution of reports of sexual violence by degree of kinship according to suspected alcohol use, MG, Brazil, 2018-2022.

	Yes N (%)	No N (%)
Degree of kinship		
Father	384 (7.36)	4.829 (92.54)
Mother	74 (1.42)	5.139 (98.57)
Stepfather	333 (6.39)	4.880 (93.58)
Stepmother	6 (0.12)	4.207 (80.57)
Spouse	376 (7.22)	4.837 (92.76)
Former spouse	180 (3.45)	5.033 (96.54)
Boyfriend or girlfriend	157 (3.01)	5.056 (96.97)
Ex-boyfriend/girlfriend	126 (2.24)	5.087 (97.57)
Son or daughter	33 (0.63)	5.180 (99.37)
Sibling	75 (1.44)	5.138 (98.58)
Friends/acquaintances	1.637 (31.41)	3.576 (68.60)
Stranger	1.361 (26.09)	3.852 (73.85)
Caregiver	14 (0.27)	5.199 (99.73)
Boss/supervisor	23 (0.44)	5.190 (99.56)
Person with an institutional relationship	20 (0.38)	5.193 (99.61)
Police officer/law enforcement officer	16 (0.31)	5.197 (99.69)
The person themselves	23 (0.44)	5.190 (99.56)
Other relationship	551 (10.57)	4.662 (89.44)

DISCUSSION

A study examining the prevalence and characteristics of sexual violence involving substance use (alcohol or drugs) conducted in the United States showed that the vast majority of people who were victims of sexual violence, whether male or female, reported that the perpetrator was intoxicated at the time of the crime.[8] Another study conducted in Spain showed that women who drink alcohol tend to be seen by men as vulnerable and/or sexually receptive.[9] This is consistent with comparative qualitative studies that concluded that alcohol is deliberately used by men as a seduction technique, regardless of whether there is consent or not.[10]

To further the discussion on the relationship between alcohol consumption and sexual violence in the Brazilian context, it is relevant to consider a study that investigated the perceptions of women victims of intimate partner violence in the city of Juiz de Fora, Minas Gerais. The study highlighted that alcohol can act as a situational factor, increasing the likelihood of violence by reducing inhibitions and impairing judgment, in addition to being frequently used as a justification for aggressive behavior. Participants reported that, in many cases, alcohol consumption by aggressors was seen as a preferred explanation for episodes of violence, which may reflect an attempt at emotional self-protection in the face of the complexity of abusive relationships.[11]

According to the results obtained in this study, there was a significant increase in reported cases of sexual violence involving alcohol consumption in 2022. In parallel with this, we should highlight that between 2020 and 2023, the WHO classified the SARS-Cov-2 outbreak, better known as Covid-19, as a Public Health Emergency of International Concern.[12]

In this context, the study that analyzed the increase in sexual violence during the Covid-19 pandemic, although focused on cases involving children and adolescents, offers some conclusions to be explored. The authors highlight that the pandemic and social isolation measures have created favorable conditions for an increase in sexual violence, especially within the households.[13]

The prevalence of victims of sexual violence was female (92%), as in Minas Gerais, a study conducted in a municipality in Colombia shows that females were the majority of victims in reports of this type of violence between 2011 and 2020. In this sense, another study indicates that violence is a manifestation of patriarchal and sexist structures that perpetuate gender inequality. For the author, this framework encourages the objectification and devaluation of women, which leads to an environment where sexual violence is mostly normalized as a form of control and domination. Furthermore, the difficulty victims face in accessing justice and effective support contributes to the perpetuation of this cycle of violence.[14] Sexual violence affects a large proportion of girls, requiring intervention that not only focuses on increasing social support for survivors, facilitating reporting, and ensuring that perpetrators are convicted, but also aims to reduce alcohol use and alleviate poverty.[15]

The predominant age group was 20 to 29 years old (24.30%), and the most common race/color was brown (47.29%). Regarding education, most records had the 'unknown/blank' field checked (25%), and among the available data, the most common level was incomplete 5th to 8th grade of elementary education (16.98%). These findings differ from the study by Sousa et al. (2021), who showed, in their study conducted in the state of Maranhão, that reports of sexual violence were more common in women aged 10 to 14 (54%), and corroborated the findings related to the brown race (70.4%) and incomplete 5th to 8th grade of elementary education (39.8%) as the majority of reports.[16]

Reflecting on these findings, it is possible to understand that sexual violence disproportionately affects women who occupy vulnerable social positions—young women, black or brown women, and women with lower levels of education. This profile is not merely statistical, but reveals structural dynamics of exclusion. The effects of public policies aimed at combating gender-based violence are not felt uniformly among all women: black women, for example, face historical and institutional processes of subordination that put them at greater risk of victimization and invisibility in terms of access to justice and social protection. These processes are exacerbated by social markers such as race, class, and gender, which are intertwined in a context of structural racism and institutionalized patriarchy.[17]

The most commonly reported type of sexual violence was rape (74.60%), which is consistent with data published by the Brazilian Forum on Public Safety in 2020, which recorded 66,348 cases of rape in Brazil, of which 5,009 occurred in Minas Gerais. Of the total, 85% of victims in the country and 86% in the state were female.[18] The results obtained are similar to the findings in the literature, with a study showing that about 78% of the cases of violence reported in Maranhão between 2009 and 2017 were violence involving rape, and in second place in the number of reports was sexual harassment, with 13.6% of cases in the nine years analyzed in this research, which also corroborates the findings of the present study.[16] Among the various forms of violence, rape is an attack that is not limited to the body, but also to the rights of the victim. Those who suffer do not have the right to choose, and the shame of what they have suffered perpetuates this silence.[19] In parallel with this, when discussing rape as gender violence, a study conducted by the Institute of Applied Economic Research in 2011 concluded that only 10% of rapes in Brazil are reported to the police. Based on this data, it can be concluded that many cases go unreported.[20]

This reality reveals an alarming and persistent issue in the country, where rape and sexual harassment are widely underreported crimes, reflecting a context of impunity and a deeply rooted culture of gender-based violence. The underreporting of rape in Brazil reflects a social structure that minimizes the severity of sexual violence, imposing significant obstacles on victims. Structural sexism, gender discrimination, and social stigma surrounding sexual abuse contribute to the silencing of victims, especially women, who make up the vast majority of rape victims.

According to the results obtained, most post-exposure procedures were not performed, with the majority consisting of blood collection (40.89%) and STD prophylaxis (38.05%). In this context, one of the serious consequences of sexual violence is the possibility of transmission of sexually transmitted infections (STIs), which causes fear and anxiety in victims. According to the Ministry of Health, it is essential to offer immediate assistance, including clinical and laboratory care, post-exposure prophylaxis (PEP) for Human Immunodeficiency Virus (HIV), viral hepatitis, and non-viral STIs (gonorrhea, syphilis, chlamydia infection, trichomoniasis, and chancroid), in addition to psychological and social support. Another important aspect is to provide prevention of unwanted pregnancy and guidance on medical procedures and legal rights, ensuring comprehensive and humanized care for victims.[21]

It is known that 7.6% of women became pregnant after sexual violence, especially those who did not access health services or receive emergency contraception. The same study described that the occurrence of STIs corresponded to 3.5%, being more common among young people aged 15 to 19 or victims of multiple aggressors.[22] In addition, the low implementation of post-exposure procedures may be related to structural and institutional factors, such as the lack of adequate preparation on the part of some health professionals, who often do not have in-depth knowledge of specific protocols for caring for victims of sexual violence. This gap compromises the quality of care provided, making it difficult to offer effective and comprehensive assistance when it is most needed. Barriers such as the scarcity of specialized services, the unequal distribution of these services throughout the country, and the lack of emotional and social support also contribute to many victims not receiving the comprehensive care to which they are entitled.

Regarding data on the likely perpetrator, higher prevalences were found for male perpetrators only. Another study describes that sexual assault against adults is about 1.62 times more frequent when involving a male perpetrator.[23] In Paraná, a study based on consultation of notification forms for cases treated at a referral hospital found that only one aggressor was identified in approximately 79% of reported cases.[24]

In this study, the perpetrator's degree of kinship was mostly acquaintances of the victim (31.41%), followed

by a high proportion of perpetrators unknown to the victim (26.09%). This result contrasts with the findings of a study conducted in the state of Espírito Santo, which indicated that sexual assault by strangers was about nine times more prevalent than that committed by perpetrators who had some connection with the victim.[23]

In another study conducted with victims of sexual violence in Piauí, although most cases also involved strangers (44.9%), the authors reported that the literature shows that a large proportion of rape cases occur within an intimate marital context, whether formal or not, and that several studies also demonstrate that the main perpetrators are family members themselves, including fathers, stepfathers, and acquaintances.[24] It is also worth mentioning that it is important to consider that the relationship between victim and perpetrator in sexual violence is complex and influenced by multiple sociocultural factors, which may explain the variability of data found in different regions and studies. Although part of the literature points to a predominance of unknown perpetrators, other studies show that sexual violence often occurs in the home or within the victim's circle of trust, which can make reporting difficult and contribute to underreporting.

Studies show that family violence associated with alcohol and drug use, violation of protective measures, and recidivism are strongly linked to alcohol consumption, both in family violence and intimate partner violence. Incidents related to alcohol use were twice as likely to involve serious physical violence, including life-threatening injuries, and were more likely to result in recidivism.[25]

Excessive alcohol consumption, by disinhibiting behavior and reducing victims' resistance, is a major facilitator of sexual assault. In this sense, accurate and detailed reporting of these cases is essential to strengthen the health surveillance system. Continuous and adequate training of health teams play an essential role in this process, ensuring that reporting forms are completed thoroughly and accurately. This practice not only improves the quality of data on cases of violence, but also ensures that they are properly investigated, referred, and treated in response to the needs of victims.

Furthermore, it is essential that government agencies invest in educational programs and projects aimed at both preventing sexual violence and providing comprehensive support to its victims. Raising public awareness and empowering individuals are essential pillars for addressing and reducing sexual violence associated with alcohol abuse. It is also important to note that such violence has impacts that go beyond physical harm, damaging the psychological and social well-being of victims, a factor that reinforces the need for a prepared health system and coordinated and effective public policies.

This study has limitations related to the use of data from SINAN, such as underreporting and gaps in records. These problems compromise the completeness of information and the effectiveness of surveillance and prevention actions. In order to mitigate this problem, it is important to highlight the importance of continuous investment in the training of health professionals, with a focus on improving the quality of notifications and ensuring more assertive care for victims. It is important to emphasize the need for this proposal for continuing education in health, as it must be accompanied by the development of interventions aimed at reducing alcohol abuse.

The results highlight the urgency of implementing integrated public policies to raise awareness about the harmful effects of excessive alcohol consumption and to support victims of sexual violence resulting from this use. Given the limitations of this study, further investigation of cases is needed to understand the other mechanisms involved and to develop appropriate intervention strategies. Finally, it is necessary to encourage professionals to, as part of good health practices, accurately complete notification forms to promote the quality of the recorded information and contribute to the effectiveness of the public health actions to be developed.

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AUTHORS' CONTRIBUTIONS

Laura Beatriz Andrade Medeiros contributed to the bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, preparation of tables, conclusions, and review. **João Gabriel Machado Silva** contributed to the literature review, writing of the abstract, interpretation and description of results, and review. **Bruna Betiatti Benatatti Eller** contributed to the literature review, writing of the abstract, methodology, interpretation of results, conclusions, statistics, and review. **Eduarda Henriques Moioli** contributed to the writing of the abstract, content review, and translation of the text. **Ana Paula Alves Goulart** contributed to content review and translation of the text. **Maria Cristina de Moura Ferreira** contributed to the project management, bibliographic research, and content review. **Carla Denari Giuliani** contributed to the project management, bibliographic research, and content review. **Mônica Rodrigues da Silva** contributed to project management, bibliographic research, and content review. **Marcelle Aparecida de Barros Junqueira** contributed to the project management, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, and review.

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Original Article

Ventilator-associated pneumonia in adult patients: development and validity of a bundle and a checklist

Pneumonia associada à ventilação mecânica no paciente adulto: elaboração e validação da aparência de bundle e checklist

Neumonía asociada a la ventilación mecánica en pacientes adultos: elaboración y validación de la apariencia del paquete y de la lista de verificación

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RESUMO

Justificativa e Objetivos: a pneumonia associada à ventilação mecânica é uma infecção pulmonar que ocorre 48 horas após o início da intubação orotraqueal e ventilação mecânica invasiva, sendo uma infecção comum em terapia intensiva. Na busca por maior qualidade assistencial e segurança do paciente, o objetivo do estudo foi elaborar e validar a aparência do *bundle* e do *checklist* para prevenção da pneumonia associada à ventilação mecânica com profissionais de Unidade de Terapia Intensiva Adulto. **Métodos:** estudo metodológico e quantitativo, que ocorreu no período de janeiro de 2023 a novembro de 2024, e foi organizado em duas etapas: (1) construção do *bundle* e do *checklist*; (2) validação dos instrumentos. A população foi composta por 15 profissionais na temática, que consentiram eletronicamente em participar da pesquisa. O instrumento para coleta dos dados foi hospedado no *Google Forms*®, com apoio da rede social *WhatsApp*® e e-mail. Realizou-se a avaliação dos critérios de clareza e relevância, aplicando-se o *Suitability Assessment of Materials* para mensuração a aparência do *bundle* e *checklist*. Considerou-se válido cada item que obteve concordância superior a 80%. **Resultados:** obtiveram-se 15 respostas: 57,1% do sexo feminino; com média de faixa etária de 32 anos; majoritariamente profissionais enfermeiros (42,9%). Nenhum dos critérios de validação demandou alterações, devido à concordância superior a 0,80 em todos os itens. Ambos os instrumentos apresentam consistência interna de 0,949, considerada excelente. **Conclusão:** o *bundle* e o *checklist* foram avaliados como instrumentos adequados, claros e relevantes, e sua incorporação na prática pode contribuir significativa para prevenção da pneumonia associada à ventilação mecânica.

Descritores: *Pneumonia Associada à Ventilação Mecânica. Cuidados Críticos. Lista de Checagem. Pacotes de Assistência ao Paciente. Estudo de Validação.*

ABSTRACT

Background and Objectives: ventilator-associated pneumonia is a lung infection that occurs 48 hours after the start of orotracheal intubation and invasive mechanical ventilation, and is a common infection in intensive care. In the search for better quality of care and patient safety, this study aimed to develop and validate the appearance of a bundle and a checklist for ventilator-associated pneumonia prevention with professionals from the Adult Intensive Care Unit. **Methods:** this was a methodological and quantitative study, which took place from January 2023 to November 2024, and was organized into two stages: (1) bundle and checklist construction; (2) instrument validity. The population consisted of 15 professionals in the field, who consented electronically to take part in the research. The instrument for data collection was hosted on Google Forms®, with support from the WhatsApp® social network and e-mail. Clarity and relevance criteria were assessed, applying the Suitability Assessment of Materials to measure bundle and checklist appearance. Each item that obtained agreement greater than 80% was considered valid. **Results:** fifteen responses were obtained: 57.1% were female; with a mean age of 32 years; and the majority were nurses (42.9%). None of the validity criteria required changes, due to agreement above 0.80 across all items. Both instruments have an internal consistency of 0.949, considered excellent. **Conclusion:** the bundle and checklist were assessed as adequate, clear, and relevant instruments, and their incorporation into practice can significantly contribute to ventilator-associated pneumonia prevention.

Keywords: *Pneumonia, Ventilator-Associated. Critical Care. Checklist. Patient Care Bundles. Validation Study.*

RESUMEN

Justificación y Objetivos: la neumonía asociada a la ventilación mecánica es una infección pulmonar que se produce 48 horas después del inicio de la intubación orotraqueal y la ventilación mecánica invasiva, y es una infección frecuente en cuidados intensivos. En la búsqueda de una mejor calidad asistencial y seguridad del paciente, el objetivo del estudio fue elaborar y validar la apariencia del paquete y la lista de verificación para la prevención de la neumonía asociada a la ventilación mecánica con profesionales de la Unidad de Cuidados Intensivos de Adultos. **Método:** un estudio metodológico y cuantitativo, que se desarrolló de enero de 2023 a noviembre de 2024, y se organizó en dos etapas: (1) construcción del paquete y lista de verificación; (2) validación de los instrumentos. La población estuvo formada por 15 profesionales con la experiencia en la temática, que dieron su consentimiento electrónico para participar en la investigación. El instrumento de recogida de datos se alojó en *Google Forms*®, con el apoyo de la red social *WhatsApp*® y del correo electrónico. Los criterios de claridad y relevancia se evaluaron mediante el instrumento *Suitability Assessment of Materials* para medir la apariencia del paquete y la lista de verificación. Cada elemento con un nivel de concordancia superior al 80% se consideró válido. **Resultados:** se obtuvieron 15 respuestas: el 57,1 % fueron mujeres, con una edad media de 32 años, y la mayoría eran profesionales de enfermería (42,9 %). Ninguno de los criterios de validación requirió cambios, debido a una concordancia superior a 0,80 en todos los ítems. Ambos instrumentos presentan una consistencia interna de 0,949, considerada excelente. **Conclusión:** el paquete de medidas y la lista de verificación se evaluaron como instrumentos adecuados, claros y pertinentes, y su incorporación en la práctica puede contribuir significativamente a la prevención de la neumonía asociada a la ventilación mecánica.

Palabras Clave: *Neumonía Asociada al Ventilador. Cuidados Críticos. Lista de Verificación. Paquetes de Atención al Paciente. Estudio de Validación.*

INTRODUCTION

Pneumonia is an acute respiratory infection caused by germs, toxic products, or allergic reactions, affecting the pulmonary alveoli, bronchi, and interstitium.[1] It affects about one in every 100 patients overall and up to one in ten patients on invasive mechanical ventilation (IMV), with *Streptococcus pneumoniae* being the main causative agent, responsible for about 60% of cases of hospital-acquired pneumonia and one of the leading causes of morbidity and mortality in nosocomial infections.[2]

Ventilator-associated pneumonia (VAP) is a lung infection that occurs more than 48 hours after the start of orotracheal intubation and IMV, and is one of the most common infections in intensive care units (ICUs), with an incidence of 6 to 52%.[3-5] The mortality rate from VAP is 70% in high-risk patients globally.[4] The incidence ranges from two to 16 episodes per 1,000 days of ventilation in the United States.[4-5] The estimated risk of VAP is 1.5% per day, decreasing to less than 0.5% per day after the 14th day of mechanical ventilation.[5] In Brazil, the incidence is 23.2 to 36.01%.[6] Mortality from VAP varies between 20 and 60%, resulting in hospital stays longer than 12 days and increased healthcare costs.[6]

The main factor for the development of pneumonia in the ICU is mechanical ventilation.[2-3] Endotracheal intubation, nasogastric tube feeding, malnutrition, and inadequate saliva flow, which lead to oropharyngeal colonization in patients, are other predisposing factors.[7] VAP increases oxygen demand and pulmonary secretion production, which can cause alveolar collapse and impair gas exchange.[7] Other consequences of VAP include prolonging the length of hospitalization and increasing the length of stay in the ICU, with a consequent increase in treatment costs, greater use of health resources, and continued IMV, thus causing high morbidity and mortality rates.[2]

The multidisciplinary ICU team is expected to play an important role in preventing VAP by using management tools such as care bundles and checklists.[8] Awareness of the use of these tools can be effective in preventing VAP, potentially reducing its incidence significantly. To this end, it is up to ICU professionals to seek reliable scientific evidence for translation and implementation in practice.

In 2022, The Society for Healthcare Epidemiology of America (SHEA) published a guideline containing best practices for the prevention of VAP based on the opinion of international experts.[2] Based on this evidence, it is possible to translate this knowledge into the construction and evaluation of bundles and checklists for care.

Bundles and checklists are characterized as care management tools that present interventions with specific care that, when grouped together, improve practices with a view to patient safety. It should be noted that the success of these tools is related to the execution of all proposed items, without fragmentation of any stage.

The production of these management tools is a systematic strategy to improve care processes in complex care environments, seeking satisfactory results for the patient. Given the above, this study aimed to develop and validate the appearance of the bundle and checklist for the prevention of VAP with adult ICU professionals.

METHODS

Methodological and quantitative research. This type of research allows for the verification of methods for obtaining, organizing, and analyzing data, with the aim of developing, validating, and evaluating instruments for care practice.[10]

The research took place from January 2023 to November 2024 and was organized in two stages: (1) development of the bundle and checklist; (2) validation of the appearance with adult ICU professionals.

Development of the bundle and checklist

The products were developed based on the recommendations published by SHEA, containing clinical care for the prevention of VAP.[2] Brazilian resolutions from the Medical, Nursing, Physiotherapy, and Dentistry Councils were also consulted to identify the ethical and legal prerogatives of the practice of each area.

The bundle was structured with the following items: objectives; scope; acronyms; glossary; knowledge base; development; methodology; management indicator; and references. SHEA is an international professional society that improves public health by establishing infection prevention measures and supporting antibiotic stewardship among healthcare professionals. In the 2022 recommendations, the quality of the evidence was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation, characterizing the bundle for the prevention of VAP in the categories high, moderate, and low (Table 1).

Table 1. Categories of evidence quality from Grades of Recommendation, Assessment, Development, and Evaluation. Curitiba, Paraná, Brazil, 2025.

CATEGORY	DEFINITION
HIGH	Highly confident that it is true, the effect is close to the estimated size and direction of the effect. Evidence is classified as "HIGH" quality when there is a wide range of studies without major limitations, there is little variation between studies, and the summary estimate has a narrow confidence interval.
MODERATE	The actual effect is likely to be close to the estimated size and direction of the effect, but there is a possibility that it could be substantially different. Evidence is classified as "MODERATE" quality when there are few studies and some have limitations, but no major flaws. In addition, there is some variation between studies, or the confidence interval of the summary estimate is wide.
LOW	The true effect may be substantially different from the estimated size and direction of the effect. Evidence is classified as "LOW" quality when supporting studies have major flaws, there is important variation between studies, the confidence interval of the summary estimate is very wide, or there are no rigorous studies.

The guideline verified the following items: avoid intubation and prevent reintubation; reduce sedation; maintain and improve physical conditioning; raise the head of the bed between 30° and 45°; perform oral care without the use of chlorhexidine; provide enteral nutrition in comparison with parenteral nutrition early on; change the ventilator circuit only when it is visibly dirty or damaged.

As for the checklist, three blocks were created, with the first containing identification data and clinical history, the second containing a description of essential practices for the prevention of VAP, containing nine items, and the third containing care referred to as additional approaches, with three items. A procedural representation was chosen to demonstrate simplicity and objectivity, helping to reduce care failures, organize processes with a focus on results, and promote higher quality care and safety for patients, family members, and professionals.

Appearance validation

The validation process, a quantitative stage, took place online in one round. The population consisted of 45 professionals specializing in the subject, selected intentionally and not probabilistically. The selection was made by searching the Lattes Platform for *résumés* from the National Council for Scientific and Technological Development.[11] Invitations were sent via WhatsApp® groups linked to intensive care professional associations, through consultation with the LinkedIn platform (social media focused on business and employment), and by referral from specialists (snowball technique).

The professionals were classified based on their technical expertise (target audience with practical experience in the context for which the bundle and checklist are intended).[11] For selection, resumes were analyzed considering the following criteria in order of priority: having a degree in nursing, medicine, physical therapy, or dentistry; working in direct care for adult patients in intensive care, preferably for more than one year; having participated in courses/training on the study topic. The choice to invite professionals from the above-mentioned areas is justified by their involvement in the production of the guideline published by SHEA.[2]

The validation sample consisted of 15 professionals who met the pre-established criteria. We sought to establish a committee of between five and 27 professionals.[11] Participants were given a period of ten days to validate the documents. When there was a delay in response, reminders were sent to identify the need for assistance in completing the form, clarifying doubts, and/or extending the deadline. Professionals who did not return the bundle and checklist validation instrument by the end of the ten-day extension were excluded.

Considering the 15 selected participants, an invitation to participate was sent electronically (via email or WhatsApp®), containing a presentation of the research, its objectives, and a link to access the Free and Informed Consent Form on Google Forms®. If accepted, the evaluator was directed to the document validation stage, with instructions for the validation process.

The data collection instrument, hosted on Google Forms®, was organized into three stages: 1) characterization of the evaluators; 2) analysis of the relevance of the bundle and checklist content in terms of clarity and relevance; 3) assessment of the appearance of the bundle and checklist based on the items in the Suitability Assessment of Materials (SAM), which are divided into the following domains: content; language; illustrations; layout; motivation; and usability.10 For the evaluation of each item, the options "inappropriate," "somewhat inappropriate," "appropriate," or "totally appropriate" were considered.[12] At the end of the survey, space was provided for "comments or suggestions for improvements to the bundle and checklist." The time to complete the forms varied between 25 and 30 minutes.

Subsequently, to complete the validation, professionals were asked to answer an open question: 1) Comments, suggestions, rewriting of any of the items and/or domains of the bundle and checklist?

The data were analyzed using descriptive statistics (absolute and relative frequencies, minimum, maximum, mean, median, and standard deviation). To validate the content and appearance of the bundle and checklist, the scores assigned to each item in the participants' evaluations were verified, considering the psychometric criteria and SAM criteria.[10,12]

The clarity and relevance of the items were calculated using the Content Validation Coefficient (CVC).[13] The CVC was calculated for each criterion (clarity and relevance/pertinence) and for each domain of the SAM, as well as the total CVC of the bundle and checklist. Items with more than 80% agreement among professionals (evaluated as adequate) and a CVC > 0.80 were considered valid.

Ethical aspects were respected, and the study was approved by the Research Ethics Committee on April 6,

2023, as stated in Opinion No. 5,988,955 and Certificate of Ethical Presentation and Appraisal No. 67399323.7.0000.5668.

The study was conducted in accordance with the Guidelines for Reporting Reliability and Agreement Studies.

RESULTS

Fifteen professionals participated in the appearance validation, predominantly nurses (47%). Regarding gender, 53.3% were female. Their ages ranged from 21 to 60 years. Regarding professional practice, 80% are involved in direct patient care, with 53% coming from public institutions. Regarding qualifications, 80% have specialization (Table 2).

Table 2. Characterization of the sample of evaluators of the bundle and checklist for the prevention of ventilator-associated pneumonia. Curitiba, Paraná, Brazil, 2025.

Variables	N (%)
Age (years) – mean ± SD	32.5 ± 12.7
Gender	
Male	7 (46.7)
Female	8 (53.3)
Profession	
Physician	4 (28.0)
Physical Therapist	3 (20.0)
Nurse	7 (47.0)
Dentist	1 (5.0)
Professional performance	
Assistance	12 (80.0)
Management	3 (20.0)
Institution that operates	
Public	8 (53.0)
Private	7 (47.0)
Length of practice (years) – median (P25 – P75)	2 (1 – 10)
Length of training (years) – median (P25 – P75)	4 (1 – 18)
Highest degree	
Specialization	12 (80.0)
Residency	3 (20.0)

Abbreviation: SD – standard deviation.

The results correspond to the responses related to the items in the bundle and checklist regarding their clarity and relevance, as perceived by the participants (Table 3). The CVC analysis showed a high degree of agreement among professionals, exceeding 80%, which allowed both instruments to be considered valid.

Table 3. Validation with professionals regarding the clarity and relevance of the bundle and checklist. Curitiba, Paraná, Brazil, 2025.

Criteria evaluated	Bundle CVC	Checklist CVC
Clarity	0.93	0.93
Relevance	0.89	0.95
Average	0.91	0.94
Cronbach's alpha	0.950	0.896

Abbreviation: CVC - Content Validation Coefficient.

The validation of the bundle and checklist appearance by professionals considered the instrument suitable for use in daily care. Validation was mediated by SAM, considering the analysis of content, language, layout, motivation, and usability. The items were evaluated with a CVC greater than 0.80, demonstrating that the products are clear and relevant tools for implementation in the clinical practice of adult ICU professionals (Table 4). Cronbach's alpha was evaluated at 0.949, indicating almost perfect reliability.

Table 4. Validation of the bundle's appearance and checklist with the target audience based on the Suitability Assessment of Materials. Curitiba, Paraná, Brazil, 2025.

Items evaluated	Agreement (%)			CVC
Content	**I**	**A**	**TA**	
1. Meets the proposed objectives	0 (0.0)	2 (13.0)	13 (87.0)	0.96
2. The content is divided coherently	2 (7.0)	3 (20.0)	11 (73.0)	0.91
3. Meets the needs of the target audience	0 (0.0)	3 (20.0)	12 (80.0)	0.95
4. There is logic in the sequence of information	4 (27.0)	11 (73.0)	0 (0.0)	0.93
5. It is relevant to inform the target audience	0 (0.0)	5 (33.0)	10 (77.0)	0.91
6. It is scientifically accurate	0 (0.0)	5 (33.0)	10 (77.0)	0.91
Language				
7. The writing style is appropriate for healthcare professionals.	0 (0.0)	5 (33.0)	10 (77.0)	0.91
8. The sentences are engaging and not tiresome.	1 (7.0)	6 (40.0)	8 (53.0)	0.86
9. The text is clear and objective.	0 (0.0)	5 (33.0)	10 (77.0)	0.91

continue

Items evaluated	Agreement (%)			CVC
Layout	**I**	**A**	**TA**	
10. The font size and typeface make it easy to read	1 (6.0)	7 (47.0)	7 (47.0)	0.85
11. The colors used in the checklist make it easy to read	1 (6.0)	4 (27.0)	10 (67.0)	0.90
12. The items are arranged in an organized manner	0 (0.0)	4 (27.0)	11 (73.0)	0.93
13. The size of the checklist is consistent	0 (0.0)	5 (33.0)	10 (77.0)	0.91
14. The visual composition is attractive and well organized	2 (13.0)	5 (33.0)	8 (53.0)	0.85
Motivation				
15. The reader is encouraged to continue reading	2 (13.0)	5 (33.0)	8 (53.0)	0.85
16. The checklist is enlightening	0 (0.0)	5 (33.0)	10 (77.0)	0.91
Usability				
17. The checklist items highlight key aspects that should be reinforced	0 (0.0)	4 (27.0)	11 (73.0)	0.93
18. It is suitable for use by healthcare professionals in the care of critically ill adult patients	0 (0.0)	5 (33.0)	10 (77.0)	0.91
Cronbach's alpha		**0.949**		

Abbreviation: CVC - Content Validation Coefficient.

After validating the bundle and checklist, the evaluators praised the instruments: clear and direct information; interesting and relevant; organized, facilitating the collection of information in an efficient and clear manner; tools that are easy to understand and useful for the ICU routine; complete, practical, and objective checklist. Based on the results, no structural adjustments to modify, include, or exclude content were made, so as not to compromise the instrument. Thus, the final version of the checklist is structured into four domains: Domain 1 - Patient identification; Domain 2 - Clinical identification; Domain 3 - Essential practices; and Domain 4 - Additional approaches (Figure 1).

PATIENT IDENTIFICATION									
Name:_____ Date of birth: __/__/____ Bed n°:_____									
CLINICAL IDENTIFICATION									
Date of admission to the ICU: __/__/____ Date and location of intubation: __/__/____ ( ) ICU ( ) PS ( ) OTHERS: _____ ( ) Reintubation: __/__/____ ( ) Extubation: ( ) Accidental ( ) Scheduled: __/__/____ ( ) Tracheostomy: __/__/____ ( ) TOT Exchange __/__/____									
Verification of the intervention: (Y) YES; (N) NO; (NA) NOT APPLICABLE.									
ESSENTIAL PRACTICES	**DATE OF THE WEEK/TIME**								
Oxygen therapy was administered via high-flow nasal cannula.**									
Oxygen was administered via non-invasive positive pressure ventilation.**									
It presents measures to minimize accidental extubation and reintubation.***									
Minimize daily sedation in patients without contraindications.***									
Exercise and early mobilization were performed.***									
The head of the bed should be kept elevated between 30° and 45°, unless medically contraindicated.*									
Brushing instructions are provided, but without chlorhexidine.**									
Early enteral nutrition provided.***									
The ventilator circuit was replaced due to visible dirt, a defect, or in accordance with institutional protocol.***									
ADDITIONAL APPROACHES									
If intubation is required, endotracheal tubes with subglottic secretion drainage are used.**									
Considered early tracheostomy (if lower extremity intubation < 10 days).**									
Post-pyloric feeding tube insertion is considered for patients intolerant to gastric feeding and at high risk of aspiration.**									
Quality of Evidence measured using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system: *High, **Moderate, ***Low									

Figure 1. Final version of the checklist for the prevention of ventilator-associated pneumonia. Curitiba, Paraná, Brazil, 2025.

DISCUSSION

The development and validation of the bundle and checklist for preventing VAP in adults represent a crucial step toward optimizing healthcare, as they provide a solid scientific basis for implementing evidence-based practices, promoting continuous improvement in healthcare processes and standardization of care.[15]

In the United States, the Centers for Disease Control and Prevention, located in Atlanta, conducted the Study on the Efficacy of Nosocomial Infection Control to analyze the effectiveness of healthcare-associated infection (HAI) control programs implemented in the country. The findings of this study indicated that HAI result in an average increase of four days in hospital stays, in addition to generating significant additional treatment costs.[16-17] Thus, the strategy of creating bundles has been adopted, aiming to systematize actions to prevent adverse events in practices associated with IMV in patients.[18]

Hospitalized patients, especially those undergoing IMV, are at increased risk for pneumonia. Estimates indicate a mortality rate of approximately 33% for patients with this infection.[19] Thus, the implementation of VAP prevention measures is essential to reduce the morbidity and mortality associated with this complication, and the lack of standardization in care practices has limited the effectiveness of these interventions.[20]

The SHEA recommendations can be classified into two main categories. The first encompasses essential practices that have a positive impact on clinical outcomes, such as reducing the duration of mechanical ventilation, length of hospital stay, and mortality. The second category covers additional approaches that

similarly have the potential to improve these outcomes, although they may be associated with additional risks.[20]

From this perspective, the development of a bundle and checklist based on up-to-date scientific evidence, capable of guiding professionals in the processes for preventing VAP, is a valuable tool for improving the quality of care and patient safety.[21] This approach allowed for the integration of the expertise of healthcare professionals and the knowledge of educators and researchers, resulting in a tool that shows great potential for improving the quality and safety of patient care in both educational and healthcare settings.

The evaluation of professionals allowed for the emergence of diverse opinions and approaches to VAP, minimizing the possibility that the topic would be based solely on the perception and interest of researchers. The instrument was validated by a multidisciplinary group, as it understands that the prevention of HAI is intrinsic to everyone.[22] However, nurses play a uniquely important role, with an indispensable role in all stages of care, from prevention to treatment and monitoring of infections. Their contribution is particularly notable in the training and education of teams, in the rigorous implementation of care protocols, and in the continuous supervision of surveillance practices, promoting quality of care and safety.

The checklist is an essential tool for ensuring that all stages of a given procedure are followed systematically. At the same time, it allows procedures to be performed in the required order, ensuring compliance with requirements and facilitating data collection for further analysis. Furthermore, it is an accessible and effective method for reducing risks arising from distractions or overconfidence, especially in standardized activities. To ensure the reliability of this instrument, making it safe, the validation process has become indispensable.[24]

This study used the patient's name, date of birth, and bed number as identifiers, considering that the patient identification protocol presented by the National Patient Safety Program recommends the use of at least two identifiers. The checklist begins with the correct identification of the patient, representing the first of the six International Patient Safety Goals. Correct identification is an extensive process, involving multiple professionals, which encompasses structural factors, work processes, professional practices, and the participation of the patient and their family members. When correctly implemented, it contributes to the prevention of errors related to care at different levels of healthcare.[25]

The second section of the study is dedicated to recommended practices for preventing intubation and reintubation. Scientific evidence supports the use of high-flow nasal oxygen or noninvasive positive pressure ventilation when safe and feasible. High-flow nasal oxygen has been shown to be effective in preventing intubation in patients with hypoxemic respiratory failure, in addition to reducing reintubation and nosocomial pneumonia in critically ill or postoperative patients, when compared to conventional oxygen. Noninvasive positive pressure ventilation has similar results and, when combined with high-flow nasal oxygen immediately after extubation, can further reduce the risk of reintubation in patients at high risk of failure.[2,6,22]

For the management of agitation in ventilated patients, a multimodal approach is recommended, avoiding the isolated use of benzodiazepines. Dexmedetomidine and propofol, in particular, have demonstrated superiority over benzodiazepines, reducing the duration of mechanical ventilation and length of stay in the ICU. Daily assessment of readiness for extubation in patients without contraindications is essential to minimize the duration of mechanical ventilation. Studies show that the use of specific protocols can accelerate extubation by up to one day, compared to the traditional approach.[2,6]

In addition to the preventive measures already discussed, promoting early mobilization emerges as a fundamental strategy to enhance the recovery of mechanically ventilated patients, reducing the length of stay in the ICU, indicating lower rates of VAP, and promoting an increase in the rate of functional recovery independently.[2,22]

Although studies indicate a positive association between raising the head of the bed and reducing the incidence of VAP, the scientific literature has not yet conclusively demonstrated a significant impact on the duration of mechanical ventilation or mortality. The scarcity of data limits understanding of the full scope of the benefits of this intervention. However, considering its simplicity, low cost, and potential benefit in preventing VAP, raising the head of the bed remains a recommended practice.[2]

The scientific literature shows a consistent association between daily oral hygiene and a reduction in the incidence of VAP. However, the use of chlorhexidine solutions as an adjunct to oral hygiene has not been shown to be effective in reducing the duration of mechanical ventilation or the length of stay in the ICU. Meta-analyses of randomized studies and observational studies point to a possible association between the use of chlorhexidine and higher mortality, although this relationship is uncertain and requires further investigation. Considering the lack of solid evidence on the benefits of routine chlorhexidine use and the possibility of adverse events, its use is not recommended as standard practice in the oral care of intubated patients.[2,6]

Research shows that early enteral nutrition in critically ill patients, compared to parenteral nutrition, is associated with a reduced risk of nosocomial

pneumonia. However, studies indicate that early parenteral nutrition, initiated within the first 48 hours of ICU admission, may be associated with increased mortality and risk of HAI when compared to late parenteral nutrition, initiated after the eighth day of admission.[6,8,22-23]

Thus, the guidelines recommend replacing the ventilator circuit only when it shows visible signs of dirt or damage. This practice, supported by high-quality evidence, aims to optimize resources and reduce costs without compromising patient safety. Routine replacement of the circuit at predetermined times has not shown any benefit in terms of preventing VAP or improving clinical outcomes.[2-8]

The third and final section is dedicated to discussing additional approaches to preventing VAP. The use of endotracheal tubes with subglottic secretion drainage is recommended to minimize the accumulation of secretions above the tracheostomy cuff in patients who may require intubation for more than 48-72 hours. This intervention is only feasible for children over 10 years of age, due to the smallest available tube (size 6.0).

Clinical research confirms that the use of these tubes reduced VAP rates by 44%, but there was no relationship with the duration of IMV or length of hospital stay. Although initial studies suggested a possible impact on mortality, this association was not confirmed in subsequent analyses. The indication for endotracheal tubes with subglottic drainage is particularly relevant for patients requiring prolonged IMV. In these cases, the use of these tubes may contribute to a reduction in the duration of ventilation. Frequent tube changes through extubation and reintubation are not recommended.[2,6,8]

Although the quality of evidence is considered moderate, several clinical studies have shown that early tracheostomy (less than ten days) is associated with lower rates of VAP, shorter ICU stays, and shorter IMV duration when compared to late tracheostomy. In addition, observational studies suggest a possible reduction in mortality rates in patients undergoing early tracheostomy.[2,8,22]

Considering the position of the post-pyloric feeding tube in patients at high risk of aspiration is a clinical practice with moderate scientific evidence. Meta-analyses show mixed results on whether post-pyloric feeding reduces the length of stay on the ventilator or in the hospital. Furthermore, post-pyloric feeding is seen as less physiological compared to gastric feeding. This type of enteral nutrition should be reserved for patients who are intolerant to gastric feeding and those at high risk of aspiration, according to the guidelines of the nutrition society.[2,6,8]

The response rate obtained from the evaluators was satisfactory. The analysis of the level of agreement indicated that both instruments, the bundle and the checklist, exceeded the recommended indices, demonstrating their effectiveness as tools for implementation in adult ICUs. These findings corroborate the relevance of using validated instruments to evaluate care practices in this context. Therefore, it should be noted that none of the evaluation criteria required changes, since all items evaluated obtained a concordance index greater than 0.80.

One limitation is the representativeness of the sample, which is limited by the geographical concentration of evaluators, who come exclusively from the state of Paraná. This characteristic restricts the generalization of the results to a broader context, covering the other four regions of the country. To overcome the limitations encountered, it is necessary to continue expanding the evaluation process, which takes place over time. As a future perspective, we suggest the development (construction, validation, and evaluation) of instruments for pediatric and neonatal contexts to complement the present study.

Based on the results of this research, it is believed that the bundle and checklist are potentially significant tools for incorporation into health services, with a view to reducing the incidence of VAP in adults, providing improvements in the quality of care and patient safety.

The results obtained in the study of the construction and evaluation of the VAP prevention bundle and checklist pointed to acceptable clarity and relevance for their incorporation and use in adult ICUs. The consensus of the professionals provided evidence for the reliability of the bundle and checklist.

It should be noted that this research contributes to the use of new care strategies, in order to translate scientific knowledge into clinical practice. This study presented an innovative instrument resulting from the adaptation of international recommendations.

The process of evaluating the content and appearance of the instruments points to their contribution to the prevention of VAP, contributing to patient safety and the continuous improvement of care processes.

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AUTHORS' CONTRIBUTIONS

Ana Carolina Pereira de Lima contributed to the literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Cléton Salbego** contributed to the literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Graciele Torezan** contributed to writing the abstract, methodology, interpretation of results, conclusions, review, and statistics. **Tierle Kosloski Ramos** contributed to the discussion, interpretation, and description of results, conclusions, review, and statistics. **Silvana Bastos Cogo** contributed to the discussion, interpretation, and description of results, conclusions, review, and statistics. **Jessika de Oliveira Cavalaro** contributed to the discussion, interpretation and description of results, conclusions, review, and statistics. **Robson Giovani Paes** contributed to the discussion, interpretation and description of results, conclusions, review, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Inovações para governança hospitalar no enfrentamento da resistência antimicrobiana: perspectivas de stakeholders

Innovaciones para la gobernanza hospitalaria para combatir la resistencia a los antimicrobianos: perspectivas de stakeholders

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ABSTRACT

Background and Objectives: Antimicrobial resistance has global health and policy implications and tackling it in hospitals requires a range of strategic governance interventions that integrate management and involve leaders in the day-to-day running of the hospital. The aim was to analyse the perspectives of local leaders and stakeholders on innovations in the governance of a teaching hospital in tackling antimicrobial resistance. **Methods:** This is a qualitative study using interviews with local leaders involved in mandatory and advisory hospital committees, conducted between September and November 2023. **Results:** 13 stakeholders from the institution were interviewed, the majority of whom were women (76.9%), all self-identified as white and in a stable union (61.5%). Innovations were grouped into: Decision making based on service evidence; Use of research in practice; Antimicrobial stewardship; Development of health care teams; and Patient-centred and timely care. **Conclusion:** The research has made an important contribution to local decision making and to the management of the hospital's response capacity. It also contributes to strengthening the policy agenda and global and local agreements. Future research could address the development of models for hospital governance, as well as the implementation and evaluation of interventions to reduce the challenges identified.

Keywords: *Governance. Antimicrobial Drug Resistance. Innovation. Hospitals Teaching.*

RESUMO

Justificativa e Objetivos: A resistência antimicrobiana tem implicações sanitárias e políticas em escala global e seu enfrentamento em âmbito hospitalar requer diversificadas ações estratégicas de governança que integram a gestão envolvendo as lideranças na interpelação com o cotidiano do hospital. Objetivou-se analisar as perspectivas das lideranças locais, *stakeholders* sobre inovações para a governança de um hospital de ensino no enfrentamento da resistência antimicrobiana. **Métodos:** Trata-se de uma pesquisa de abordagem qualitativa por entrevistas com lideranças locais atuantes junto às comissões hospitalares obrigatórias e assessórias que ocorreram entre setembro e novembro/2023. **Resultados:** Foram entrevistadas 13 stakeholders da instituição, a maioria eram mulheres (76,9%), todos com a cor da pele autorreferida branca e em união estável (61,5%). As inovações foram agrupadas em: tomada de decisão baseada por evidências do serviço; utilização de pesquisas na prática; gestão de antimicrobianos; desenvolvimento das equipes de saúde e cuidado centrado e oportuno aos pacientes. **Conclusão:** A pesquisa demonstrou importante contribuição para a tomada de decisão local e para orientar a capacidade de resposta do hospital. Contribui ainda com o fortalecimento da agenda política e dos acordos mundiais e locais. Pesquisas futuras podem abordar o desenvolvimento de modelos para a governança hospitalar, como também implementar e avaliar intervenções para a redução dos desafios expostos.

Descritores: *Governança Em Saúde. Resistência Microbiana A Medicamentos. Inovações. Hospitais De Ensino.*

RESUMEN

Justificación y Objetivos: La resistencia a los antimicrobianos tiene implicaciones sanitarias y políticas a escala mundial, y abordarla en los hospitales requiere diversas acciones estratégicas de gobernanza que integren la gestión e impliquen a los líderes en el día a día del hospital. El objetivo era analizar las perspectivas de los líderes locales y las partes interesadas sobre las innovaciones para la gobernanza de un hospital universitario en la lucha contra la resistencia a los antimicrobianos. **Método:** Se trata de un estudio cualitativo mediante entrevistas con líderes locales que trabajan en los comités hospitalarios obligatorios y consultivos, que tuvieron lugar entre septiembre y noviembre de 2023. **Resultados:** Se entrevistaron 13 actores de la institución, la mayoría mujeres (76,9%), todas autodeclararon que su color de piel era blanco y estaban en unión estable (61,5%). Las innovaciones se agruparon en: Toma de decisiones basada en la evidencia del servicio; Uso de la investigación en la práctica; Manejo de antimicrobianos; Desarrollo de equipos de salud y Atención oportuna y centrada en el paciente. **Conclusión:** La investigación contribuyó de manera importante a la toma de decisiones a nivel local y a orientar la capacidad de respuesta del hospital. También contribuye a reforzar la agenda política y los acuerdos globales y locales. Futuras investigaciones podrían abordar el desarrollo de modelos de gobernanza hospitalaria, así como la aplicación y evaluación de intervenciones para reducir los retos expuestos.

Palabras Clave: *Gobernanza. Resistencia Microbiana A Las Drogas. Innovaciones. Hospitales De Enseñanza.*

INTRODUCTION

The Pan American Health Organization (PAHO) and the World Health Organization (WHO) has defined antimicrobial resistance (AMR) as the ability of microorganisms (bacteria, fungi, viruses, and parasites) to alter themselves when exposed to antimicrobials (antibiotics, antifungals, antivirals, antimalarials, or anthelmintics), rendering them "ineffective".[1] Thus, it is a global health emergency established by the World Health Organization, due to its spread requiring a coordinated local and international response, which is increasingly important, a situation that was further exacerbated by the Covid-19 pandemic, given the high consumption of prescription and self-medication. In this way, AMR presents itself as a threat to global health, and its aggravation was observed in the context of the SARS-CoV-2 pandemic.[2]

However, antimicrobial resistance has health and political implications on a global scale. Furthermore, the challenges of infection control in healthcare services are compounded by the need for coordinated and multi-sectoral efforts involving clinical-biological, socioeconomic, and political perspectives. In this context, a quadripartite global alliance is gaining strength, comprised of: the World Health Organization, the World Organization for Animal Health, the Food and Agriculture Organization of the United Nations, and the United Nations Environment Programme. This articulation is based on the "One Health" approach, a socio-ecological approach to human, animal, plant, and environmental health, expressed through inter-institutional commitments that prioritize the issue of adverse drug reactions (ADRs). Therefore, sustainable solutions are sought through a political agenda, intersectoral and transdisciplinary actions in addressing AMR.[1]

There are gaps in the production of research that addresses the political agenda of AMR, its implementation, and how it has been carried out in a post-pandemic scenario within health services.[2,3,4] It is added that, according to a literature review conducted by Murray and colleagues based on the World Health Organization's global action plan, 2015, the gaps found relate to: improving laboratory infrastructure, improving patient management and data quality in local and global surveillance, reinforcing national plans; prevention and control of infections, especially in healthcare settings; education and improvement of communication, surveillance and research, and increased production and analysis of data to support strategies and policy decisions; optimization of antimicrobial use, strengthening antimicrobial stewardship programs; and investment in new medicines.[5,6]

Thus, in light of the pandemic's repercussions, it is necessary to better understand the complex relationships between hospital governance and the management of AMRs. When discussing AMR management in hospitals nationwide, it is necessary to contextualize them within the Unified Health System (SUS).[7] It is worth emphasizing that in Brazil, SUS teaching hospitals occupy a strategic position for innovations in AMR management. They are traditional loci of teaching-service integration, and as part of their mission, they develop the teaching-research binomial to achieve qualified training and care.[8,9]

Reducing the incidence of AMRs and improving infection control in hospitals requires diverse actions. Above all, the term hospital governance is understood here from a systemic point of view, which integrates the hospital's senior management or strategic management, the organization's leadership, and its control mechanisms. This apparatus is interrelated with the hospital's daily routine, personnel management, quality of care, financial management, patient services, among others. Added to this vision are aspects such as the operation of health networks and hospital networks, the organization of the health system itself, as well as its political and regulatory frameworks.[10]

In a recent scoping review, in 2024, on innovations in the management of antimicrobial resistance in teaching hospitals, it was evidenced that there are gaps in the production of the subject regarding studies developed in Brazil or Latin America. The main innovations identified there were activities usual to the fight against AMR, such as: reinforcement of precautions and cleaning and disinfection routines; professional training and education; forms and guides for prescription control; active audits and institutional epidemiological surveys and institutional committees and quality indicators.[11]

The question stems from how to improve this fight. In this sense, innovation in health services presents itself as a complex challenge, since it consists of obtaining performance superior to the usual. The forces that shape services to innovate and, consequently, to have superior performance must be considered. The actors influencing this change, local leaders or stakeholders, must be considered.[12] Above all, when working at the local level to manage RAM, it becomes crucial to involve hospital governance actions.

In this sense, the objective is to analyze the perspectives of local leaders and stakeholders on innovations for the governance of a teaching hospital in addressing RAM.

METHODS

This is a qualitative research study using interviews, to be reported in accordance with the guidelines of the Consolidated Criteria for Reporting Qualitative Research (COREQ) in its version valid for Portuguese

spoken in Brazil.[13] In this type of investigation, the aim is to capture particularities, with an interest in the conceptions, experiences, and interactions of the participants. An important aspect in this context is the position of the researcher himself. He is an integral part of the research, and his personal presence and immersion in the analyzed scenario influence the reflection and production of the results of qualitative research.[13,14]

As for the study setting, it is a public teaching hospital from SUS — general and high complexity, totaling 342 beds, with emergency room and heliport, oncology, obstetrics, Adult, Pediatric and Neonatal Intensive Care Units. In addition, the hospital complex has five annexes, with specialty and rehabilitation clinics, and around 173 consulting rooms. Furthermore, it has been part of the Brazilian Hospital Services Company network since 2013, and is a reference for the health macro-region of the Southern Triangle of Minas Gerais, composed of 27 municipalities, with an approximate population of 800,000 inhabitants.[15]

To answer the question about innovations to address RAM, which permeate the governance of a SUS teaching hospital, its stakeholders were interviewed. This is a purposive sample, in which the leaders active in the mandatory and advisory hospital committees were identified, these committees being active with the hospital's senior management in their deliberative processes, as well as being composed of representatives of the hospital's workforce.

The survey of the committees took the form of a scientific publication, based on a document analysis entitled "Public governance practices in addressing antimicrobial resistance in a teaching hospital of the Brazilian Unified Health System: a document analysis," which identified the governance mechanisms in addressing antimicrobial resistance in a teaching hospital.[4] Fourteen committees were identified (Table 1), and their coordinators or, in their absence during the data collection period, their deputy coordinators were included in the purposive sample. The exclusion criterion was the absence or vacation of both the coordinator and deputy coordinator at the time of the interview. The main guideline was that participants should speak from a perspective related to their work on the committee, not just their personal view. Those with at least one year of experience were included. All invitees agreed to this criterion.

Table 1. Commissions surveyed.

Commission/committee/core group	Acronym[1]
Strategic Master Plan	PDE
Hospital Infection Control Committee	CCIH
Pharmacy and Therapeutics Committee	CFT
Drug Standardization Committee	CPM
Internal Committee for Accident and Harassment Prevention	CIPA
Internal Quality Assessment Committee	AVAQUALI
Antimicrobial Use and Control Committee	CUCA
Patient Safety Center	NSP
Epidemiological Surveillance Center	NUVE
Health Technology Assessment Center	NAT's
Clinical Analysis Laboratory	UACAP
Teaching and Research Management	GEP
Nursing Education Service	SEE
Multiprofessional Care Protocols Committee	CPAM

Abbreviation: Strategic Master Plan (PDE), Hospital Infection Control Committee (CCIH), Pharmacy and Therapeutics Committee (CFT), Medication Standardization Committee (COM), Internal Committee for Accident and Harassment Prevention (CIPA), Internal Quality Assessment Committee (AVAQUALI), Committee for the Use and Control of Antimicrobials (CUCA), Patient Safety Center (NSP), Epidemiological Surveillance Center (NUVE), Health Technology Assessment Center (NAT's), Clinical Analysis Laboratory (UACAP), Teaching and Research Management (GEP), Nursing Education Service (SEE), Multiprofessional Care Protocols Committee (CPAM).

The interviews took place between September and November 2023, by prior appointment. To ensure privacy and minimize external interference, the meetings were held at the hospital itself, in a room reserved for this purpose. A single meeting was held, lasting approximately 60 minutes, and there were no refusals to participate. Prior to data collection, a pilot application was carried out among the researchers themselves in order to adjust approaches, application time, and standard concepts.

The approach began with the application of a structured questionnaire for the sociodemographic characterization of the participants. Next, the question was: "Regarding the management of RAM within our hospital and considering your role in the Hospital Committee/Commission/Device, what potential, innovations, and/or technological horizons are used and/or desired?" The interviews were conducted in an open manner, allowing for a more fluid conversation. When doubts arose about the concepts, these were clarified by the interviewer. The interviews were audio-recorded.

The interviewer, one of the authors of this study, underwent prior training and participated in an elective course in a professional master's degree program in public administration (PROFIAP), entitled "Special Topics in Public Organization Administration - Qualitative Research," with a workload of 60 hours. In addition, she is a public servant, has worked at the researched hospital as a biologist for 22 years, and has been part of the hospital's unit leadership team for 5 years. These aspects of the interviewer ultimately broaden her immersion and experience within the studied context. This, it is believed, enabled the participants' access and adherence to the study.

interview, since the interviews were leader-to-leader, a horizontal approach, minimizing judgments and constraints due to hierarchy.

For data analysis, the interviews were transcribed in full using the Transkriptor® application. At the end, a report was compiled with the full transcripts in a Word® document. Participants were coded according to their representation on hospital committees. In-depth readings of the report were carried out jointly and by a pair of researchers from this study, in a meeting for scrutiny and consensus, in November 2023. The pair produced a single textual record that portrayed the understanding of the stakeholders as a whole, through the context they narrated, always in accordance with the content analysis structure proposed by Minayo.[14] In this way, the aim was to identify, in addition to the semantic structures, the interactions that these presented with the context of the sociological structures of message production.[14] The description of the narratives was presented in a table. The sociodemographic characteristics of the interviewees were analyzed using statistics. descriptive.

Regarding ethical aspects, this study is part of a larger research project entitled "Convergent care research for the implementation of evidence-based practice among the teams of a public teaching hospital," approved on June 9, 2017, CAAE number: 64910317.6.0000.5154 and substantiated opinion number 2.110.319, from the *Universidade Federal do Triângulo Mineiro*, in accordance with the resolution of the National Health Council 466/2012. The research also followed resolutions 510/2016, of the National Health Council, and 580/2018. Data were collected after understanding and signing the Informed Consent Form by the participants. Fourteen potential respondents representing stakeholders from the committees were identified.

RESULTS

Thirteen stakeholders from the institution were interviewed, one of whom represented two committees: NAT and Multiprofessional Protocol. The majority were women (76.9%), all with self-reported white skin color and in stable relationships (61.5%). They work as nurses (38.5%), pharmacists (30.8%), doctors (15.4%), physiotherapists and law graduates (7.7%, both). 84.6% have more than 20 years of experience in the field, with the highest degree distributed among doctorates (38.5%), master's degrees and specializations (30.8%, both).

The responses given by the interviewees were not limited to expressions of agreement with the current situation. Furthermore, there were not only expressions of apparent cordiality or agreement out of fear of potential retaliation. This was understood as something positive, since the mediation of the interviews aimed to achieve this result. It is believed that greater horizontality was achieved in the chosen method due to the interviewer's characteristics and immersion in the scenario, as she was also a stakeholder in the hospital institution. The perspectives indicated by the interviewees regarding the potential for innovations and/or technological horizons of the public teaching hospital in addressing RAM were outlined in five areas as described (Table 2).

Table 2. Stakeholder Perspectives.

Innovations	Perspectives	Stakeholders
Evidence-Based Decision Making in the Service	• It must be an action foreseen in the Strategic Master Plan or other institutional planning of the hospital; • Develop an internal contract with the hospital's care units in which actions to combat antimicrobial resistance are agreed upon; • Have a panel on hospital quality indicators that are sensitive to the topic of antimicrobial resistance, resistance/sensitivity profile of germs to antimicrobials.	PDE, AVAQUALI, CCIRAS, NUVE
Using Research in Practice	• Promote institutional research on the topic within the hospital itself; • Have summarized and easily accessible reports, such as on a website, about research already conducted at the hospital on the topic; • Support the development of new classes of antibiotics and drugs; • Establish partnerships with Postgraduate Programs at the affiliated University.	CFT, GEP, CUCA, NAT's, CCIRAS
Antimicrobial Stewardship	• Strengthen hospital practice in accordance with antimicrobial stewardship as an antibiotic management program; • Promote drug-therapy reconciliation for antibiotic therapy; • Have applications that produce timely and systematic reports on the use of antimicrobials in the hospital; • Have control over the release of antimicrobials through an auditable application.	CFT, CUCA, NUVE, CCIRAS
Development of healthcare teams	• · Provision of training in different modalities – including in a virtual environment, as well as continuing education for hospital health teams; • Development of campaigns to raise awareness throughout the hospital community, such as those on patient safety, with an emphasis on hand hygiene and zero adornment; • Supervision with health teams on the subject, holding meetings to discuss the reality of each unit and adjust the course of action; • Maintaining updated Precaution Protocols, Infection Control Protocols, and other related institutional routines in accordance with scientific evidence and ANVISA recommendations.	NSP, CFT, CPM, CIPA, AVAQUALI, LABORATÓRIO, SEE

continue

Innovations	Perspectives	Stakeholders
Patient-Centered and Timely Care	• Strengthen multidisciplinary-oriented discharge of patients; • Strengthen networking, with shared responsibility of hospitals for the health of communities in their territories; • Implement alert systems for ADR cases during hospitalization; • Implement diagnostic improvements for ADRs using methods such as molecular biology.	CPM, CUCA, NUVE, CCIRAS, LABORATÓRIO

Abbreviation: Strategic Master Plan (PDE), Hospital Infection Control Committee (CCIH), Pharmacy and Therapeutics Committee (CFT), Medication Standardization Committee (COM), Internal Committee for Accident and Harassment Prevention (CIPA), Internal Quality Assessment Committee (AVAQUALI), Committee for the Use and Control of Antimicrobials (CUCA), Patient Safety Center (NSP), Epidemiological Surveillance Center (NUVE), Health Technology Assessment Center (NAT's), Clinical Analysis Laboratory (UACAP), Teaching and Research Management (GEP), Nursing Education Service (SEE), Multiprofessional Care Protocols Committee (CPAM).

DISCUSSION

It is relevant, in the view of leaders, that efforts be made to advance technology, such as more efficient tools for such control. Research applied to clinical practice is a major factor in improving the situation, aligned with real local needs, promoting innovation in the face of the challenges experienced.

Reducing the incidence of AMRs and improving infection control in hospitals requires diverse coordinated actions, including intersectoral strategies and government leadership.[4] Above all, innovation is crucial to tackling AMRs. The need to reconcile innovation, improvements, quality of care, and patient safety in the management of AMRs is emphasized.[16,17,18]

According to a study by Freitas and colleagues (2024), improving decision-making skills is directly related to better patient outcomes and a reduction in clinical errors. The implementation of evidence-based practices and advanced technologies results in improvements in diagnostic accuracy and care efficiency.[19]

The innovative perspectives pointed out reflect the focus on improvement in the face of local needs. Evidence-based decision-making in the service indicates innovations ranging from action planning to technologies that provide a timely view of infection indicator monitoring, demonstrating that these actions optimize financial and, especially, human resources, contributing primarily to the prevention of increased infections.

The implication for practice suggests the need to create training programs that promote knowledge about evidence-based practice and its translation process to clinical contexts, as well as organizational projects that support formal leaders in this process.[20]

The use of research in practice demonstrates the importance of teaching hospitals as research settings. They are traditional loci of teaching-service integration that have as part of their mission the development of the teaching-research binomial to achieve qualified academic training and care.[9] Service-teaching partnerships provide comprehensiveness in clinical discussions with updated and contextualized scientific references according to official norms and guidelines.

Necessary strategies are pointed out, such as evidence-based educational programs. Cohesive collaboration between professionals and managers is necessary, including in the development of protocols, as it reduces risks to patients' health and enhances the institution's credibility.[21]

Academia should prioritize communication skills in all its forms, as this is a fundamental strategy for the integration process between teaching and health services, just as the SUS (Brazilian Unified Health System) as a school should integrate with teaching, stimulating the commitment to the training of health professionals. The qualification and sustainability of the health system, in times of so many challenges, is a task for all of us.[22]

Regarding antimicrobial stewardship, this is the main strategy used to address AMR (Antimicrobial Resistance) in health services, known worldwide as stewardship. In Brazil, Collegiate Board Resolution RDC No. 7 of 02/24/2010, article 45, is the legislation that regulates the rational and appropriate use of antimicrobials.[23] Information technology appears as a technological horizon for better management of these.

In this approach, it is recommended that hospitals have specific forms and guides for controlling antibiotic prescriptions. In order to establish in these guidelines a universal checklist for the hospital setting regarding antibiotic prescription therapy and timely detection for infection control, including the management of AMRs. In this way, it is possible to establish the level of compliance regarding the use of antibiotics and the limits established by control and audit programs.[24,25]

With a patient-centered focus, all the actions mentioned reflect quality of care. The World Health Organization (WHO) in its report points globally to the focus on patient-centered care in terms of quality of health, ensuring health care, safety, timely care, effectiveness, efficiency, among others, guaranteeing rights and needs in a balanced way.[6]

However, the engagement of stakeholders - understood here as active leaders within hospital committees, their mobilization towards participation in the interviews of this study, promoted among them a reflection-action on the topic addressed. Influencing greater proactivity from these leaders, thereby strengthening and expanding the hospital's response capacity in addressing AMRs. Furthermore, given the research method adopted, the immersion that the interviewer presented in the scenario enabled the respondents' engagement and facilitated the unveiling of reality.

Regarding the limitations of the research, these were those expected by the very nature of the method adopted, especially those associated with the interpretation of the findings, affected by the subjectivity of the researchers in translating reality, since the results depend on the understanding of the research participants.

However, the entire intentional sample was reached. Thus, this research makes an important contribution to local decision-making and to guiding the response capacity of the analyzed hospital in its governance to address AMR. Furthermore, even though the responses were not validated by uninvolved peers, the dual position of the interviewer (researcher and field participant) did not seem to have compromised the study. With this, this research contributes to strengthening the political agenda and global and local agreements in the face of this growing global health threat. Future research can address the development of models for hospital governance, as well as implement and evaluate interventions to reduce the challenges presented here.

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AUTHORS' CONTRIBUTIONS

Tatiana da Silva Campos contributed to the bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables and references. **Fernanda Carolina Camargo** contributed to the bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusion and final review. **Alessandra Cabral Nogueira Lima** contributed to the research with methodology, interpretation and description of results. **Regiane Máximo Siqueira** contributed to the research with methodology, interpretation and description of results.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Original Article

Changes in tuberculosis control in the state of Bahia following the onset of Covid-19

Mudanças no controle da tuberculose no estado da Bahia após o início da Covid-19
Cambios en el control de la tuberculosis en el estado de Bahía tras la aparición de la Covid-19

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ABSTRACT

Background and Objectives: The Covid-19 pandemic reversed years of progress in tuberculosis control worldwide, and for the first time in over a decade, tuberculosis-related deaths increased. This study aimed to compare the epidemiological, clinical, and laboratory variables of pulmonary tuberculosis before and after the onset of Covid-19 in two territories in southern Bahia, Brazil. **Methods:** This ecological study utilized data from the Notifiable Diseases Information System (Sinan) and the Hospital Information System of the Unified Health System (SIH/SUS). The data included new pulmonary tuberculosis cases reported between 2017 and 2022, which were compared across the pre-pandemic period (2017–2019) and the post-pandemic onset period (2020–2022) in the *Costa do Descobrimento* and *Extremo Sul* territories of Bahia. **Results:** Between January 2017 and December 2022, 1,682 new pulmonary tuberculosis cases were reported, with an annual mean incidence rate of 33.5 cases per 100,000 population, and a mean mortality rate of 1.1 deaths per 100,000 population. Following the onset of Covid-19, a 3.3% increase in incidence and a 20.5% increase in mortality were observed, along with a 5.7% decrease in cure rates and a 38.6% reduction in hospital case fatality rates. Notifications of tuberculosis-HIV/Aids co-infection and cases among individuals with more than eight years of schooling increased during the pandemic. **Conclusion:** Diagnostic and treatment gaps caused by Covid-19 may have contributed to the increased incidence and mortality of tuberculosis in southern Bahia.

Keywords: *Pulmonary Tuberculosis. Epidemiological Monitoring. Communicable Disease Control. Ecological Studies.*

RESUMO

Justificativa e Objetivos: A pandemia de Covid-19 reverteu anos de progresso no controle da tuberculose no mundo e, pela primeira vez em mais de uma década, as mortes relacionadas com a tuberculose aumentaram. Este estudo teve como objetivo comparar as variáveis epidemiológicas, clínicas e laboratoriais da tuberculose pulmonar antes e após o início da Covid-19 em dois territórios do sul da Bahia, Brasil. **Métodos:** Estudo ecológico utilizando dados do Sistema de Informação de Agravos de Notificação (Sinan) e do Sistema de Informação Hospitalar do Sistema Único de Saúde (SIH/SUS). Os dados incluíram casos novos de tuberculose pulmonar notificados entre 2017-2022, que foram comparados entre o período pré-pandemia (2017–2019) e o pós-pandemia (2020–2022) nos territórios da Costa do Descobrimento e Extremo Sul da Bahia. **Resultados:** Entre janeiro de 2017 e dezembro de 2022 foram notificados 1.682 casos novos de tuberculose pulmonar, com taxa de incidência média anual de 33,5 casos por 100 mil habitantes e taxa de mortalidade média de 1,1 óbitos por 100 mil habitantes. Após o início da Covid-19 observou-se aumento de 3,3% na incidência e de 20,5% na mortalidade, juntamente com redução de 5,7% na taxa de cura e de 38,6% na taxa de letalidade hospitalar. As notificações de coinfecção tuberculose-HIV/Aids e de casos entre indivíduos com mais de oito anos de escolaridade aumentaram durante a pandemia. **Conclusão:** As lacunas de diagnóstico e tratamento causadas pela Covid-19 podem ter contribuído para o aumento da incidência e mortalidade por tuberculose no sul da Bahia.

Descritores: *Tuberculose Pulmonar. Monitoramento Epidemiológico. Controle de Doenças Transmissíveis. Estudos Ecológicos.*

RESUMEN

Justificación y Objetivos: La Covid-19 revirtió años de progreso en el control de la tuberculosis en el mundo y, por primera vez en más de una década, aumentaron las muertes relacionadas con la tuberculosis. Este estudio tuvo como objetivo comparar las variables epidemiológicas, clínicas y de laboratorio de la tuberculosis pulmonar antes y después de la aparición de la Covid-19 en dos territorios de Bahía, Brasil. **Métodos:** Estudio ecológico utilizando datos del Sistema de Información de Enfermedades de Declaración Obligatoria (Sinan) y del Sistema de Información Hospitalaria del Sistema Único de Salud (SIH/SUS). Los datos incluyeron nuevos casos de tuberculosis pulmonar notificados entre 2017-2022, comparados entre el período prepandemia (2017-2019) y el período pospandemia (2020-2022) en la *Costa do Descobrimento* y *Extremo Sul* de Bahía. **Resultados:** Entre enero de 2017 y diciembre de 2022 se notificaron 1.682 nuevos casos de tuberculosis pulmonar, con una tasa de incidencia promedio anual de 33,5 casos por 100 mil habitantes y de mortalidad promedio de 1,1 muertes por 100 mil habitantes. Tras la aparición de la Covid-19, hubo un aumento del 3,3% en la incidencia y del 20,5% en la mortalidad, junto con una reducción del 5,7% en la curación y del 38,6% en la letalidad hospitalaria. Durante la pandemia aumentaron las notificaciones de coinfección tuberculosis-VIH/Sida y los casos entre personas con más de ocho años de educación. **Conclusiones:** Las brechas de diagnóstico y tratamiento causadas por la Covid-19 pueden haber contribuido al aumento de la incidencia y la mortalidad por tuberculosis en Bahía.

Palabras Clave: *Tuberculosis Pulmonar. Monitoreo Epidemiológico. Control De Enfermedades Transmisibles. Estudios Ecológicos.*

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by bacteria from the *Mycobacterium tuberculosis* complex and is transmitted via airborne droplets expelled through coughing, speaking, or sneezing by individuals with untreated active pulmonary TB.[1,2] The pulmonary form is the most prevalent and is responsible for sustaining the disease's transmission chain.[1,3] The extrapulmonary form, which affects other organs and tissues, primarily occurs in individuals infected with the Human Immunodeficiency Virus (HIV).[1,3]

Considered a severe public health problem, TB has reemerged as the leading global cause of death from a single infectious agent.[4] Estimates for 2022 indicate that TB affected 10.6 million people worldwide, representing a 4.5% increase compared to 2021, and caused 1.1 million deaths.[2] Brazil accounts for one-third of TB cases in the Americas, reporting 78,000 new cases and 4,500 deaths in 2022.[2,5]

The Northeast is the region in Brazil with the second-highest number of new pulmonary TB cases, with an incidence rate of 34.9 cases per 100,000 population.[5] In the state of Bahia, where the incidence rate is 27 cases per 100,000 population, the disease predominantly affects males aged 30–49 years, individuals with brown skin color/race, low educational attainment, and negative HIV serology.[5-7] Within the state, clusters of new TB cases are concentrated in municipalities with incidence rates exceeding 40 cases per 100,000 population.[8]

Currently, research on the epidemiological profile of TB in Bahia primarily focuses on the capital, Salvador, and larger cities, making it challenging to assess the disease's status in other territories.[6,7,9,10] It is also known that TB programs worldwide faced challenges in providing essential diagnostic and treatment services during the Covid-19 pandemic.[11,12] Therefore, epidemiological monitoring of pulmonary TB in southern Bahia before and after the onset of Covid-19 is crucial for understanding the pandemic's impact on TB control in the state's socially vulnerable areas.

This study aimed to compare the epidemiological, clinical, and laboratory variables of pulmonary TB before and after the onset of Covid-19 in two territories in southern Bahia, Brazil.

METHODS

This study is an ecological analysis utilizing data from the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* - SINAN) and the Hospital Information System (*Sistema de Informações Hospitalares* - SIH) of the Unified Health System (*Sistema Único de Saúde* – SUS), accessed via the online portal of the Department of Informatics of SUS. These data included new pulmonary TB cases reported among residents of municipalities within the *Costa do Descobrimento* and *Extremo Sul* territories of Bahia from 2017 to 2022. New cases of extrapulmonary tuberculosis were excluded.

Costa do Descobrimento and *Extremo Sul* are territories located in the southern region of Bahia state, comprising 21 municipalities with an estimated population of 853,039 inhabitants.[13] *Costa do Descobrimento* includes eight municipalities: Belmonte, Eunápolis, Guaratinga, Itabela, Itagimirim, Itapebi, Porto Seguro and Santa Cruz Cabrália. *Extremo Sul* consists of 13 municipalities: Alcobaça, Caravelas, Ibirapuã, Itamaraju, Itanhém, Jucuruçu, Lajedão, Medeiros Neto, Mucuri, Nova Viçosa, Prado, Teixeira de Freitas and Vereda.

Sociodemographic (age, sex, race/skin color, education level), clinical (person with Aids), and laboratory (sputum smear microscopy, culture, rapid molecular test for TB, histopathology, drug susceptibility test, HIV test) data on pulmonary TB were compared between the pre-pandemic period (2017–2019) and the post-pandemic period (2020–2022). Population estimates from 2017 to 2021, and the 2022 Population Census were used to calculate incidence and mortality rates. Hospitalizations and hospital deaths due to pulmonary TB were identified using codes A15.0 to A15.3 from the International Classification of Diseases (ICD-10).[14] The hospital case fatality rate for pulmonary TB was calculated by dividing the number of hospital deaths by the number of hospitalizations for the disease, with the result multiplied by 100.[15] The spatial distribution of pulmonary TB incidence and mortality rates was analyzed using QGIS software version 3.32.3.

Data were presented as measures of central tendency and dispersion for quantitative variables and as absolute and relative frequencies for qualitative variables. To compare the number of new cases, cured cases, deaths among new cases, and hospital deaths before and after the onset of Covid-19, the Shapiro-Wilk test was used to assess data distribution. Upon confirming normality, Student's t-test was applied. Pearson's Chi-square test and Fisher's Exact test were used to evaluate associations between sociodemographic, clinical, and laboratory variables across the two periods. Statistical analyses were conducted using the RStudio programming language version 2023.06.0 (RStudio Team, 250 Northern Ave, Boston, MA, USA), with a significance level of $p \leq 0.05$.

The use of secondary databases exempts this study from approval by a Research Ethics Committee, in accordance with Resolutions No. 466/2012 and No. 510/2016 of the Brazilian National Health Council.

RESULTS

From 2017 to 2022, 2,169 cases of pulmonary TB were reported, of which 1,682 (77.5%) were new cases, 166 (7.7%) were transfers, 161 (7.4%) were reentries after abandonment, 126 (5.8%) were relapses, 17 (0.8%) were postmortem entries, and the remaining 17 (0.8%) did not have their entry type specified.

The new pulmonary TB cases annual mean was 280 (±42.7). In the period before Covid-19, the mean was 274.3 (±47.3), while after its onset, it rose to 286.3 (±47.3) (Table 1). *Costa do Descobrimento* reported 862 new cases, with 438 (50.8%) occurring before the pandemic and 424 (49.2%) afterward. *Extremo Sul* da Bahia reported 820 new cases, with 385 (46.9%) reported before Covid-19 and 435 (53.1%) after the pandemic began.

Table 1. Comparison of the mean number of new pulmonary tuberculosis cases, cured cases, deaths, and hospital deaths before (2017–2019) and after the onset of the novel coronavirus disease (Covid-19) (2020–2022) in *Costa do Descobrimento* and *Extremo Sul*, Bahia, Brazil.

Variables	Mean	SD	CV (%)	p-value
New cases				
2017-2019	274.3	47.3	17.3	0.772
2020-2022	286.3	47.3	16.5	
Cured cases				
2017-2019	188.0	33.9	18.0	0.663
2020-2022	177.3	18.2	10.3	
Deaths				
2017-2019	7.7	2.1	27.1	0.234
2020-2022	10.0	2.0	20.0	
Hospital deaths				
2017-2019	5.00	1.00	20.0	**0.021**
2020-2022	2.00	1.00	50.0	

Abbreviation: CV: Coefficient of Variation. SD: Standard Deviation.

The mean incidence of new pulmonary TB cases was 33.5 (±5.4) cases per 100,000 population. Costa do Descobrimento recorded a mean incidence of 34.7 (±8.2) cases per 100,000 population, while Extremo Sul had a mean of 26.5 (±5.9) cases per 100,000 population (figure 1A). After the onset of Covid-19, the mean incidence of new pulmonary TB cases in the evaluated territories increased by 3.3% compared to the pre-pandemic period. In *Costa do Descobrimento*, the incidence decreased by 19.6%, whereas in *Extremo Sul,* it increased by 29.8% (Table 2). The largest increases in incidence occurred in the municipalities of Itanhém, Lajedão, and Ibirapuã, while the largest decreases were observed in Itagimirim, Guaratinga, and Itapebi (Table 2 and Figure 2).

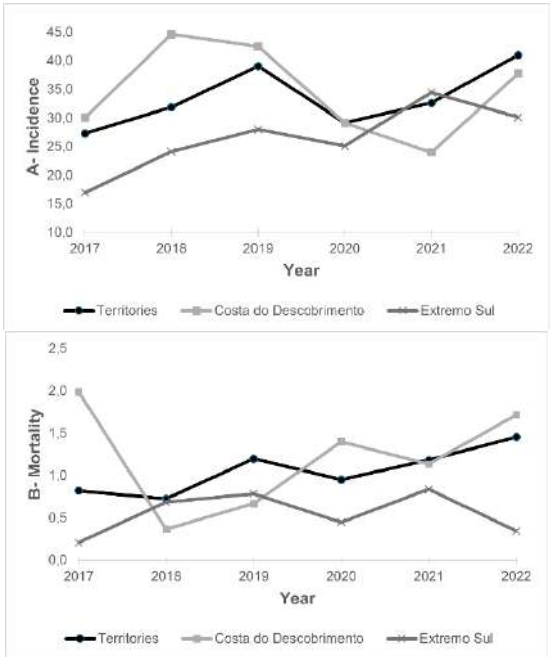

Figure 1. Distribution of pulmonary tuberculosis incidence (A) and mortality (B) rates reported in *Costa do Descobrimento* and *Extremo Sul*, Bahia, Brazil – 2017 to 2022 (N = 1,682).

Table 2. Comparison of pulmonary tuberculosis incidence, mortality, and hospital case fatality rates before (2017–2019) and after the onset (2020–2022) of the novel coronavirus disease (Covid-19) in *Costa do Descobrimento* and *Extremo Sul*, Bahia, Brazil.

	Incidence		Mortality		Hospital case fatality rate	
Location	**2017-2019**	**2020-2022**	**2017-2019**	**2020-2022**	**2017-2019**	**2020-2022**
Alcobaça	39.5	41.6	3.0	0.0	-	0.0
Belmonte	36.7	36.0	0.0	4.5	0.0	-
Caravelas	40.6	47.7	0.0	0.0	0.0	0.0
Eunápolis	38.8	29.8	1.2	0.0	27.1	19.8
Guaratinga	21.8	8.3	0.0	0.0	-	0.0
Ibirapuã	11.6	30.4	0.0	0.0	-	0.0
Itabela	46.6	44.0	0.0	2.7	0.0	16.7
Itagimirim	57.4	14.6	4.6	0.0	0.0	0.0
Itamaraju	36.1	34.3	0.5	0.5	10.0	0.0
Itanhém	5.1	18.0	0.0	1.7	-	0.0
Itapebi	25.6	20.7	0.0	0.0	0.0	-
Jucuruçu	17.8	29.3	0.0	0.0	0.0	-
Lajedão	8.4	25.1	0.0	0.0	-	-
Medeiros Neto	23.2	19.2	0.0	1.5	11.1	0.0
Mucuri	20.0	19.9	0.0	0.0	-	0.0
Nova Viçosa	22.3	20.9	0.0	0.8	16.7	0.0
Porto Seguro	36.4	43.6	1.1	3.5	11.1	4.2
Prado	27.0	37.7	2.4	2.4	0.0	0.0
Santa Cruz Cabrália	49.0	45.5	1.2	1.1	0.0	0.0
Teixeira de Freitas	31.6	37.9	1.4	0.2	29.6	11.1
Vereda	16.1	27.5	0.0	0.0	-	-
Costa do Descobrimento	***40.3***	***32.4***	***1.0***	***1.4***	***4.8***	***5.1***
Extremo Sul	***23.0***	***29.9***	***0.6***	***0.5***	***5.2***	***0.8***
Territories of Bahia	**29.1**	**30.1**	**0.7**	**0.9**	**13.8**	**8.4**

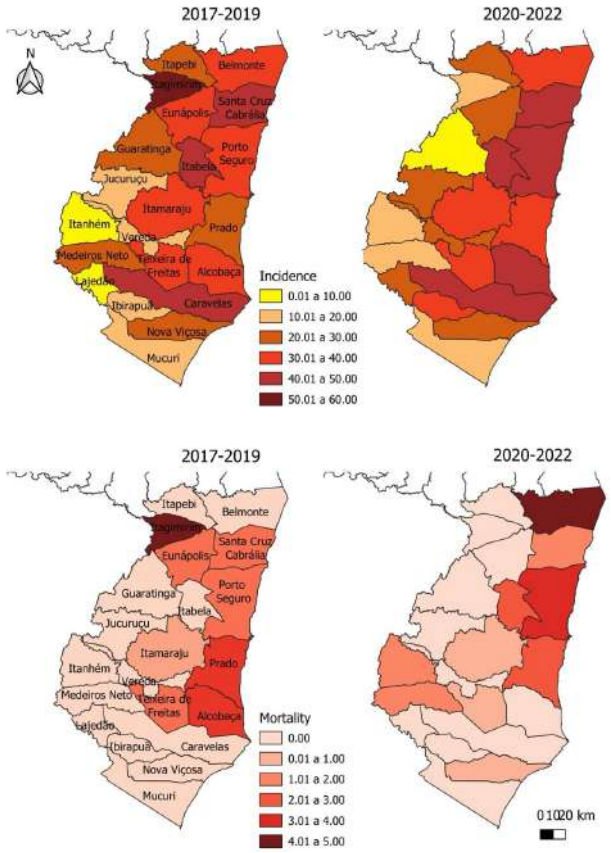

Figure 2. Comparison of incidence and mortality rates of new pulmonary tuberculosis cases in the municipalities of Costa do Descobrimento and Extremo Sul, Bahia, Brazil – 2017–2019 and 2020–2022.

Regarding sociodemographic characteristics, the majority of cases occurred among men (69.1%; n=1,163), individuals aged 20–59 years (75.7%; n=1,274), individuals of Black or mixed race (71.7%; n=793), and those with low educational attainment (71.7%; n=793).

In the analysis of associated comorbidities, 314 (18.7%) individuals reported alcoholism, 310 (18.4%) tobacco use, 148 (8.8%) illicit drug use, 145 (8.6%) diabetes, 107 (6.4%) acquired immunodeficiency syndrome (Aids), and 60 (3.6%) mental illness. After the onset of Covid-19, a 65.7% increase in TB-HIV/Aids coinfection was observed (p = 0.026), along with a 10.1% increase in individuals with low educational attainment (p = 0.005) (table 3). Although not statistically significant, there were increases of 43.9% in individuals with mental illness, 36.4% with diabetes, 15.2% among tobacco users, 7.3% among individuals with alcoholism, and 3.7% among illicit drug users.

Table 3. Comparison of sociodemographic, clinical, and laboratory characteristics of new pulmonary tuberculosis cases before (2017–2019) and after (2020–2022) the onset of the novel coronavirus disease (Covid-19) in *Costa do Descobrimento* and *Extremo Sul*, Bahia, Brazil (N = 1,682).

Variables	2017-2019 N (%)	2020-2022 N (%)	p-value
Age			
Up to 19 years	76 (9.2)	74 (8.6)	0.127
20 to 39 years	367 (44.6)	347 (40.4)	
40 to 59 years	269 (32.7)	291 (33.9)	
60 years or older	111 (13.5)	147 (17.1)	
Sex			
Male	565 (68.7)	598 (69.6)	0.707
Female	258 (31.3)	261 (30.4)	
Race/skin color			
Brown/Black	708 (88.7)	717 (87.2)	0.396
Other	90 (11.3)	105 (12.8)	
Unknown or blank*	25	37	
Education level			
≤ 8 years	455 (76.7)	338 (69.0)	**0.005**
8 years	138 (23.3)	152 (31.0)	
Unknown or blank*	218	359	
Not applicable**	12	10	
Aids			
Yes	39 (5.4)	68 (8.5)	**0.026**
No	681 (94.6)	734 (91.5)	
Unknown or blank*	103	57	
Sputum Smear Microscopy			
Positive	508 (63.8)	465 (55.7)	0.550
Negative	147 (18.4)	147 (17.6)	
Performed	655 (82.2)	612 (73.4)	**<0.001**
Not performed	142 (17.8)	222 (26.6)	
Unknown or blank*	26	25	
Culture			
Positive	109 (13.2)	143 (6.6)	1.000
Negative	42 (5.1)	55 (6.4)	
Performed/in progress	163 (19.8)	220 (26.6)	**0.005**
Not performed	660 (80.2)	639 (74.4)	
RMT-TB			
Detectable	63 (8.7)	256 (32.7)	**0.001**
Non-detectable/Inconclusive	34 (4.8)	52 (6.6)	
Performed/in progress	97 (13.3)	308 (39.4)	**<0.001**
Not performed	630 (86.7)	474 (60.6)	
Unknown or blank*	96	77	
Histopathology			
Positive	146 (19.0)	118 (15.0)	0.635
Suggestive	48 (6.2)	33 (4.2)	
Not suggestive	8 (1.0)	4 (0.5)	
Performed/in progress	241 (31.3)	206 (26.1)	**0.027**
Not performed	529 (68.7)	583 (73.9)	
Unknown or blank*	53	70	
Drug Susceptibility Test			
Resistant	4 (1.3)	4 (1.2)	0.719
Susceptible	76 (24.0)	110 (31.8)	
Performed/in progress	105 (33.2)	149 (43.1)	**0.012**
Not performed	211 (66.8)	197 (56.9)	
Unknown or blank*	507	513	
HIV Test			
Positive	44 (5.3)	71 (8.3)	0.065
Negative	634 (77.0)	696 (81.0)	
Performed/in progress	683 (83.0)	775 (90.2)	**<0.001**
Not performed	140 (17.0)	84 (9.8)	

Abbreviation: *Not included in the statistical analysis. **Individuals not of school age. HIV: Human Immunodeficiency Virus. Aids: Acquired Immunodeficiency Syndrome. RMT-TB: Rapid Molecular Test for Tuberculosis.

In the territories of *Costa do Descobrimento* and *Extremo Sul*, TB-HIV/Aids coinfection notifications increased by 50% and 100%, respectively.

Regarding laboratory findings, most individuals had negative HIV serology (79%) and positive sputum smear microscopy (59.7%). Sputum culture, histopathology, and rapid molecular testing for tuberculosis (RMT-TB) were positive in 72.2%, 73.9%, and 78.8% of the cases analyzed, respectively. After the onset of Covid-19, both the utilization of RMT-TB and the detection of mycobacteria through this method significantly increased ($p < 0.001$) (Table 3). In *Costa do Descobrimento*, there was a 36% increase in HIV positivity and a significant reduction in sputum smear

microscopy ($p = 0.003$) and RMT-TB performance ($p = 0.002$). In *Extremo Sul*, a significant decrease was observed in sputum smear microscopy ($p = 0.003$) and histopathological examinations ($p < 0.001$), alongside an increase in HIV testing ($p < 0.001$). Notably, there was a 1,592.9% increase in RMT-TB positivity ($p = 0.001$) in *Extremo Sul*.

Regarding case closure outcomes for new pulmonary TB cases, 1,096 (65.2%) resulted in cure, 199 (11.8%) were lost to follow-up, 106 (6.3%) were transferred, 71 (4.2%) resulted in death from other causes, 53 (3.2%) resulted in death from pulmonary TB, 39 (2.3%) had a change in diagnosis, 10 (0.6%) were primary abandonments, nine (0.5%) had a change in treatment regimen, six (0.4%) had drug-resistant TB, and four (0.2%) were due to treatment failure. Additionally, 89 (5.3%) cases had an unspecified closure type.

The annual mean number of cured cases was 182.7 (±25.0), with 564 (51.5%) reported before Covid-19 and 532 (48.5%) after its onset. The annual mean number of deaths from pulmonary TB was 8.8 (±2.2) across both territories, with 23 (43.4%) deaths reported before the pandemic and 30 (56.6%) afterward. During the study, 180 hospitalizations for pulmonary TB were recorded, of which 109 (60.6%) occurred before Covid-19 and 71 (39.4%) afterward. Twenty-one hospital deaths from pulmonary TB were reported, with 15 (71.4%) occurring before and six (28.6%) after the pandemic began. The mean number of hospital deaths was significantly higher before the pandemic ($p = 0.021$) (Table 1).

The mean mortality rate in the territories was 1.1 (±0.3) deaths from new cases per 100,000 population (figure 1B). *Costa do Descobrimento* recorded a mean mortality rate of 1.2 (±0.6) deaths per 100,000 population, while *Extremo Sul* recorded a mean of 0.5 (±0.2) deaths per 100,000 population. The mortality rate increased from 0.7 deaths per 100,000 population before the pandemic to 0.9 deaths per 100,000 population afterward, representing a 22.2% increase. During this period, the mortality rate increased by 40.6% in *Costa do Descobrimento* and decreased by 3.6% in *Extremo Sul*. The largest increases in mortality were observed in the municipalities of Itabela, Porto Seguro, and Belmonte, while the largest decreases were in Itagimirim, Alcobaça, and Eunápolis (Table 2 and Figure 2).

The hospital case fatality rate was 11.7%. After the onset of Covid-19, the hospital fatality rate decreased by 38.6% across both territories, increased by 6.3% in *Costa do Descobrimento*, and fell by 83.6% in *Extremo Sul*. The largest decreases in the hospital fatality rate were observed in the municipalities of Nova Viçosa, Medeiros Neto, and Itamaraju (Table 2).

DISCUSSION

To expand the understanding of the sociodemographic and clinical-laboratory characteristics of pulmonary TB before and after the onset of the Covid-19 pandemic in two endemic territories in southern Bahia, this study identified an increase in incidence and mortality rates, along with a reduction in cured cases during the pandemic period. Despite TB being a disease with universal and free diagnosis and treatment provided by the Unified Health System (SUS), barriers to healthcare access persist, with 280 new cases and 8.8 deaths reported annually in *Costa do Descobrimento* and *Extremo Sul* da Bahia.

The emergence of Covid-19 reversed years of progress in TB control worldwide.[2] Globally, during the first year of the pandemic, the reallocation of human and financial resources to address Covid-19 reduced TB control and reporting efforts, as healthcare systems focused on responding to the emergency.[11,12,16] This study aimed to identify the effects of Covid-19 in the investigated territories to inform strategies for improving coverage and access to public policies provided by SUS.

From 2017 to 2019, TB incidence rates in Brazil increased by 3.6%, contrary to the declining trend observed since 2012. In 2020, pulmonary TB incidence decreased by 9% compared to the previous year due to the pandemic. However, in 2021 and 2022, with the partial recovery of the TB care network, pulmonary TB rates increased by 14.2%, rising from 28 to 32 cases per 100,000 population.[5] Contrary to the global and Brazilian trends of increasing TB incidence, a 19.6% decrease was observed in the *Costa do Descobrimento* territory.[2] Additionally, in 2022, pulmonary TB incidence in the two evaluated territories reached 41 cases per 100,000 population, exceeding the rates calculated for the state of Bahia (23.6) and Brazil (32).[5] This high incidence may be related to an increase in undiagnosed and untreated cases during the pandemic, potentially resulting in greater community transmission.[4] Regional inequalities in healthcare access and social vulnerabilities likely contribute to the disparity between the territories' incidence rates and national data.[8,17]

The SUS provides free access to TB diagnosis and treatment throughout the country, but these actions occur unequally. Since access to health services is related to the social and residential conditions of the population, individuals living in areas with lower socioeconomic development and greater income vulnerability may face greater difficulties in accessing health care, especially in pandemic situations.[4,5] Furthermore, TB imposes an economic burden on families of patients with expenses related to indirect costs of treatment or incapacity to work, demonstrating the catastrophic costs of the disease. This economic

burden can be even more damaging for individuals with precarious living conditions.[8,9]

The sociodemographic characteristics of the studied population align with observations in other parts of Bahia, with a predominance of individuals aged 20 to 39 years (42.5%), male (69.1%), self-identified as Black or mixed race (88%), and with low educational attainment (71.7%).[6,7] Low educational attainment increases vulnerability to infection as it hinders understanding of disease transmission and adherence to treatment.[8,9] However, after the onset of Covid-19, a significant increase in new pulmonary TB cases was observed among individuals with more than eight years of schooling, likely due to the interruption of healthcare services across the system, regardless of education level or income.[18]

During this period, there was also an increase in new cases among individuals aged 60 years or older, potentially related to immunosenescence and the aging population in Bahia, as the proportion of individuals in this age group has increased by nearly 50% over the past 12 years.[13] In this segment of the population, surveillance actions in primary healthcare are recommended for the early identification of respiratory symptoms, as TB's incubation period can be shortened depending on the degree of immunosuppression.[17]

People living with HIV are up to 20 times more likely to develop active TB and exhibit lower therapeutic success rates, making them a priority group for surveillance and treatment.[2] Contrary to the decreasing trend in TB/HIV coinfection observed nationally during the pandemic, this study found an increase in coinfection in the *Costa do Descobrimento* and *Extremo Sul* regions of Bahia.[19] This increase may be linked to low social development indices, as areas with inadequate socioeconomic, housing, and sanitation conditions tend to show a greater overlap of these issues.[9,18,21] The rise in coinfection cases after the onset of Covid-19 may also have resulted from expanded HIV testing coverage and the incorporation of RMT-TB in these regions, which could lead to increased dual reporting.[5]

From 2020 to 2022, diagnostic methods for TB underwent changes in the territories of interest. Despite reduced access to TB diagnostic tools during the pandemic, an increase in RMT-TB usage was observed in *Extremo Sul*.[11,12,16] This shift may have contributed to the detection of new cases after a decline during the first year of the pandemic, as RMT-TB is more sensitive in identifying mycobacteria and can also detect resistance to rifampin, the primary drug used in TB treatment regimens.[3] The reduction in histopathological testing may be attributed to difficulties in obtaining tissue samples. When RMT-TB is available, it often becomes the preferred diagnostic method.[3] Despite the increased use of RMT-TB, sputum smear microscopy remains the most widely used diagnostic method in both territories, as it is the fastest and most cost-effective test. However, its sensitivity is lower and depends on the extent of lesions.[3]

The diagnostic and treatment gaps caused by Covid-19 led to an additional 1.5 million TB-related deaths worldwide.[2,4] Compared to 2017, Brazil's TB mortality rate increased by 22.5% in 2022, reversing years of progress achieved prior to the pandemic. In both territories, a 5.7% decrease in the number of cured new cases was observed, aligning with national and state trends.[12,21]

The 40.6% increase in the mortality rate in *Costa do Descobrimento* may have been influenced by a higher proportion of treatment abandonment and the subsequent reduction in cured cases observed in Brazil and Bahia since 2020.[12,21] Conversely, the 3.6% decrease in the mortality rate in *Extremo Sul* may have resulted from technical challenges faced by healthcare professionals in accurately classifying TB-related deaths during the pandemic, as Covid-19 was prioritized.[12]

The clinical presentation of pulmonary TB includes signs and symptoms that resemble those of Covid-19, which can interfere with proper management and accurate reporting of hospital deaths caused by TB.[3,22] During the pandemic, there was a significant reduction in the number of hospital deaths from TB in both evaluated territories, resulting in a 38.6% decrease in the hospital case fatality rate. It is worth noting that in Brazil, as in other countries, the increase in Covid-19-related hospitalizations, combined with the decline in TB-related hospitalizations, may have contributed to the reduced hospital case fatality rate for TB, even as the overall TB mortality rate increased.[23] Furthermore, active or latent TB has been identified as a risk factor for fatal outcomes in patients with Covid-19. As a result, even when TB was the underlying cause of hospital death, the death coding may have been attributed to Covid-19.[24]

The *Extremo Sul* region of Bahia demonstrated better performance in hospital case fatality and mortality rates after the onset of Covid-19. This improvement may reflect a higher number of pulmonary TB notifications with associated comorbidities, enabling a more individualized approach to patient care and, consequently, better treatment outcomes. Additionally, this region exhibited greater testing coverage and higher positivity rates for pulmonary TB, with a significant increase in RMT-TB usage starting in 2020, which may have facilitated an improved management of close contacts.

The contribution of this study lies in identifying changes in the incidence, mortality, and hospital case fatality rates of pulmonary TB in two territories characterized by socially vulnerable populations and significant tourist activity. Although the observed

changes occurred after the onset of the pandemic, the use of aggregated data does not allow for establishing Covid-19 as the direct cause or for controlling confounding variables.

Among the limitations of this study is the ecological fallacy, as the results, based on aggregated data, cannot be extrapolated to the individual level. The research analyzed notifications of new pulmonary TB cases obtained from the Sinan database, which may contain incomplete entries originating from Basic Health Units, potentially contributing to underreporting. However, Sinan distinguishes deaths from new pulmonary TB cases from other types of entries, which is not the case for notifications in the Mortality Information System.[25] Underreporting also occurs in the records of hospitalizations and hospital deaths obtained from the SUS Hospital Information System, as it only includes users admitted to public SUS facilities.

After the emergence of Covid-19, an increase was observed in the proportion of new cases among individuals with more than eight years of schooling and those with Aids, as well as greater use of RMT-TB at the expense of sputum smear microscopy and histopathological testing. TB is a significant cause of death among individuals living with HIV, and the increased detection of TB/HIV coinfection during the pandemic underscores the importance of monitoring and preventive treatment in these individuals.[19] At the municipal level, discrepancies in these measures were observed when comparing the pre- and post-Covid-19 periods. These differences may be attributed to the performance of primary healthcare in case detection and management, as well as to socio-spatial and economic inequalities. In light of these findings, this study conducted a comprehensive epidemiological evaluation of TB after the emergence of Covid-19 to assist in adapting strategies and goals for prevention, diagnosis, and treatment to combat the disease. Brazil, like other countries, has committed to eradicating TB in accordance with the targets set by the United Nations' Sustainable Development Goals and the World Health Organization's End TB Strategy.[2,5] In this context, the study identified increased use of RMT-TB and HIV detection testing after 2020, which has contributed to greater disease detection and may support Brazil's efforts to reduce TB incidence and mortality.

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AUTHORS' CONTRIBUTIONS

Marília Caixeta de Araujo contributed to the bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Renata Soares Passinho** contributed to project management, writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics. **Karina Simone Souza Vasconcelos** contributed to project management, review, and statistics. **Delio José Mora** contributed to project management, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Original Article

Epidemiological profile of sepsis in a reference hospital in Paraná

Perfil epidemiológico da sepse em um hospital de referência do Paraná
Perfil epidemiológico de la sepsis en un hospital de referencia de Paraná

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ABSTRACT

Background and Objectives: To describe the clinical and epidemiological characteristics of patients who developed sepsis and/or septic shock admitted to two adult ICUs of a reference hospital in Paraná. **Methods:** This descriptive-exploratory, documentary field research used a quantitative approach, developed through the analysis of medical records of patients hospitalized in ICUs from January 2014 to December 2023. **Results:** A total of 5,423 medical records were analyzed, identifying 687 patients who developed sepsis. These patients were 56.3% male and 70.7% older adults, with 82.2% having previous comorbidities. Upon admission, 75.4% had a clinical etiology, predominantly due to respiratory pathologies (24.1%). There was a higher prevalence of septic shock (59.1%). Cases were primarily of community origin (68.1%), had a primary focus of pulmonary infection (37.6%), and resulted in death (64.6%). **Conclusion:** Sepsis is a serious public health problem and presents high morbidity and mortality rates, especially when associated with cases of septic shock. The importance of developing epidemiological studies is highlighted in order to support the construction of new protocols and public policies.

Keywords: *Sepsis. Septic Shock. Intensive Care Unit. Hospital Infection. Epidemiology.*

RESUMO

Justificativa e Objetivos: Descrever as características clínicas e epidemiológicas dos pacientes que desenvolveram sepse e/ou choque séptico internados em duas UTIs adultas de um hospital de referência do Paraná. **Métodos:** Pesquisa de campo, descritivo-exploratória, documental, retrospectivo, com abordagem quantitativa, que foi desenvolvida por meio da análise de prontuários dos pacientes hospitalizados nas UTIs no período de janeiro de 2014 a dezembro de 2023. **Resultados:** Foram analisados 5.423 prontuários, destes, 687 eram de pacientes que desenvolveram sepse, sendo 56,3% do sexo masculino, 70,7% idosos, 82,2% com comorbidades prévias, 75,4% com etiologia clínica de admissão, predominantemente por patologias respiratórias, com 24,1%. Houve uma maior prevalência de choque séptico com 59,1%, de origem comunitária (68,1%), com foco primário de infecção pulmonar (37,6%) e com desfecho de óbito (64,6%). **Conclusão:** A sepse consiste de um grave problema de saúde pública e apresenta altas taxas de morbimortalidade, principalmente quando associadas aos casos de choque séptico. Ressalta-se a importância do desenvolvimento de estudos epidemiológicos a fim de subsidiar a construção de novos protocolos de diagnóstico precoce e manejo da sepse.

Descritores: *Sepse. Choque Séptico. Unidade de Terapia Intensiva. Infecção Hospitalar. Epidemiologia.*

RESUMEN

Justificación y Objetivos: Describir las características clínicas y epidemiológicas de los pacientes que desarrollaron sepsis y/o shock séptico ingresados en dos unidades de cuidados intensivos (UCI) de adultos de un hospital de referencia de Paraná (Brasil). **Método:** Investigación de campo, descriptiva-exploratoria, documental, retrospectiva, con enfoque cuantitativo, la cual se desarrolló mediante el análisis de historias clínicas de pacientes hospitalizados en UCI en el periodo de enero de 2014 a diciembre de 2023. **Resultados:** Se analizaron 5.423 historias clínicas, de las cuales 687 trataban de pacientes que desarrollaron sepsis, el 56,3% hombres, el 70,7% ancianos, el 82,2% con comorbilidades previas, el 75,4% con etiología clínica al ingreso, predominantemente por patología respiratoria en el 24,1%. Hubo mayor prevalencia de shock séptico (59,1%), de origen comunitario (68,1%), con foco primario de infección pulmonar (37,6%) y con desenlace de muerte (64,6%). **Conclusión:** La sepsis es un grave problema de salud pública y tiene altas tasas de morbimortalidad, especialmente cuando la asocia a casos de shock séptico. Se destaca la importancia de desarrollar estudios epidemiológicos para apoyar la construcción de nuevos protocolos de diagnóstico temprano y manejo de la sepsis.

Palabras Clave: *Sepsis. Choque Séptico. Unidade de Cuidados Intensivos. Infección Hospitalaria. Epidemiología.*

INTRODUCTION

The Intensive Care Unit (ICU) is a hospital environment designed to receive critically ill or at-risk patients who require uninterrupted care from a multidisciplinary team. These patients are exposed to various invasive procedures and the administration of immunosuppressive drugs, which makes them five to ten times more susceptible to acquiring infections, which frequently progress to sepsis.[1]

According to the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM), sepsis results from an exaggerated response of the organism to an infectious stimulus.[2]

This syndrome is characterized by an organic imbalance between the inflammatory process and anti-inflammatory actions, leading to systemic release of cytokines and chemical mediators, oxidative stress, and hemostasis-affecting mechanisms. These factors contribute to the activation of the coagulation process and complement system, leading to systemic dysfunction and even death in more serious cases, such as septic shock.[3]

Septic shock is characterized by the presence of hypotension associated with organ, cellular, and metabolic dysfunctions, and is directly related to high morbidity and mortality rates worldwide. The diagnosis of septic shock is established when vasopressors are required to maintain mean arterial pressure (MAP) >65 mmHg and serum lactate levels greater than 2 mmol/L.[4]

According to the Sepsis Prevalence Assessment Database (SPREAD) by the Latin American Sepsis Institute (LASI), at least one-third of ICU beds are occupied by patients with sepsis and/or septic shock, with an overall mortality rate of 55%. This condition accounts for between one-third and half of deaths in hospitals in the United States. In Brazil, the prevalence rate is 30%, with a mortality rate of 55%, making it the leading cause of mortality in noncardiac hospitalizations at the ICUs and the main burden to healthcare.[5]

Given this, characterizing the epidemiological profile of sepsis is crucial for directing prevention programs, as its occurrence varies by age group, sex, and location. In Brazil, a previous study found that the profile with the highest sepsis incidence is older adults aged 80 or older, male, White, with most cases concentrated in Southeastern Brazil.[2]

In light of the above, the guiding question of this study was: What are the clinical and epidemiological characteristics of patients who developed sepsis, from January 2014 to December 2023, in two ICUs of a public hospital in Southwest Paraná?

Thus, this research aimed to describe the clinical and epidemiological characteristics of patients who developed sepsis and/or septic shock admitted to two adult ICUs of a reference hospital in Paraná.

METHODS

This is a descriptive-exploratory, documentary, cross-sectional, and retrospective field research. It uses a quantitative approach and was conducted in a Reference Hospital in inland state of Paraná.

The institution has 146 active hospital beds and serves as a reference for 42 municipalities in the care of trauma; low-, medium-, and high-complexity orthopedic surgeries; vascular surgeries; intermediate- and high-risk pregnancies; pediatric surgeries; urology, and maxillofacial surgery. It has two adult ICUs, one pediatric ICU, and one neonatal ICU, and serves as an undeniable reference for the Mobile Urgent Care Service (SAMU), the Integrated Emergency Trauma Care Service (SIATE), and the Bed Management Center, serving approximately 600,000 inhabitants.

The study sample consisted of medical records of patients admitted to the two adult ICUs and diagnosed with sepsis from January 2014 to December 2023.

The inclusion criteria were medical records of patients hospitalized in the aforementioned sectors who developed sepsis and/or septic shock during the study period and who presented the variables of interest. Records that did not contain all the necessary information or indicated that the patients were affected by other diseases were excluded.

Data collection was performed using a checklist developed by the investigators that included the following variables: age, sex, comorbidities, length of stay, origin, etiology of admission, use of devices, signs and symptoms, infectious focus, isolated microorganisms, sepsis classification, origin of sepsis, and clinical outcome.

Sepsis diagnosis required two or more clinical criteria, including leukocytosis or leukopenia, a heart rate greater than 90 beats per minute (BPM), a core temperature above 38°C or below 36°C, and a respiratory rate greater than 20 respirations per minute (RPM).

Septic shock is characterized by the need for vasopressor use to maintain MAP >65 mmHg, even after adequate fluid administration, in addition to a serum lactate level greater than 2 mmol/L.[1,4] The quickSOFA (qSOFA) instrument was applied to predict sepsis severity. qSOFA is a practical and straightforward bedside tool used to assess the risk of clinical deterioration in patients with infection, such as sepsis. This instrument considers parameters such as: respiratory rate ≥ 22 RPM, systolic blood pressure ≤ 100 mmHg, and Glasgow Coma Scale < 15. Each parameter scores 1 point, ranging 0 to 3; a score of 2 or more indicates a higher risk of mortality and ICU stay for the patient.[6]

The data were analyzed using the Statistical Package for Social Sciences – 25.0 program, via descriptive frequency analyses. Furthermore, categorical variables were compared using the Chi-squared test. Univariate and multivariate analyses were performed to assess independent risk factors for mortality and sepsis classification. A p-value < 0.05 was considered statistically significant.

This study was previously sent to the research institution for the institutional consent form to be signed, and then submitted to the Ethics Committee of the Paranaense University for evaluation, and was approved under Opinion No. 6,713,924/2024. Thus, all ethical and legal principles were followed in accordance with Resolution 466/2012 of the Brazilian National Health Council.

RESULTS

This study evaluated 5,423 medical records of patients admitted to adult ICUs. Of these, 687 (12.6%) were patients who developed sepsis and/or septic shock during hospitalization. The clinical profile showed a predominance of male patients (56.3%) and older patients (70.7%), with a mean age of 66.13 ± 17.16 years. Most were hospitalized for clinical conditions (75.4%) and had previous comorbidities (82.2%), with systemic arterial hypertension (SAH) being the most prevalent (49.3%), followed by diabetes mellitus (DM) (27.8%), renal failure (19.4%), heart disease (16.7%), and chronic obstructive pulmonary disease (COPD) (13%). In some cases, patients had more than one associated comorbidity.

Regarding the length of stay, most patients remained hospitalized for up to 15 days (68.9%). As for the etiology of admission, most were due to respiratory pathologies (24.1%), followed by postoperative causes (20%) and sepsis (17%). Regarding the use of invasive devices, most patients used both invasive and therapeutic devices (Table 1).

Table 1. Clinical profile of patients with sepsis and/or septic shock admitted to adult ICUs at a hospital in Paraná. 2024.

Parameter	N (%)
Sex	
Male	387 (56.3)
Female	300 (43.7)
Age	
Young	201 (29.1)
Older adult	486 (70.7)
Comorbidities	
Yes	565 (82.2)
No	122 (17.8)
Patient	
Clinical	518 (75.4)
Surgical	146 21.3)
Trauma	23 (3.3)
Length of stay	
Up to 15 days	473 (68.9)
More than 15 days	214 (31.1)
Etiology of admission	
Respiratory pathologies	165 (24.1)
Postoperative	138 (20)
Sepsis	117 (17)
Septic shock	62 (9)
Renal/urinary pathologies	55 (8)
Neurological pathologies	49 (7.1)
Gastrointestinal/abdominal pathologies	37 (5.4)
Trauma	20 (2.9)
Cardiovascular pathologies	19 (2.8)
Other	25 (3.7)
Use of invasive devices	
Mechanical ventilation	562 (81.8)
Central line	646 (94)
Indwelling urinary catheter	676 (98.4)
Nasoenteral/nasogastric tube	579 (84.3)
Vasoactive drug	599 (87.2)
Parenteral nutrition	61 (8.9)

According to the sepsis classification criteria, 59.1% of the sample had septic shock, and most cases were community-acquired (68.1%). The primary source of infection was pulmonary (37.6%).

The qSOFA was used to predict sepsis severity. While it is not useful as a diagnostic tool for sepsis, it remains an important indicator of severity. In this study, qSOFA was calculated in 81.8% of the sample, and in most cases (33.2%), the score was 2 points, suggesting higher mortality and increased length of stay in intensive care.

Regarding clinical signs, a significant portion of patients presented with hypotension (92.6%), tachycardia (69.7%), tachypnea (43.8%), and leukocytosis (79.3%). Evaluation of clinical outcomes revealed a high mortality rate, with 64.6% of patients dying, while 35.4% were discharged from the hospital (Table 2).

Table 2. Clinical characteristics of sepsis and/or septic shock cases in patients admitted to adult ICUs at a hospital in Paraná. 2024.

Parameter	N (%)
Sepsis classification	
Sepsis	281 (40.9)
Septic shock	406 (59.1)
Sepsis origin	
Community-acquired	468 (68.1)
Nosocomial	219 (31.9)
Primary source of infection	
Pulmonary	258 (37.6)
Abdominal	140 (20.4)
Urinary tract	94 (13.7)
Cutaneous	42 (6.1)
Unspecified	118 (17.2)
Other	35 (5.0)
qSOFA performed	
Yes	562 (81.8)
No	125 (18.2)
qSOFA score	
<2*	211 (37.5)
≥ 2*	351 (62.5)

continue

Parameter	N (%)
Clinical signs of sepsis	
Hyperthermia	283 (41.2)
Tachypnea	301 (43.8)
Leukocytosis	545 (79.3)
Hypotension	636 (92.6)
Hypothermia	86 (12.5)
Tachycardia	479 (69.7)
Leukopenia	8 (1.2)
Decreased level of consciousness	233 (33.9)
Dyspnea	210 (30.6)
Hyposaturation	242 (35.2)
Bradycardia	57 (8.3)
Outcome	
Discharge	243 (35.4)
Death	444 (64.4)

Abbreviation: *qSOFA score: < 2 indicates a lower probability of poor prognosis and/or organ dysfunction; ≥ 2 indicates a higher probability of poor prognosis and/or organ dysfunction.

The data below show the statistical association between sepsis severity/classification and the use of invasive devices (Table 3).

Table 3. Frequency, percentage, and significant association of patients who progressed to septic shock (n=447), according to the use of invasive devices in patients admitted to adult ICUs at a hospital in Paraná. 2024.

Parameter	Total	N (%)	p-value
Use of invasive devices			
Indwelling urinary catheter	676	403 (59.7)*	0.001
Vasoactive drug	598	391 (65.4)*	0.000
Nasoenteral/nasogastric tube	580	373 (64.3)	0.000
Mechanical ventilation	562	374 (66.5)	0.000
Central line	645	402 (62.3)*	0.000

Abbreviation: *Significant association

A statistical association was also found between deaths related to age (stage of life), as well as clinical conditions (presence of comorbidities, sepsis classification, and use of invasive devices) (Table 4).

Table 4. Frequency, percentage, and significant association of patients with sepsis who died (n=447), according to age (stage of life) cycle and clinical conditions of patients admitted to adult ICUs at a hospital in Paraná. 2024.

Parameter	Total	N (%)	p-value
Age			
Young	201	103 (51.2)	
Older	486	344 (70.8)*	0.000
Comorbidities	565	385 (68.1)	0.001
Sepsis classification			
Sepsis	281	142 (50.5)	
Septic shock	406	305 (75.1)	0.000
Use of invasive devices			
Indwelling urinary catheter	676	444 (65.7)	0.010
Vasoactive drug	598	437 (73.1)	0.000
Nasoenteral/nasogastric tube	580	417 (71.9)	0.000
Mechanical ventilation	562	421 (74.9)	0.000
Central line	645	440 (68.2)	0.000

Abbreviation: *Significant association

DISCUSSION

Sepsis and septic shock are recognized as significant public health problems, affecting millions worldwide and associated with high mortality rates. The epidemiological profile of this syndrome may vary by region and population, making critical to characterize those affected.

When evaluating the clinical profile of patients affected by sepsis in this study, in relation to sex, the male population was found to be predominant in 56.3% of cases. This result is consistent with other Brazilian regions, as evidenced by a study conducted in the state of Tocantins, which found that males accounted for 55.0% of the cases.[7]

This data can be explained by the lifestyle and habits preferred by men, such as low adherence to and seeking of healthcare services, in addition to the everyday use of substances such as tobacco and alcohol, which, in the long term, impair the integrity and functioning of vital organs.[8]

When analyzing the age group, older adults (> 60 years) were the most affected by sepsis, representing 70.7% of cases. This number is consistent with Brazilian reality, as a nationwide study between 2010 and 2019 found that 53% of hospitalizations were among older people.[5]

It is scientifically established that the older population is naturally more susceptible to illness and, consequently, to health complications. Studies conducted in England and Wales point to factors such as immunosenescence — the decline of the immune system with age — and inflammaging — persistent, low-grade chronic inflammation — as facilitators of serious infections.[9]

Other factors, such as pre-existing comorbidities, diminished physiological reserves associated with aging, malnutrition, and even polypharmacy, are also listed.[9]

The susceptibility and frailty of older adults to the high mortality rate related to sepsis were evident in this study, which identified a significant association between older adults and the number of deaths (p=0.000), with 70.8% of total deaths related to this population.

An equally important and relevant factor in explaining the high mortality rate present in sepsis cases was the presence of comorbidities associated with hospitalized patients. This study showed that among patients affected by sepsis, 82.2% had comorbidities, which was also significantly associated with mortality, with 68.1% of patients with comorbidities dying.

Regarding relationship between sepsis and underlying comorbidities, German investigators concluded that sepsis was the exclusive and sole cause of death in only six (12%) cases. When comorbidities were present, sepsis accounted for 54 (76%) cases.[10] Thus, the presence of pre-existing comorbidities can increase case severity and worsen prognosis, since pre-existing diseases, such as DM and SAH, are associated with several physiological changes in the body.[11]

Regarding origin of hospitalized patients, those with clinical complications accounted for 75.4% of admissions. The same was observed in a private hospital in the state of Sergipe between 2016 and 2017, where

94.5% of the analyzed hospitalizations shared the same origin.[12] The severity of the admission conditions, combined with a delay in treatment initiation, can worsen the clinical picture and necessitate prolonged hospitalization.

According to data obtained on sepsis from SIH/DATASUS, the average length of hospital stay for patients varies according to the region of Brazil, being, on average, 11 days in the North region; 10.9 days in the Northeast region; 13 days in the Southeast region; 10.6 days in the South region; and 12.6 days in the Midwest region.[13] Internationally, studies show that hospital stays are longer in developed countries, such as the United States and China, than in middle- and low-income countries, a difference primarily associated with more advanced ICU care and better prognoses.[14]

This study found that most patients (68.9%) had a hospital stay of less than 15 days. This shorter length of stay can be directly attributed to early mortality, as a consequence of the severity of septic conditions.[15]

Regarding the etiology of ICU admission, this study found that respiratory pathologies were the leading cause (24.1%). These data differ from those of a study conducted in Belo Horizonte, state of Minas Gerais, which identified other traumas as the main causes.[16]

The discrepancy in the data can be explained by the study hospital's patient profile. Furthermore, the primary cause of hospitalization alone is not sufficient to justify a septic condition. However, clinical causes, especially those related to the respiratory and cardiac systems, are associated with prolonged hospital stays and the use of invasive devices, both of which contribute to infectious outcomes.[16]

Regarding use of invasive devices, in a study conducted in João Pessoa, state of Paraíba, 100% of patients diagnosed with sepsis used a central line and an indwelling urinary catheter (IUC). In comparison, 72% used mechanical ventilation (MV).[17] A similar study was conducted in Asia, where more than 70% of patients with sepsis used MV, supporting this research, which found high rates of use of invasive devices.[18]

This study also showed that sepsis related to the use of invasive devices is significantly associated with mortality, specifically the use of IUC (p=0.010) and MV and CVC (p=0.000).

The use of these devices is considered a significant risk factor for acquiring healthcare-associated infections (HAIs). Although it contributes to patient prognosis, prolonged use of these devices, coupled with inadequate protocols, insufficient hand hygiene, and incorrect procedure performance, significantly increases the risk of infection, which can subsequently progress to sepsis. Globally, one in four cases of sepsis in hospitals and one in two cases of sepsis in ICUs are the result of HAIs.[18]

Regarding sepsis classification, septic shock is prevalent in 59.1% of cases. This high rate was also found in research conducted at a trauma hospital in Belo Horizonte, where a septic shock rate of 35% was observed.[16]

This growing trend in the number of septic shock cases is directly linked to the emergence of new bacterial strains resistant to antibiotic therapy, the aging of the population due to increased life expectancy, and improvements in healthcare systems' capacity to diagnose more cases of this syndrome and its complications.[19]

Furthermore, it is proven that septic shock considerably increases the chance of death. In this study, a significant association with mortality was observed (p=0.000), as 75.1% of individuals with septic shock died, in line with a study carried out in the state of Piauí, which indicated a 90.5% mortality rate in cases of septic shock, highlighting the severity of this syndrome.[20]

Regarding origin, sepsis can be acquired in the community or in the hospital setting. Community-acquired sepsis is the one identified upon admission or within 72 hours of hospitalization.[21] In this study, it accounted for 68.1% of cases, consistent with a study conducted in Ethiopia, which also found the predominant source of infection to be community-acquired.[14]

This data may vary depending on the population and the predominant admission etiology. Furthermore, with the pandemic and social isolation measures, there was a decrease in the number of surgeries and patients hospitalized for trauma. However, many got infected with Covid-19 and became severely ill, triggering a septic condition, mostly of pulmonary origin.[21]

The respiratory tract is considered a primary site of infections and is directly related to the use of invasive devices, such as endotracheal tubes.[15] The pulmonary tract was highlighted in this study as a primary source of infection (37.6%), in accordance with the national profile, as evidenced in a study carried out in Teresina, state of Piauí, which found a rate of 44.4% of primary pulmonary focus.[20]

The large number of pulmonary infections is mainly due to the region's characteristics, which favor the infectious process and bacterial proliferation. Furthermore, the study population primarily comprised older individuals with associated comorbidities, thus presenting a higher risk of acquiring respiratory infections, as well as requiring the use of mechanical ventilation and ICU stay.[20] Moreover, although MV is important for patient prognosis, it is associated with the acquisition of ventilator-associated pneumonia (VAP) and, subsequently, with the progression to sepsis.[22]

According to the Surviving Sepsis Campaign Guidelines, hospitals and healthcare services must

include sepsis screening systems for critically ill and high-risk patients, such as SOFA or qSOFA. SOFA has high predictive validity, but it is not an easy tool to apply, as it requires laboratory tests. qSOFA, on the other hand, is faster and more practical to use at the bedside to assess the risk of clinical deterioration in patients with infections.[23]

Of the medical records analyzed, from those in which was possible to apply the qSOFA score, 51.1% presented values ≥ 2, which represents a high risk of death. In Spain, a study conducted among inpatients at a general hospital identified that 24% of the sample already presented qSOFA ≥ 2 upon admission. In this case, a significant association was observed between patients with altered qSOFA and the number of deaths, underscoring the importance of applying the score initially, but not as an isolated diagnostic method.[24]

The disparity between this study's results and those of other studies can be explained primarily by differences in the sectors analyzed, since ICUs have more complex and invasive procedures than regular wards. In view of this, it was also not possible to apply qSOFA to all medical records analyzed, as some data were incomplete.

In the analysis of sepsis-related clinical signs, hypotension (92.6%), leukocytosis (79.3%), and tachycardia (69.7%) stood out, which may be related to circulatory and inflammatory impairment. In an analysis of data from the literature, tachycardia and tachypnea were identified as the most frequent clinical signs in septic patients.

The signs and symptoms of sepsis generally affect several organ systems, as the intense release of inflammatory mediators during the septic episode results in multiple organ failures, thereby causing the classic signs observed in this study.[25]

The outcome of patients with sepsis in this study revealed a high mortality rate (64.6%), reflecting the severity and potentially lethal impact of this condition. Recent studies of sepsis mortality trends in Brazil and its regions, covering the period from 2010 to 2019, revealed an incidence rate of 51.3 deaths per 100,000 inhabitants.[5]

These results reinforce what is advocated by the World Health Organization (WHO), placing sepsis as a serious global public health problem and one of the main causes of death in ICUs, reinforcing the need for emergency measures involving infrastructure, protocols, and trained professionals who can act quickly in the face of signs of sepsis, aiming at timely rescue measures.[7]

Regarding the study's limitations, there was insufficient information, incomplete or inaccurate medical record documentation, and a lack of information on the origin or primary source of sepsis, all of which significantly affected data collection and analysis. Thus, the importance of accurately completing medical records is emphasized to improve understanding of sepsis risk factors and, consequently, to enhance prevention measures.

Furthermore, the relevance of research focused on describing the epidemiological profile of sepsis is highlighted, to assist in guiding care, fostering new investigations into the syndrome, and supporting the development of new health policies aimed at the early detection of risk factors and the implementation of early interventions, so that there is a decrease in morbidity and mortality rates.

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AUTHORS' CONTRIBUTIONS

Djúlia Raissa Seitz contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics. **Gilmar Godinho dos Santos Azevedo** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics. **Géssica Tuani Teixeira** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics. **Franciele Nascimento Santos Zonta** contributed to project management, bibliographic research, abstract writing, methodology, discussion, interpretation and description of results, conclusions, review, and statistics. **Stefany de Oliveira** contributed to abstract writing, data collection, review, and statistics. **Allan Pantano** contributed to data collection and statistics. **Géssica Tuani Teixeira** contributed to project management, fundraising, bibliographic research, review, and statistics. **Djúlia Raissa Seitz, Gilmar Godinho dos Santos Azevedo,** and **Géssica Tuani Teixeira** contributed to project management, bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Original Article

Retrospective study of the impact of KPC and NDM genes on multidrug-resistant infections: in a reference hospital in Piauí, Brazil

Estudo retrospectivo do impacto dos genes KPC e NDM em infecções multirresistentes: em um hospital de referência no Piauí, Brasil

Estudio retrospectivo del impacto de los genes KPC y NDM en infecciones multirresistentes: en un hospital de referencia en Piauí, Brasil

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ABSTRACT

Background and Objectives: *Klebsiella pneumoniae carbapenemase* (KPC) and *New Delhi metallo-beta-lactamase* (NDM) carbapenemases confer resistance to last-line antibiotics, compromising treatment and worsening clinical outcomes. This retrospective and descriptive study aimed to analyze the frequency of multidrug-resistant bacteria in cultures from patients admitted to a reference hospital in Piauí, Brazil, and their correlation with patient outcomes, including affected hospital sectors, clinical progression, and length of stay. **Methods:** Conducted in a reference tertiary hospital and through data analysis covering the period from January 2021 to December 2022, it highlights the prevalence and resistance mechanisms of bacterial species, with an emphasis on the KPC and NDM genes. **Results:** KPC was predominantly found in *Pseudomonas aeruginosa* and *K. pneumoniae*, whereas NDM was mainly detected in *K. pneumoniae* and *Serratia marcescens*. Some species, particularly *K. pneumoniae*, exhibited dual resistance genes. The study revealed higher mortality rates when both KPC and NDM genes were present: 45.83% for KPC, 43.75% for NDM, and 65.71% for infections with both genes. It also explored hospital stay lengths, showing KPC infections averaged 58.9 days, NDM infections 69 days, and dual gene infections 49 days. **Conclusion:** This research provides critical insights into the challenges of antibiotic-resistant organisms in hospitals, underscoring the need for effective patient management and resource allocation strategies. To the best of our knowledge, this study uncovers the first documented cases of NDM gene infections in Piauí.

Keywords: *Antibiotic resistance. Resistance genes. Klebsiella pneumoniae. Outcome Assessment. Health Care.*

RESUMO

Justificativa e Objetivos: As carbapenemases *Klebsiella pneumoniae carbapenemase* (KPC) e *metalo-beta-lactamase de Nova Delhi* (NDM) conferem resistência a antibióticos de última linha, comprometendo o tratamento e agravando os desfechos clínicos. Este estudo retrospectivo e descritivo teve como objetivo analisar a frequência de bactérias multirresistentes em culturas de pacientes internados em um hospital de referência no Piauí, Brasil, e sua correlação com os desfechos dos pacientes, incluindo setores afetados, evolução clínica e tempo de internação. **Métodos:** Realizado em um hospital terciário de referência e por meio de análise de dados do período de janeiro de 2021 a dezembro de 2022, o estudo destaca a prevalência e os mecanismos de resistência das espécies bacterianas, com ênfase nos genes KPC e NDM. **Resultados:** O mecanismo de resistência KPC foi predominantemente encontrado em *Pseudomonas aeruginosa* e *K. pneumoniae*, enquanto o NDM foi identificado principalmente em *K. pneumoniae* e *Serratia marcescens*. Algumas espécies, particularmente *K. pneumoniae*, exibiram genes de resistência dupla. O estudo revelou taxas de mortalidade mais altas quando ambos os genes KPC e NDM estavam presentes: 45,83% para KPC, 43,75% para NDM e 65,71% para infecções com ambos os genes. A pesquisa também explorou a duração das internações hospitalares, mostrando que infecções por KPC tiveram uma média de 58,9 dias, infecções por NDM 69 dias e infecções com genes duplos 49 dias. **Conclusão:** Esta pesquisa fornece insights críticos sobre os desafios dos organismos resistentes a antibióticos em hospitais, sublinhando a necessidade de estratégias eficazes de gerenciamento de pacientes e alocação de recursos. Até onde sabemos, este estudo revela os primeiros casos documentados de infecções pelo gene NDM no Piauí.

Descritores: *Resistência a antibióticos. Genes de resistência. Klebsiella pneumoniae. Avaliação de Resultados em Cuidados de Saúde. Atenção à Saúde.*

RESUMEN

Justificación y Objetivos: Las carbapenemasas *Klebsiella pneumoniae carbapenemasa* (KPC) y *metalo-beta-lactamasa de Nueva Delhi* (NDM) confieren resistencia a los antibióticos de última línea, lo que compromete el tratamiento y empeora los resultados clínicos. Este estudio retrospectivo y descriptivo tuvo como objetivo analizar la frecuencia de bacterias multirresistentes en cultivos de pacientes ingresados en un hospital de referencia en Piauí, Brasil, y su correlación con los desenlaces de los pacientes, incluyendo los sectores afectados, la evolución clínica y el tiempo de estancia. **Métodos:** Realizado en un hospital terciario de referencia y mediante análisis de datos del período de enero de 2021 a diciembre de 2022, el estudio destaca la prevalencia y los mecanismos de resistencia de las especies bacterianas, con énfasis en los genes KPC y NDM. **Resultados:** KPC se encontró predominantemente en *Pseudomonas aeruginosa* y *K. pneumoniae*, mientras que NDM se identificó principalmente en *K. pneumoniae* y *Serratia marcescens*. Algunas especies, particularmente *K. pneumoniae*, exhibieron genes de resistencia dual. El estudio reveló tasas de mortalidad más altas cuando estaban presentes ambos genes KPC y NDM: 45,83% para KPC, 43,75% para NDM y 65,71% para infecciones con ambos genes. También se exploraron las duraciones de las estancias hospitalarias, mostrando que las infecciones por KPC tuvieron un promedio de 58,9 días, las infecciones por NDM 69 días y las infecciones con genes duales 49 días. **Conclusiones:** Esta investigación proporciona información crítica sobre los desafíos de los organismos resistentes a antibióticos en hospitales, subrayando la necesidad de estrategias efectivas de manejo de pacientes y asignación de recursos. Hasta donde sabemos, este estudio revela los primeros casos documentados de infecciones por el gen NDM en Piauí.

Palabras Clave: *Resistencia a antibióticos. Genes de resistencia. Klebsiella pneumoniae. Evaluación de Resultado en la Atención de Salud. Atención a la Salud.*

INTRODUCTION

Multidrug-resistant organisms are defined as species with acquired insensitivity to at least one agent in 3 or more different classes of antimicrobials, responsible for an increasing number of hospital- and community-acquired infections.[1] In this context, there is an impact on mortality rates, leading to increased treatment costs, hospitalisation, diagnostic tests, and therapeutic challenges. It is estimated that approximately 20% to 30% of hospital-acquired infections in developing countries are associated with bacteria resistant to multiple classes of antimicrobials, which directly impacts mortality rates and increases the costs of treatment, hospitalization, diagnostic testing, and therapeutic challenges.[1]

These infections are treated with antimicrobials; however, the excessive, inappropriate, and unnecessary use of these agents has contributed to high bacterial resistance rates, progressively rendering treatments ineffective.[2,3] A significant milestone was the spread of the pandemic caused by SARS-CoV-2, where the widespread use of antimicrobial therapies as part of the clinical care package was observed, increasing resistance rates.[4-7]

In Brazil, Gram-negative bacilli producing the NDM-1 enzyme have been detected with alarming frequency since 2013, with 81 clinical isolates reported across nine states and 11 bacterial species—all confirmed as multidrug-resistant.[8] Colistin and amikacin remain among the few antibiotics with activity against these strains, highlighting the scarcity of effective therapeutic options.

Monitoring and early intervention with appropriate treatment in healthcare units are fundamental strategies to prevent and control the spread of these bacteria.[9] Thus, epidemiological surveillance and mandatory reporting of suspected cases of healthcare-associated infections become essential mechanisms for the control of Healthcare-Associated Infections (HAIs) enabling the investigation of outbreak causes, the identification of locations with higher occurrences of these infections, and the prevention of new cases.[10-12]

In light of the above, the present study aimed to analyze the frequency of multidrug-resistant bacteria in cultures from patients at a reference hospital in Piauí, Brazil, and their correlation with patient outcomes, including affected hospital sectors, clinical progression, and length of stay.

Given the above, this study aimed to describe the frequency of multidrug-resistant bacteria isolated from clinical cultures of patients admitted to a referral hospital in the state of Piauí, Brazil, and to examine their correlation with patient outcomes, including affected hospital sectors, clinical evolution, and length of hospital stay.

METHODS

Study Design

This was a retrospective descriptive study conducted over 2 years, based on records from January 2021 to December 2022. The primary objective of this investigation was to elucidate the frequency of multidrug-resistant bacteria in the mentioned healthcare unit, analyse the hospitalisation time of diagnosed patients, and identify the most affected sectors.

Study Setting

The research was conducted at the University Hospital of the Federal University of Piauí, covering the pharmacy and microbiology laboratory sectors. It is noteworthy that this hospital is a tertiary referral centre in the state, offering both outpatient and inpatient services, with a total of 190 beds, incorporating clinical and surgical care in regular and intensive care units. The institution is structurally organized into four inpatient nursing stations, an outpatient care area, and an Intensive Care Unit (ICU). Nursing Station 1 is dedicated to orthopedic and neurosurgical patients; Nursing Station 2 focuses on oncology patients; Nursing Station 3 serves internal medicine (clinical) patients and Nursing Station 4 accommodates surgical patients. Additionally, during the Covid-19 pandemic, a separate ICU was established for patients with SARS-CoV-2 infection.

The study covered all inpatient units (including wards and ICUs) where cultures were routinely collected and processed by the microbiology laboratory.

Study Population

All hospitalized patients from whom microbiological cultures were collected and who had confirmed hospital-acquired infections caused by multidrug-resistant bacteria were eligible for inclusion regardless of age or sex, as long as they met the criteria for nosocomial infection (i.e., culture collected ≥48 hours after admission).

Inclusion Criteria

Patients admitted to HU-UFPI between January 2021 and December 2022 who had a positive culture for multidrug-resistant bacteria, with microorganisms identified as hospital-acquired (cultures collected ≥48 hours after admission).

Exclusion Criteria

Community-acquired infections, defined as positive cultures obtained within the first 48 hours of admission; duplicate isolates, considering only the first isolate of each species per patient; and cultures with insufficient data for analysis, such as missing information on clinical evolution or sector of admission. No sampling

strategy was applied, as all eligible cases during the study period were included, and no patient-identifiable information was used at any stage of data collection.

Data Collection

Microbiological data are routinely collected from patient records, laboratory test results, and local surveillance systems. Samples are collected and sent to the microbiology laboratory, where it is inoculated into culture media and analysed by the VITEK® 2 COMPACT, an automated system for routine microbial identification and antibiogram testing, standardised according to BrCAST based on the identified species.13 These data are linked to the patient's history, resulting in a spreadsheet with diagnostic information that will be manually entered into the hospital's IT system. The investigation of resistance genes is carried out for five types: KPC (*Klebsiella pneumoniae carbapenemase*), NDM (New Delhi metallo-beta-lactamase), OXA-48 (OXA-48 beta-lactamase), IMP (Imipenemase), and VIM (Verona imipenemase) through immunochromatographic testing (VITEK®2 COMPACT - bioMérieux, France). Although the detection of resistance genes included KPC, NDM, OXA-48, IMP, and VIM, only KPC- and NDM-producing isolates were identified during the study period. No samples tested positive for OXA-48, IMP, or VIM. Therefore, while all carbapenemases were considered eligible for inclusion, the final dataset contained only cases involving KPC and NDM.

Data such as admission location, identified microorganism, case outcome, culture site, among others, were processed to generate overall secondary indicators, including: i) prevalence of microorganisms in the hospital, ii) outcomes of patients with the clinical condition of multidrug-resistant infection, iii) number of hospitalisation days when an infection is diagnosed, iv) mortality rate, and v) sector with the highest number of identified cases.

To avoid data duplication, only the first isolate per species per patient was considered. Secondary infections or subsequent isolates from the same hospitalization were excluded.

Data Analysis

Data analysis was exclusively descriptive. Data were extracted from tables provided by the hospital's microbiology department and manually compiled into Microsoft Excel® 2019 spreadsheets. Categorical variables, such as bacterial species, presence of resistance genes, hospitalization unit, and patient clinical outcomes, were analyzed using simple sums and expressed as absolute and relative frequencies (n and %). Confidence intervals for proportions were calculated using the Agresti–Coull method. No hypothesis testing was performed, as the study was not inferential in nature.

The data processing was carried out using the R programming language.

Ethical Considerations and Other Information

The project was duly reviewed and approved by the Ethics Committee of HU-PI under authorisation number 66872123.6.0000.8050. During the preparation of this work the authors used ChatGPT-3.5 as a writing assistance tool. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

RESULTS

The study assessed the prevalence of resistant bacterial infections and the distribution of resistant species among 187 patients admitted to the hospital from January 2021 to December 2022. Among the 187 samples that received such a diagnosis, urine culture yielded 62 positive results, while blood culture recorded 57, being the collection sites with the highest number of diagnoses (Table 1). In 2021, a higher prevalence is evident with 113 cases compared to 2022, which had only 74 identified cases (Figure 1).

Table 1. Type of isolated culture and number of bacterial samples with any type of resistance gene.

Bacteria found in the type of culture	Number of cases found
Urine culture	62
Blood culture	57
Wound secretion	31
Tracheal aspirate	6
Rectal swab	6
Stool culture	5
Catheter tip	4
Cerebrospinal fluid (CSF)	3
Ascitic fluid	1
Bacteriological	1
Abdominal collection	1
Tendon	1
Pleural effusion	1
Bronchoalveolar lavage (BAL)	1
Tissue biopsy	1

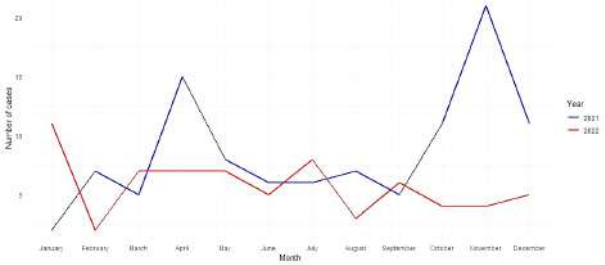

Figure 1. Number of Identified Cases of Multidrug-Resistant Bacteria. Monthly distribution of identified cases of multidrug-resistant bacteria at the Piauí University Hospital in 2021 and 2022.

Nursing Station 3 allocates patients from the medical clinic, and among all stations, it is the one that yielded the highest number of positive results for multidrug-resistant infections, totaling 59 identified patients. The ICU, on the other hand, is the location with the highest prevalence of this clinical condition, registering 61 cases in the investigated years, highlighting the need for specific measures for prevention and control, particularly in environments with critically ill patients.

The categorisation of bacterial species into different resistance mechanisms demonstrated that the KPC gene was present in the following species: *Pseudomonas aeruginosa* with a total of 24 cases, along with *K. pneumoniae* with a total of 20 cases, making the two species the most prevalent, followed by the species *Serratia marcescens* (2 cases), *Proteus hauseri* (1 case), *Escherichia coli* (1 case) and *Citrobacter koseri* (1 case) with a lower prevalence of this resistance enzyme (Figure 2). The NDM gene was found in the following species: *K. pneumoniae* with a total of 79 cases, being the most prevalent, followed by *S. marcescens* with of 7 cases, and the species *Enterococcus faecium* (1 case), *Enterococcus spp*. (2 cases), *Enterobacter cloacae* (2 cases) and *K. ozaenae* (1 case) also found with the gene but in smaller quantities (Figure 2). Importantly, a single patient could harbour isolates carrying more than one resistance gene, meaning that cases are not mutually exclusive across resistance mechanisms.

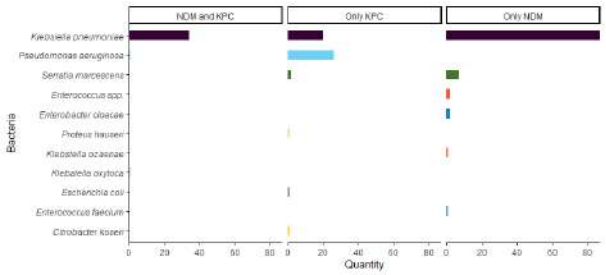

Figure 2. Prevalence of bacteria by type of resistance gene. Quantity of bacterial species found separated by type of resistance mechanism, being with only KPC (enzyme that confers resistance to carbapenems), only with NDM (enzyme belonging to the class of metallo-beta-lactamases that confers resistance to various antimicrobials, including carbapenems), and microorganisms that have both types of genes together.

In the studied samples, it was possible to verify that some species contain both resistance genes, conferring a high degree of resistance. The most prevalent species with both resistance genes was *K. pneumoniae* with a total of 20 cases, followed by *P. aeruginosa* and *K. oxytoca*, with at least one case of each species (Figure 2).

The progression of patients according to the resistance gene was also investigated. Analysing the investigated cases, the mortality rate was observed, where, upon acquiring KPC, the mortality rate was 45.83% [32.6% - 59.7%]. Among cases with the NDM gene, the mortality rate was 43.75% [34.3% - 53.7%]. When analysing cases where both resistance genes were present in the same infection, the chance of progressing to death increased to 65.71% [49.1% - 79.2%], highlighting a higher mortality rate and worse outcome for this type of infection (Figure 3).

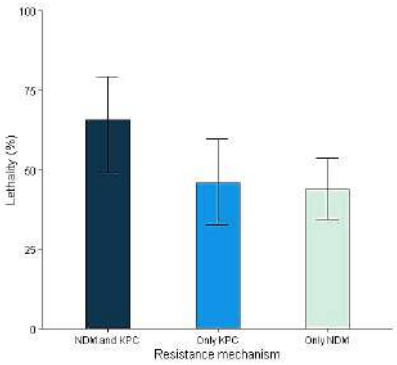

Figure 3. Mortality Rates by Resistance Gene. Lethality (%) among hospitalized patients, according to the type of investigated resistance gene.

Additionally, it was possible to analyse the length of hospital stay according to the type of acquired infection (Figure 4). KPC exhibited the highest number of cases with an average hospitalisation period of 59 days [34.5 - 73], when the condition progressed to hospital discharge and 51 days [29.5 - 75] for cases that evolved to death. In the case of NDM, the average length of hospitalisation varies according to the patient's prognosis; when linked to hospital discharge, the average time is 69 days [36 - 85.25], while for cases resulting in hospital death, the average is 46 days [30.25 - 54]. On the other hand, when investigating infections with both resistance genes, the average length of hospital stay was 49 days [24.75 - 78] for cases that were discharged and 50 days [21.5 - 85] for those that resulted in death (Figure 4).

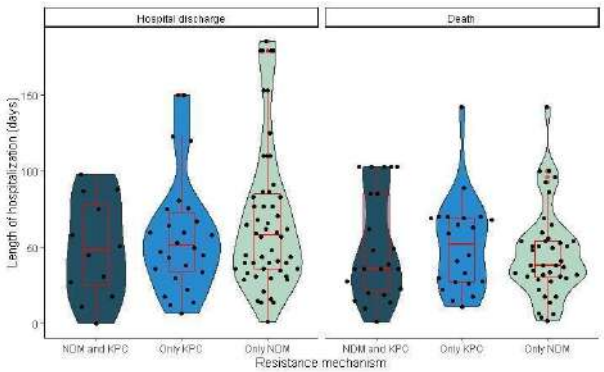

Figure 4. Average Length of Hospital Stay. Average number of days patients were hospitalized based on the type of resistance gene and patient outcome (discharge or death).

DISCUSSION

In this study, it was possible to identify a higher chance of death when a species acquires both KPC and NDM strains, which may be related to the restriction

that the patient faces regarding treatment alternatives for the condition. Furthermore, we had a greater number of cases reported in 2021, with a high prevalence of *K. pneumoniae*, containing the KPC resistance gene and an average number of days of hospitalisation reaching 58.9 days.

The diagnosis of an infectious condition is based on clinical, epidemiological, and laboratory results. Among these epidemiological characteristics, both the most prevalent bacteria and the sensitivity profile of the hospital's microorganisms significantly contribute to the formulation of empirical treatment protocols when the patient's health status cannot afford the wait for culture test results.[14] This underscores the fundamental importance of establishing a comprehensive database with the hospital's or region's historical clinical data. Our data play a crucial role in helping to develop effective empirical treatment protocols.

It is worth highlighting the high influence of hospital infections on management costs, as they drastically impact the period of hospitalisation. For example, the average length of stay researched within the hospital varies according to the type of infection, reaching, in some cases, such as bacteria with the NDM gene, around 69 days. During this period, considering the length of stay, the consumption of antibiotics, the duration of isolation, laboratory tests, and human resources, these are all costs generated by this clinical condition. Reducing infection rates can play a fundamental role in mitigating the economic challenges faced by public hospitals, in addition to benefiting the reduction of the patient's hospitalisation time, increasing bed turnover rates, and the availability of places in ICUs.

Since the 1980s, pharmaceutical companies have gradually shifted focus from antimicrobial research to concentrate on drug therapy for chronic non-communicable diseases.[15] Carbapenems, such as meropenem and imipenem, are a class of beta-lactam antibiotics with a broad spectrum of action, being effective against many gram-positive and gram-negative bacteria and generally reserved for the treatment of severe infections.[16,14] Due to increasing resistance to third-generation cephalosporins, fluoroquinolones, and aminoglycosides, carbapenems have progressively established themselves as the main option for potentially fatal infections by multidrug-resistant *E. coli.*[16] As carbapenems become an increasingly common therapeutic choice, it is crucial to establish monitoring programmes to prevent the emergence and spread of resistance to these drugs, especially as the emergence of new antibiotics has been increasingly scarce.

Both KPC and NDM genes are carbapenem resistance genes; they encode an enzyme capable of hydrolysing beta-lactam antibiotics, including carbapenems. KPC-like enzymes are capable of hydrolysing all β-lactams, and strains harbouring this gene often acquire resistance to fluoroquinolones, aminoglycosides, and trimethoprim-sulfamethoxazole, creating multidrug-resistant organisms.[17] On the other hand, bacteria carrying the NDM enzyme are highly transmissible and, due to their dissemination through environmental sources in community settings in low-income countries, they are currently considered endemic worldwide. Treatment becomes a challenge due to the limited availability of effective antimicrobials for these clinical conditions, sometimes requiring a combination of antimicrobials to obtain an efficient result.[15] However, this increases the risk of side effects and the possibility of selecting new resistant strains.[18] Therefore, the presence of both strains increases the patient's morbidity and mortality.

Regarding prevalence, the results found showed a high prevalence of *K. pneumoniae* in the three investigated forms of resistance. This is the most common species found in hospital infections, especially in intensive care units and in patients with compromised immune systems. This is partly due to its ability to colonise hospital surfaces and survive in these environments for long periods.[19] Infections occur due to an imbalance between the host's immune defences and the pathogen, which, upon invading the patient, trigger local reactions that initiate the infectious process. In patients hospitalised in the ICU, the risk of this imbalance is much higher due to underlying conditions, compromised immunity, extensive use of antibiotics, and exposure to invasive devices. The invasive procedures often used for treatment, such as tracheal intubation, mechanical ventilation, and intravascular catheters, become susceptible surfaces for the colonisation of enterobacteria, justifying this increased vulnerability to nosocomial infections in ICU patients.[20] Examples of this include bloodstream infections by bacteria and urinary infections, which are commonly related to catheter use. [20]

In addition to the ICU, Nursing Station 3, responsible for medical clinic patients, also had a notably high prevalence of multidrug-resistant infections, with 59 cases identified during the study period. This station is the only one equipped with isolation beds, which likely contributes to the higher absolute number of cases, as these beds are designated for patients with known or suspected resistant infections. The high number of infections can also be attributed to the profile of patients admitted to this unit: frequently polymorbid, elderly, or immunosuppressed, with longer hospital stays and greater exposure to antibiotics—well-known risk factors for colonization and infection by resistant pathogens.[1] This reinforces the importance of infection control protocols in clinical wards.

Another data point studied was that, when comparing the years 2021 and 2022, a significant reduction in the

number of cases presented with multidrug-resistant infection was suggested, going from 113 patients to 74 patients in 2022. In this last year, Brazil began its vaccination campaign against Covid-19 in the second half of January 2021, increasing the vaccination rate in the country.[21] As already reported in other studies, individuals who were not fully vaccinated or who did not receive any vaccine against Covid-19 had an excess risk of hospitalisation and death from the disease.[22] In this context, the introduction of the vaccine triggered a significant transformation in the patterns of hospital admissions, resulting in a notable reduction in the number of infections, justifying this reduction in cases.[23]

This study provides unprecedented data on the epidemiology of multidrug-resistant bacteria in the state of Piauí, Brazil, filling an important gap in national surveillance. To our knowledge, existing research on the distribution of NDM-1-producing Gram-negative bacteria in the Brazilian clinical setting did not include data from the state of Piauí. [24]

Our study has some limitations. First, the hospital only evaluates specific resistance genes—NDM, KPC, OXA-48, IMP, and VIM—and restricts its analysis to bacteria, disregarding other resistant microorganisms. Furthermore, it was not possible to identify any readmissions of patients to other healthcare institutions after their initial hospitalization. The high prevalence of *K. pneumoniae* and the identification of resistance genes such as NDM, KPC, and dual combinations highlight a critical scenario for infection control and antimicrobial stewardship. The findings reveal a worrying association between the presence of these genes and adverse clinical outcomes, including high mortality rates and reduced hospital stays resulting from death. The detection of combined resistance genes further highlights the need for targeted interventions, given their clinical impact.

Although the analysis was limited to bacterial isolates, the data reinforce the urgent need for continued molecular surveillance, expanded rapid diagnostic capabilities, and strengthened regional health monitoring systems. Furthermore, the limited scope of genotypic testing in the hospital setting highlights the importance of expanding molecular diagnostics to encompass other emerging determinants of resistance and neglected microbial species.

This contribution is crucial to filling existing gaps in understanding the spread of these resistant strains in the Brazilian clinical setting. This information may be useful for research aimed at improving antimicrobial stewardship and developing effective strategies to control the spread of resistant bacteria.

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AUTHORS' CONTRIBUTIONS

Ruana Stephany Macedo Santos contributed to the literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, preparation of tables, conclusions, revision, and statistical analysis. **Eduardo Lima de Sousa** contributed to project administration, literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, conclusions, revision, and statistical analysis. **Thallyta Maria Tavares Antunes** contributed to writing of the abstract, revision, and statistical analysis. **José Felipe Pinheiro do Nascimento Vieira** contributed to writing of the abstract, revision, and statistical analysis. **Samara Belchior Gaído** contributed to writing of the abstract, revision, and statistical analysis. **Bruno Guedes Alcoforado Aguiar** contributed to project administration, literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, conclusions, revision, and statistical analysis.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

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Original Article

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Higiene de manos en una institución de enseñanza superior en Salvador, BA, Brasil: conocimiento de los estudiantes

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ABSTRACT

Background and Objectives: Hand hygiene (HH) is a pillar of quality, safety and infection prevention in health services and the object of interest to Higher Education Institutions offering undergraduate health programs. The purpose of this study was to investigate the knowledge of undergraduate nursing students on the subject of HH with a view to contributing to health safety. **Methods:** This is a cross-sectional study with undergraduate nursing students from a public institution located in the city of Salvador, BA. Variables studied: academic characterization and student performance. Data collection: direct observation of the HH technique and application of a form. **Results:** The sample consisted of 82.9% of the students enrolled. Predominance of female students (84%), aged 18 to 24 years (66.2%). Of the six steps recommended for the HH technique, only 3.6% of the students performed all the steps. A statistical correlation was identified between the semester of study and increased adherence to correct HH technique steps. Rubbing the palms of hands together interlacing fingers was the most performed step, most students (40.8%) sanitized their hands in less than 20 seconds, and although 58% identified the five moments for HH during health care, 87% did not know the recommended time for HH. **Conclusion:** While HH technique proficiency improved as students progressed through the semesters, overall knowledge and performance of HH techniques remained inadequate. These findings suggest that the institution must implement multidimensional teaching strategies to enhance the acquisition and retention of these essential skills in the studied program.

Keywords: *Hand hygiene. Nursing. Infection control.*

RESUMO

Justificativa e Objetivos: A higienização das mãos (HM) é pilar da qualidade, segurança e prevenção de infecções em serviços de saúde e objeto de interesse também das Instituições de Ensino Superior dos cursos de graduação em saúde. Este estudou objetivou investigar o conhecimento dos discentes de Curso de Graduação em Enfermagem acerca da temática da HM, com vista a contribuir para a segurança em saúde. **Métodos:** Estudo transversal, com discentes de Curso de Graduação em Enfermagem de uma Instituição pública localizada na cidade de Salvador, BA. Variáveis estudadas: caracterização acadêmica e desempenho discente. Coleta de dados: observação direta da técnica de HM e aplicação de formulário. **Resultados:** A amostra constou de 82,9% dos alunos matriculados. Predominância de alunos do sexo feminino (84%), idade 18 a 24 anos (66,2%). Dos seis passos recomendados para a técnica de HM, apenas 3,6% dos alunos realizaram todos os passos. Identificou-se correlação estatística entre semestres cursados pelos discentes e aumento na realização dos passos da técnica de HM. A fricção entre as palmas das mãos foi a etapa mais executada; a maioria dos alunos (40,8%) higienizou as mãos em menos de 20 segundos; 58% identificaram os cinco momentos para a HM durante os cuidados em saúde, entretanto, 87% desconhecem o tempo preconizado para HM. **Conclusão:** A despeito da técnica de HM melhorar com o avanço de semestres cursados, os discentes estudados apresentaram conhecimento e técnicas inadequadas de HM, o que sinaliza a necessidade de implementar estratégias multidimensionais de ensino e aprendizagem nessa temática no curso investigado.

Descritores: *Higiene das mãos. Enfermagem. Controle de infecções.*

RESUMEN

Justificación y Objetivos: La higiene de manos (HM) es un pilar de la calidad, la seguridad y la prevención de infecciones en los servicios de salud, y objeto de interés para las instituciones de educación superior que ofrecen programas de salud de pregrado. El propósito de este estudio fue investigar el conocimiento de los estudiantes de enfermería de pregrado sobre el tema de la HM con el fin de contribuir a la seguridad sanitaria. **Método:** Estudio transversal con estudiantes de enfermería de pregrado de una institución pública ubicada en la ciudad de Salvador, Bahia. Variables estudiadas: caracterización académica y desempeño de los estudiantes. Recopilación de datos: observación directa de la técnica de HM y aplicación de un formulario. **Resultados:** La muestra estuvo compuesta por el 82,9% de los estudiantes matriculados. Predominaron las mujeres (84%), con edades comprendidas entre los 18 y los 24 años (66,2%). De los seis pasos recomendados para la técnica de HM, solo el 3,6% de los estudiantes los realizó en su totalidad. Se identificó una correlación estadística entre el semestre de estudio y una mayor adherencia a los pasos correctos de la técnica de HM. Frotarse las palmas de las manos fue el paso más realizado. La mayoría de los estudiantes (40.8%) se desinfectaron las manos en menos de 20 segundos. Si bien el 58% identificó los cinco momentos para la HM durante la atención médica, el 87% desconocía el tiempo recomendado para la HM. **Conclusión:** A pesar de la mejora en la técnica de HH con el avance de los semestres cursados, los estudiantes demostraron conocimientos y técnicas inadecuados de HM. Los hallazgos sugieren que la institución debe implementar estrategias de enseñanza multidimensionales para mejorar la adquisición y retención de estas habilidades esenciales en el programa estudiado.

Palabras Clave: *Higiene de manos. Enfermería. Control de infecciones.*

INTRODUCTION

Hand hygiene (HH) is the primary infection prevention and control measure in healthcare settings, recognized as the cornerstone of quality and patient safety.[1] Although preventable, healthcare-associated infections (HAIs) constitute a public health problem. Data from the World Health Organization (WHO) estimate rates of around 3.5 to 12% in patients from high-income countries and 5.7 to 19.1% in low- and middle-income countries. These indicators are likely to increase due to underreporting of these infections in many countries.[2]

Healthcare-associated infections are mainly transmitted through the contaminated hands of healthcare professionals; consequently, strategies for maintaining clean hands have been one of healthcare's greatest challenges since the era of Ignaz Semmelweis and Florence Nightingale.[1]

The economic burden of HAIs on healthcare systems, especially those with universal access, is enormous, and data on financial costs vary between countries, but equally impact nation-states in their mission to protect their citizens.[3]

In this context, the prevention and control of HAIs should be a priority goal for managers and healthcare professionals. As contaminated hands constitute the main mode of transmission of pathogens within healthcare services, this practice is the key procedure for interrupting the transmission of microorganisms during healthcare.[1-3]

Contaminated hands transmit microorganisms, some of great epidemiological relevance, such as *Clostridium difficile*, vancomycin-resistant *Enterococcus*, or Methicillin-resistant *Staphylococcus aureus*. The contamination of healthcare professionals' hands results directly from contact with patients or indirectly through touching contaminated environmental surfaces.[2,4-7]

Despite its importance, lack of adherence to HH is a reality in healthcare services worldwide and data report adherence rates of approximately 20 to 40%.[1-3,8] In this context, education is central to behavioral change, and since 2009 the WHO has encouraged the updating of curricula in undergraduate health programs with the inclusion of disciplinary components that address the theme of patient safety, prevention of errors and adverse events in healthcare.[7,9-10]

Thus, health curricula at Brazilian Higher Education Institutions must urgently integrate the topic of HH to train professionals committed to patient safety and the prevention of HAIs.

To address this need, the present study aimed to investigate undergraduate nursing students' knowledge of HH to contribute to improved health safety.

METHODS

This is a cross-sectional descriptive quantitative study. It was conducted with undergraduate students of a Nursing Program at a state public university located in Salvador, Bahia, Brazil.

This Nursing Program is part of the Department of Life Sciences at this university, along with other undergraduate health programs: Medicine, Nutrition, Pharmacy, Physiotherapy, and Speech Therapy. Student admission occurs semiannually through a public selection process (university entrance exam), special categories (affirmative action policies), and the Unified Selection System (SISU). This is a full-time program and offers 60 seats annually, 30 in each semester. Its Pedagogical Project foresees the completion of the curriculum in 10 to 14 semesters with a total workload of 4,335 hours. Among the curricular components, this Nursing Program has an elective course entitled "Infection Control and Safety in Health Services", offered as "Special Topics" with a workload of 30 hours, where the topic of HH is addressed.

The convenience sample included all students enrolled in this program, according to the inclusion criteria: age over 18 years, being duly enrolled and attending the program during the data collection period. Exclusion criteria included students on leave due to leave of absence, maternity leave, or medical leave during the data collection period, or students with physical limitations that prevented them from performing the HH technique.

Theoretical and practical knowledge of students about HH was defined as the dependent variable.

Theoretical knowledge was assessed by the number of correct answers obtained in a self-administered questionnaire with six questions. The questions referred to: (i) the concept of HH; (ii) the relationship between the technique and the recommended time for HH; (iii) microbial activity of antiseptic solutions; (iv) indication for the use of alcohol-based antiseptic solution; (v) effectiveness of HH with alcohol solution; and (vi) on the five moments of HH recommended by the WHO (Annex or supplementary material 1).

Practical knowledge was measured by the number of steps recommended by the WHO performed during HH with alcohol solution. Participating students were asked to sanitize their hands with alcohol solution.[7,9] This procedure was observed by trained scholarship holders, who verified and recorded the completion of each of the six steps. Only the number of steps and areas of the sanitized hands were recorded. The sequence of the technique, as recommended by the WHO, was not considered for counting the correct answers.[7,9] The HH time was measured with a stopwatch. The observation data were recorded on an observation form (Appendix A or supplementary material 1).

Data relating to the academic characterization of participants were collected as independent variables.

Academic characterization was performed based on the information provided by students during data collection. The information gathered referred to sex at birth, age, current semester, and practical experience in health services through curricular or extracurricular internships. There were also open-ended questions inquiring about attendance in the "specific curricular component on Healthcare-Associated Infection (HAI)" course and another about the existence of any "curricular component in which the topic of HH in health services was addressed". Data were collected by four students previously trained by the researchers for 60 days. The collection took place in person between August and November 2023 in a specific room on the premises of this higher education institution. Two stages were carried out sequentially: 1st: direct observation of the HH technique using an alcoholic preparation (liquid solution), and 2nd: application of a self-administered questionnaire with semi-structured questions about the students' characterization and theoretical knowledge about HH. The HH technique using an alcohol-based solution was selected for its ease of observation, eliminating the need for a sink with soap and water.

Data collection appointments were scheduled in advance, on specific days, times, and locations according to a schedule created by the data collectors. After processing and recoding, data were processed using the IBM SPSS (Statistical Package for the Social Sciences) software. Initially, data on sex, age, current semester, experience in healthcare services, steps performed for HH, number of steps performed, correct answers to knowledge questions, and total number of correct answers were presented as absolute and relative frequencies. The range, mean, median, and standard deviation were used to assess the time students spent performing HH.

The normality of data distribution for correlation was assessed using the Shapiro-Wilk test. Given the lack of normality in the distribution of variables, the Spearman's correlation coefficient was used to analyze the relationship between the semester, the number of correct answers, and the correct steps. The significance level adopted was 5% ($p < 0.05$).

Each participating student signed the Informed Consent Form (ICF) before data collection. This study was submitted to Plataforma Brasil under CAAE No. 63764522.9.1001.0057 and was approved by the Research Ethics Committee of the Universidade do Estado da Bahia on February 24, 2022, according to Opinion No. 5.261.425.

RESULTS

This study included 169 of the 204 enrolled and eligible students of the Undergraduate Nursing Program, representing a sample of 82.8% of the sample universe.

The sociodemographic characteristics and semesters attended by the students participating in this study are presented below (Table 1).

Table 1. Sociodemographic characteristics and current semester of students in the Undergraduate Nursing program at the Higher Education Institution. Salvador, BA. Brazil. 2023.

Variables	N (%)
Sex	
Female	142 (84)
Male	27 (16)
Age range	
18 to 24 years	112 (66.2)
≥ 25 years	57 (33.7)
Current semester	**Participants/enrolled**
1º Semester	19/23 (82.6)
2º Semester	13/16 (81.2)
3º Semester	10/14 (71.4)
4º Semester	11/18 (61.1)
5º Semester	18/19 (94.7)
6º Semester	35/43 (81.3)
7º Semester	15/18 (83.3)
8º Semester	16/19 (84.2)
9º Semester	13/14 (92.8)
10º Semester	19/21 (90.4)
Practical experience in healthcare*	
Yes	120 (71)
No	49 (29)

Abbreviation: *Curricular component with practical experience in health services.

The HH technique is demonstrated below, based on non-participant observation.

Table 2. Steps of the hand hygiene technique performed by students, according to direct observation. Higher Education Institution. Salvador (BA). Brazil. 2023.

Hand hygiene steps	N (%)
Rub the palms of hands together with fingers interlaced	
Yes	164 (97)
No	05 (2.9)
Rub the back of each hand with the opposite palm, interlacing fingers	
Yes	136 (80,5)
No	33 (19.5)
Rub palms together with fingers interlaced	
Yes	58 (34,3)
No	111 (65.7)
Interlock fingers and rub the backs of the fingers against the opposing palms	
Yes	60 (35.5)
No	109 (64.5)
Rub each thumb rotationally, clasped in the opposite palm	
Yes	117 (69.2)
No	52 (30.8)
Rub fingertips and nails in the opposite palm in a rotational movement	
Yes	86 (50.9)
No	83 (49.1)

The following shows the number of steps in the HH technique performed by students during direct observation.

Table 3. Number of steps in the hand hygiene technique performed by students according to the current semester of the program. Higher Education Institution. Salvador, BA. Brazil, 2023.

Current semester	Number of HH steps performed						
	Step 1 N (%)	Step 2 N (%)	Step 3 N (%)	Step 4 N (%)	Step 5 N (%)	Step 6 N (%)	Total number of students per semester N (%)
1st semester	2 (1.2)	7 (4.14)	6 (3.6)	3 (1.8)	1 (0.6)	0 (0.0)	19 (11.2)
2nd semester	2 (1.2)	5 (3.0)	3 (1.8)	1 (0.6)	2 (1.2)	0 (0.0)	13 (7.7)
3rd semester	0 (0.0)	1 (0.6)	8 (4.7)	1 (0.6)	0 (0.0)	0 (0.0)	10 (5.9)
4th semester	0 (0.0)	2 (1.2)	5 (3.0)	3 (1.8)	1 (0.6)	0 (0.0)	11 (6.5)
5th semester	0 (0.0)	2 (1.2)	8 (4.7)	6 (3.6)	2 (1.2)	0 (0.0)	18 (10.7)
6th semester	1 (0.6)	1 (0.6)	11 (6.5)	11(6.5)	9 (5.3)	2 (1.2)	35 (20.7)
7th semester	0 (0.0)	1 (0.6)	3 (1.8)	8 (4.7)	2 (1.2)	1 (0.6)	15 (8.9)
8th semester	0 (0.0)	0 (0.0)	0 (0.0)	7 (4.14)	6 (3.6)	3 (1.8)	16 (9.5)
9th semester	0 (0.0)	1 (0.6)	1 (0.6)	4 (2.4)	7 (4.14)	0 (0.0)	13 (7.7)
10th semester	0 (0.0)	1 (0.6)	1 (0.6)	11 (6.5)	6 (3.6)	0 (0.0)	19 (11.2)
Total number of steps performed	5 (3.0)	21 (12.4)	46 (27.2)	55 (32.5)	36 (21.3)	6 (3.6)	169 (100)

When we correlated the number of steps performed by these students and their current semester, a rho of 0.531 (p<0.0001) was found, indicating a moderate correlation between the number of steps performed and the current semester in which the student is enrolled (Figure 1).

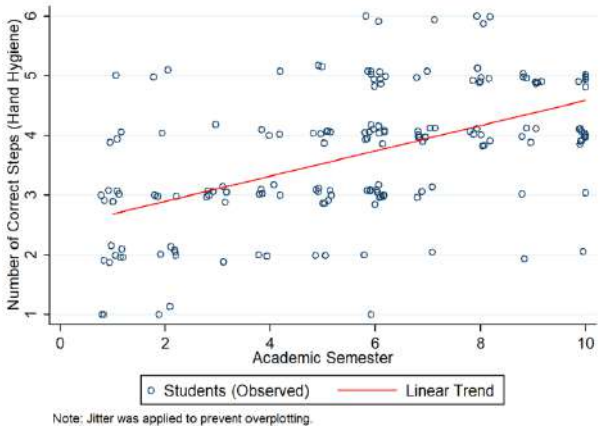

Figure 1. Correlation between the students' current semester X number of hand hygiene steps performed. Undergraduate Nursing Program. Higher Education Institution. Salvador, BA.

During direct observation, the time students spent performing HH with an alcohol solution ranged from seven to 63 seconds, mean of 23.2 seconds, median of 22 seconds, and a standard deviation of 9.8 seconds.

When categorizing the time, 40.8% (69) of the students performed HH in less than 20 seconds, 39.6% (67) within the recommended time, between 20 and 30 seconds; and 19.5% (33) exceeded 30 seconds.

The students' theoretical knowledge about HM is presented below (Table 4).

Table 4. Students' knowledge about the hand hygiene practice. Higher Education Institution. Salvador, BA. Brazil. 2023.

Knowledge Questionnaire Questions	N (%)
Concept of hand hygiene	
Correct	97 (57.3)
Incorrect	72 (42.6)
Relationship between hand hygiene technique and recommended time for its performance	
Correct	22 (13.0)
Incorrect	147 (86.9)
Microbial activity of alcohol-based antiseptic solution	
Correct	24 (14.2)
Incorrect	145 (85.7)
Indication of rubbing with alcohol-based antiseptic solution in hand hygiene	
Correct	116 (68.6)
Incorrect	53 (31.3)
On the effectiveness of hand hygiene with alcohol-based rubbing	
Correct	46 (27.2)
Incorrect	123 (72.7)
5 moments for hand hygiene recommended by the WHO	
Correct	98 (57.9)
Incorrect	71 (42.0)

Regarding the open-ended questions in the questionnaire, 101 (59.7%) students responded they had taken a specific component on HAIs and 99 (58.5%) stated there was a component that addressed the topic of HH. When describing this component, they cited Biosafety (18); Microbiology (1), Pathology (1), Care Process (1), Infectious Diseases and Immunization (29), Infection Control and Safety in Health Services (49).

Of the six questions related to students' knowledge of the topic of HH, out of a total of 169 evaluated, none managed to answer all six questions correctly. The average number of correct answers was 2.38, ranging from 0 to five questions. The median was two and the standard deviation was 1.16.

It was found that 57.3% of students are familiar with the concept of HH, 68.6% with the indication for alcohol-based hand rubbing preparation, and 58% are familiar with the five moments for HH recommended by the WHO during healthcare.

When comparing the number of correct answers to the questions in relation to the current semester, a rho of 0.291 (p=0.0001) was identified, indicating a weak correlation between the number of correct answers and the current semester of the student (Figure 2).

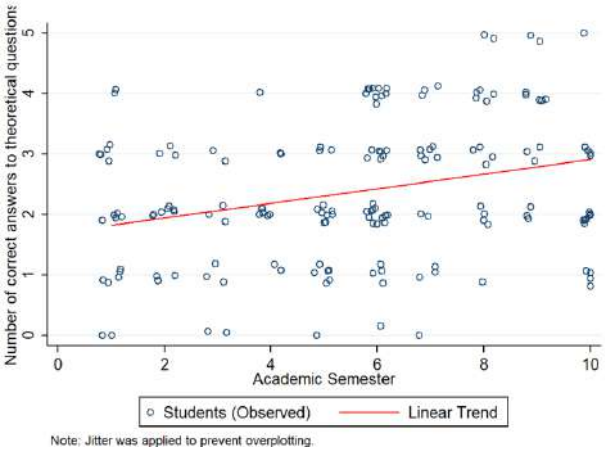

Figure 2. Correlation between students' current semester and number of correct answers to theoretical questions on hand hygiene. Undergraduate Nursing Program. Higher Education Institution. Salvador, BA.

DISCUSSION

The sociodemographic distribution of students in this Undergraduate Nursing Program shows a predominance of those aged 18 to 24 years (66.2%), mostly female (84%), reflecting the profile of Brazilian nursing, a relatively young workforce, in which 38% of professionals are under 35 years of age and 87% are female.[11]

The variable "academic characterization" sought to correlate the profile of the students and the inclusion of the HH topic in the theoretical-practical components of this Program. It was found that 59.7% of the students took a specific component on HAIs and 58.5% of these were exposed to the theoretical constructs of HH during participation in various other curricular components, showing that this Undergraduate Program has a curriculum that responds to the demands of the WHO. This organization calls upon its member countries to "improve education in patient safety, its principles and approaches", considering the need for training healthcare professionals in line with the accelerated pace of the various challenges in the healthcare sector and its demands for workforce change.[12]

The sample included students from all semesters of the Program, with the highest frequency of students from the fifth, ninth, and 10th semesters, (94.7%, 92.8%, and 90.4%), of whom 71% had practical experience in healthcare services and 29% had no curricular practice. In other words, a student body where the majority had been exposed to various theoretical curricular components and with practical clinical experience, conditions that, a priori, may favor knowledge about HH.

The WHO considers the HH technique adequate when the six complete steps are performed in a time between 20 and 30 seconds.[7,9] This recommendation is based on the rationale that the six recommended steps, regardless of the sequence performed, result in contact of the

alcoholic antiseptic solution with all areas/spaces of the hand and consequent reduction of the microbial load, compared to incomplete steps.[7,9,13-17]

Observation of the students' HH technique revealed that only 3.6% of the total students evaluated performed all six recommended steps, 32.5% four steps, and 27.2% three steps, highlighting the non-compliance with the correct HH technique by the vast majority in this study. However, Pearson's correlation test revealed that the more students advance through the semesters of the Program, the more steps of the HH technique are performed, pointing to the importance of reinforcing this knowledge throughout the evolution of the curriculum of this Program.

Of the recommended steps, rubbing the palms of hands together (step 1) was the most frequently performed by students (97%), followed by step 2, rubbing the back of each hand with the opposite palm, interlacing fingers (80.5%). The least frequently performed HH steps were rubbing palms together with fingers interlaced (65.7%), interlocking fingers and rubbing the back of fingers against the opposing palms (64.5%), and rubbing the fingertips and nails in the opposite palm in a rotational movement (49.1%), demonstrating negligence or lack of knowledge regarding the hygiene of heavily colonized areas of the hand implicated in pathogen transmission, such as the subungual and interdigital spaces.[2,7,9]

In healthcare settings, HH compliance among healthcare professionals, particularly the nursing staff, is crucial to prevent pathogen transmission, considering this professional category is responsible for 24-hour patient care, and their interventions require direct contact with patients and their surroundings.

Nursing students are considered healthcare professionals in training, and during their practice, they can also transmit microorganisms between patients if they are unfamiliar with HH or practice it incorrectly. In this sense, higher education institutions in the health field need to implement curricula, such as the one identified in this Program, that address issues of clinical practice and the culture of safety and error prevention in healthcare, reinforcing the encouragement of the WHO and regulatory bodies, such as the National Health Surveillance Agency.[11,16]

The duration of HH using an alcohol-based preparation is also a determining factor in the adequacy of this practice, considering the WHO recommendation of an exposure time of 20 to 30 seconds for the solution to achieve germicidal action. In relation to the HH technique, most students (40.8%) sanitized their hands for less than 20 seconds, falling short of the recommended duration; 39.6% of the students performed HH within the standard 20 to 30-second range; and 19.5% exceeded 30 seconds. These numbers also revealed time-related inadequacies for HH with alcohol-based solution.

Of the six questions that sought to identify the students' theoretical background regarding HH, out of a total of 169 students evaluated, none answered all six questions correctly. However, 57.3% of the students know the concept of HH, 68.6% know how to distinguish the indications for the use of hand rubbing with alcohol-based antiseptic preparation, and 58% recognize the five moments recommended by the WHO for HH during healthcare. A comparison between the number of correct answers to questions and the students' current semester revealed a weak statistical correlation; this suggests that progression through the Program does not significantly enhance knowledge regarding HH and the prevention of related HAIs.

Additionally, the recommended time for HH with an alcohol-based preparation and the microbial activity of this solution are unknown topics for 87% and 86.9% of students, respectively, as is the effectiveness of the alcohol-based preparation for HH for 72.8% of them.

Although most of these students understand the concept of HH and the indication for this practice, crucial information such as the biocidal action of alcohol and the necessary contact time with the hands is ignored, as revealed by the percentage of 40.8% of students who sanitized their hands in less than 20 seconds.

The change from handwashing with soap and water to rubbing with an alcohol-based preparation significantly reduces the microbial load on the hands. In addition, it decreases the time required from at least one minute to reach the sink, wash hands, dry them, and return to the patient, to just 20-30 seconds with the use of alcohol.[2] Therefore, despite the advantage of the minimum contact time of 20 to 30 seconds required for HH with the use of the alcohol solution, this is not followed by the vast majority of students.

This study reveals that this Undergraduate Nursing Program has a specific component on Infection Control and Health Safety, and students are exposed to various components that address the topic of HH. However, the students studied fail to comply with the technique by not performing all the recommended steps, neglecting the hygiene of hand areas involved with a higher microbial load, and not following the time required for the biocidal action of the alcohol solution. This situation constitutes poor HH practice on their part and signals the need to change teaching and learning models or to incorporate multimodal strategies into HH teaching practice, as well as those implemented in health services.

Our study diverges from previous international research regarding the evaluation of students and their knowledge in three primary aspects: i) the nursing curricula analyzed differ in duration and core

components; ii) while we evaluated HH practices through direct observation, other studies relied on self-reported data; iii) whereas those studies applied a form developed by the WHO, our study employed an instrument specifically designed by the authors.[2,18-20]

Despite the methodological differences, both international studies and our study identified gaps and/or moderate knowledge among students regarding the topic of HH. In a study with nursing students from Saudi Arabia, 58.6% of knowledge about HH was identified.[19] Another study using the WHO form in Switzerland revealed low scores on knowledge about HH (25% and 63% for students and 48.8% for nurses).[18] These data confirm the need to revise undergraduate nursing curricula and the continuing education for health professionals offered by health institutions.

Since the theoretical and practical content of HH passed on to students during the curricular components was not accessed in this study, the learning process and teaching methodological strategies are also unknown, which constituted a limitation and perhaps explains the results found.

Despite the aspects mentioned above, the objective of investigating students' knowledge about HH and contributing to national data on this topic was achieved.

Hand hygiene is also emblematic in the academic field, because even in an Undergraduate Nursing Program with a curriculum that includes disciplinary components addressing this topic, students do not have adequate HH practice, both in technique and in the recommended time. This finding signals the need to incorporate multidimensional teaching and learning strategies on this topic in this Program.

For the consolidation of the HH culture and the immersion of academia in the global fight for the control of HAIs, this study points not only to the importance of including HH constructs in the training of future nurses, but also of rethinking teaching in light of Paulo Freire's affirmation that "*teaching is not transferring knowledge, but creating the possibilities for its own production or construction*".

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AUTHORS' CONTRIBUTIONS

Eliana Auxiliadora Magalhães Costa contributed to the conception, data collection, data analysis, article writing, and revision for publication. **Tássia Teles Santana de Macedo** contributed to the data collection, data analysis, article writing, and revision for publication. **Mariana de Almeida Moraes** contributed to the data collection, data analysis, article writing, and revision for publication. **Adriana Cristina Oliveira** contributed to the data collection, data analysis, article writing, and revision for publication. **Rafael Lima Rodrigues de Carvalho** contributed to the data collection, data analysis, article writing, and revision for publication. **Rebeca Assis** contributed to the data collection and revision for publication. **Renata Gomes** contributed to the data collection and revision for publication. **Jaqueline Brazil Leite** contributed to the data collection and revision for publication. **Angela Gabriela da Silva Santana** contributed to the data collection and revision for publication.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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APPENDIX A

Observation Guide

Hand hygiene with alcohol-based antiseptic solution

Observer code:	**Student code:**	**Hand hygiene time (seconds):**

	Hand hygiene with alcohol-based antiseptic solution	**Yes**	**No**
	Rub the palms of hands together with fingers interlaced		
	Rub the back of each hand with the opposite palm, interlacing fingers		
	Rub palms together with fingers interlaced		
	Interlock fingers and rub the backs of the fingers against the opposing palms		
	Rub each thumb rotationally, clasped in the opposite palm		
	Rub fingertips and nails in the opposite palm in a rotational movement		

APPENDIX B

To be completed by the students of the Data Collection	
Institution code:	**Participant code:**

Student characterization

Age: _____years old

Sex: ( ) Female ( ) Male

Current semester: _____

( ) No practical experience in health services

( ) With practical experience in health services

Knowledge about healthcare-associated infections (HAIs) and hand hygiene (HH).

1. **Have you had a specific curricular component on the control of healthcare-associated infections (HAIs) during the program?**
   ( ) No
   ( ) Yes. Specify: _____

2. **Have you had a curricular component that addressed the topic of HH in healthcare services during the program?**
   ( ) No

   ( ) Yes. Specify: _____

3. **Hand hygiene refers to the following procedures (choose ONLY one of the options):**
   a) Hand washing with soap and water
   b) Rubbing with an alcohol-based antiseptic solution
   c) Hand washing with an antiseptic degerming solution (PVPI or chlorhexidine)
   d) a+b are correct
   e) a+b+c are correct
   f) I don't know

4. **Regarding the hand hygiene technique and the recommended time for its performance (choose one of the options):**
   a) Rubbing hands with an alcohol-based antiseptic solution should last between 20 and 30 seconds
   b) Washing with soap and water should last between 20 and 40 seconds
   c) Hand hygiene is guaranteed as long as the palms and backs of the hands are well rubbed
   d) Vigorous hand rubbing with soap and water should not be inferior to 10 seconds
   e) All of the above statements are correct
   f) I don't know

5. **Hand rubbing with an alcohol-based antiseptic solution has good or excellent antimicrobial activity against all microorganisms, except for (choose one option):**
   a) Viruses
   b) Fungi
   c) Mycobacteria
   d) *Clostridium difficile*
   e) Gram-positive and Gram-negative bacteria
   f) I don't know

6. **Hand rubbing with an alcohol-based antiseptic solution is indicated for all the situations described below, except for (choose one option):**
   a) When hands are visibly dirty
   b) Pre-surgical hand preparation
   c) Before performing aseptic procedures
   d) Before preparing medication
   e) I don't know

7. **Mark the incorrect statement (choose one of the options):**
   - **a)** Rubbing with an alcohol-based antiseptic solution is more effective in reducing the microbial load than washing hands with soap and water
   - **b)** Rubbing hands with an alcohol-based antiseptic solution requires less time than washing hands with soap and water
   - **c)** The use of wrist or finger accessories significantly reduces the effectiveness of rubbing with an alcohol-based antiseptic solution
   - **d)** Rubbing hands with an alcohol-based antiseptic solution is effective only if performed for 60 seconds
   - **e)** I don't know

8. **Which of the following options confirms the 5 moments for hand hygiene as recommended by the World Health Organization (choose one option):**
   - **a)** Before touching a patient; before a clean/aseptic procedure; after risk of exposure to body fluids, secretions, excretions, mucous membranes, non-intact skin or dressing; after touching a patient; after touching objects and equipment in the patient's surrounding environment.
   - **b)** Before entering the service area; before a clean/aseptic procedure; after risk of exposure to body fluids, secretions, excretions, mucous membranes, non-intact skin, or dressings; after touching a patient; after touching objects and equipment in the patient's surrounding environment.
   - **c)** Before touching a patient; before a clean/aseptic procedure; after risk of exposure to secretions in an isolated patient; after touching a patient; after touching objects and equipment in the patient's surrounding environment.
   - **d)** Before touching a patient; before a clean/aseptic procedure; after risk of exposure to body fluids, secretions, excretions, mucous membranes, non-intact skin, or dressings; after touching a patient; after using sanitary facilities.
   - **e)** I don't know

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Original Article

Anosmia in Covid-19 and its association with chronic diseases and infectious disease symptoms

Anosmia na Covid-19 e sua associação com doenças crônicas e outros sintomas de infecções
Anosmia en Covid-19 y su asociación con enfermedades crónicas y otros síntomas de infecciones

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ABSTRACT

Background and Objectives: Anosmia in Covid-19 may indicate a more favorable prognosis, highlighting the importance of understanding associated factors to support clinical decisions. This study aimed to analyze the prevalence and factors related to anosmia in individuals tested for Covid-19. **Methods:** Data from a university extension program that provided molecular testing services for Covid-19 diagnosis were used. Data collected between April 2020 and January 2023 were used. The chi-square test (p<0.05) was used by grouping participants according to the molecular test result: positive and negative for Covid-19. **Results:** A total of 6.5% (n=2252) of the population had anosmia, of which 1228 tested positive for Covid-19. Most participants with anosmia were adult females. There was a significant association between Covid-19 anosmia and the variant change milestone in February 2021. Among chronic diseases in individuals with anosmia and Covid-19, there was a significant association (p<0.05) with high blood pressure and diabetes. Among the symptoms of individuals with anosmia and Covid-19, ageusia, headache, and cough were directly associated; while runny nose, sore throat, dyspnea, diarrhea, and vomiting were inversely associated (p<0.05). **Conclusion:** In this study, chronic diseases related to Covid-19 anosmia included high blood pressure and diabetes, and the associated symptoms were ageusia, headache, and cough. Runny nose, sore throat, dyspnea, diarrhea, and vomiting appeared less frequently than expected in individuals with anosmia and Covid-19.

Keywords: *SARS-CoV-2. Pandemic. Smell disorders. Ageusia. Dysgeusia.*

RESUMO

Justificativa e Objetivos: A anosmia na Covid-19 pode indicar prognóstico mais favorável, o que ressalta a importância de conhecer os fatores associados para apoiar decisões clínicas. O objetivo deste estudo foi analisar a prevalência e os fatores associados à anosmia em indivíduos que realizaram o teste para a Covid-19. **Métodos:** Foram utilizados os dados de um programa de extensão universitário, que prestou o serviço de realização de testes moleculares para diagnóstico da Covid-19. Foram utilizados dados coletados entre abril de 2020 e janeiro de 2023. Para as análises utilizou-se o teste qui-quadrado (p<0,05), agrupando os participantes conforme o resultado do teste molecular: positivo e negativo para Covid-19. **Resultados:** O total de 6,5% (n=2252) da população apresentou anosmia, dos quais 1228 tiveram o teste positivo para Covid-19. A maioria dos participantes com anosmia era adulta do sexo feminino. Houve associação significativa da anosmia da Covid-19 com o marco de mudança de variantes em fevereiro de 2021. Entre as doenças crônicas nos indivíduos com anosmia e Covid-19, houve associação significativa (p<0,05) com a hipertensão arterial e diabetes. Dentre os sintomas dos indivíduos com anosmia e Covid-19, ageusia, cefaleia e tosse se associaram diretamente; e coriza, dor de garganta, dispneia, diarreia e vômito se associaram inversamente (p<0,05). **Conclusão:** As doenças crônicas associadas à anosmia da Covid-19 foram hipertensão arterial e diabetes, e os sintomas associados foram ageusia, cefaleia e tosse. Coriza, dor de garganta, dispneia, diarreia e vômito apareceram menos do que o esperado para os indivíduos com anosmia e Covid-19.

Descritores: *SARS-CoV-2. Pandemia. Transtornos de olfato. Ageusia. Disgeusia.*

RESUMEN

Justificación y Objetivos: La anosmia en Covid-19 puede indicar un pronóstico más favorable, lo que resalta la importancia de conocer los factores asociados para respaldar la toma de decisiones clínicas. El objetivo de este estudio fue analizar la prevalencia y los factores asociados a la anosmia en personas que hicieron la prueba de Covid-19. **Métodos:** Se utilizaron datos de un programa de extensión universitaria que brindó el servicio de realización de pruebas moleculares para el diagnóstico de Covid-19. Se utilizaron datos recopilados entre abril de 2020 y enero de 2023. Para los análisis se utilizó la prueba de chi-cuadrado (p<0,05), agrupando a los participantes según el resultado de la prueba molecular: positivos y negativos para Covid-19. **Resultados:** El 6,5% (n=2252) de la población presentó anosmia, de los cuales 1228 resultaron positivos a Covid-19. La mayoría de los participantes con anosmia eran mujeres adultas. Hubo una asociación significativa de la anosmia de Covid-19 con el hito del cambio de variante en febrero de 2021. Entre las enfermedades crónicas en individuos con anosmia y Covid-19, hubo una asociación significativa (p<0,05) con la presión arterial alta y la diabetes. Entre los síntomas de los individuos con anosmia y Covid-19, la ageusia, el dolor de cabeza y la tos se asociaron directamente, mientras que la secreción nasal, el dolor de garganta, la disnea, la diarrea y los vómitos se asociaron inversamente (p<0,05). **Conclusiones:** Las enfermedades crónicas asociadas a la anosmia por Covid-19 fueron la hipertensión arterial y la diabetes, y los síntomas asociados fueron ageusia, dolor de cabeza y tos. Secreción nasal, dolor de garganta, disnea, diarrea y vómitos se presentaron con menos frecuencia de lo esperado en personas con anosmia y Covid-19.

Palabras Clave: *SARS-CoV-2. Pandemia. Trastornos del olfato. Ageusia. Disgeusia.*

INTRODUCTION

The increasing reporting of anosmia in individuals infected with SARS-CoV-2 has led the World Health Organization to consider the condition a symptom of Covid-19 (the disease caused by the SARS-CoV-2 coronavirus). Anosmia may be associated with other infectious agents or health conditions, such as smoking habits and underlying diseases like type 2 diabetes, gastroesophageal disorders, and rhinitis.[1] However, one study reported that individuals affected by Covid-19 were more likely to present olfactory symptoms than those with other respiratory illnesses.[2] Another study conducted in a municipality in the interior of Rio Grande do Sul (RS) showed that almost 30% of the studied population reported at least one comorbidity prior to Covid-19, and there was a significant association between SARS-CoV-2 infection and the symptoms of anosmia and ageusia.[3]

A study of the association of anosmia in Covid-19 positive patients with other symptoms showed that the most prevalent were cough and dyspnea. The predominant comorbidities reported were overweight, hypertension, and type 2 diabetes mellitus, in descending order.[4] However, the number of anosmia cases varied across continents, making it important to investigate the factors associated with anosmia in Covid-19 patients in different regions and ethnicities. The prevalence of anosmia among those positive for Covid-19 was lower in India compared to figures from Europe, for example.[5]

The occurrence of anosmia in Covid-19 was influenced by SARS-CoV-2 variants. With the progression of the pandemic, the emergence of more efficient variants led to increased transmissibility, which may have also influenced the symptomatology and clinical prognosis of the disease. The Omicron variant, for example, which prevailed in Brazil from December 2021 onwards, had a high transmission rate and was associated with fewer cases of olfactory dysfunction compared to other variants such as Alpha and Delta.[6,7]

The complaint of anosmia was frequently associated with a better prognosis for Covid-19, with less disease severity and a lower rate of admission to intensive care units.[8,9] Thus, understanding the health status of individuals with anosmia associated with Covid-19 could contribute to the clinical diagnosis of the disease and indicators of its severity, and thus guide healthcare professionals in decision-making.[1]

In Brazil, Covid-19 has affected over 38 million individuals and resulted in more than 700,000 fatalities as of mid-2024.[10] Greater control of the infection was achieved after mass vaccination of the population. However, disease-related factors must be better understood to prevent new outbreaks. Although information on the behavior and prevalence of anosmia in Covid-19 is available in the literature, the association of this condition with comorbidities and other symptoms caused by SARS-CoV-2 still requires further investigation and consolidation.

The university extension program called UFSM-Detecta was developed as part of an institutional task force to minimize the impacts of the pandemic in the North and Northwest region of Rio Grande do Sul, with the main objectives of conducting molecular analysis of SARS-CoV-2, as well as educational and scientific dissemination activities within the public university. Nearly 50,000 people from 50 partner municipalities were served through these actions.[11] The analysis of the data generated in the project is important to understand the impacts of Covid-19 on the region and thus improve knowledge for other related challenges. Many studies on the subject are restricted to limited regions with a smaller number of individuals evaluated, making more comprehensive studies, such as the one proposed here, necessary. Therefore, the objective of this study was to analyze the prevalence and factors associated with anosmia in individuals who underwent molecular testing for Covid-19 diagnosis and attended by the UFSM-Detecta extension program.

METHODS

This is a cross-sectional, retrospective documentary study that analyzed the prevalence of anosmia in individuals who tested positive for Covid-19 and the frequency of other symptoms and/or comorbidities in these patients. In addition, individual factors such as sex, race/color, age, and date of diagnosis were analyzed. Data from an extension program (UFSM-Detecta – Universidade Federal de Santa Maria, Palmeira das Missões campus), which provided RT-qPCR (real-time quantitative polymerase chain reaction) molecular testing for Covid-19 diagnosis to approximately 50 municipalities in the North and Northwest regions of Rio Grande do Sul during the Covid-19 pandemic, were used.[11] The data analysis was simple descriptive, using data collected between April 2020 and January 2023. The region has an estimated population of approximately 310,000 inhabitants and is located about 300 km from Porto Alegre, the state capital.

Data collection occurred at the time of the diagnostic test request, based on identification forms completed by professionals from the health units served by the UFSM-Detecta program. This information accompanied the biological samples sent to the Microbiology and Molecular Biology laboratories of UFSM-PM. After the tests were performed, data were stored in physical and digital formats (online database).

The study included 49,611 users of the health services served by the UFSM-Detecta extension program in the

period between April 23, 2020, and January 27, 2023. Individuals with incomplete data, asymptomatic negatives, inconclusive RT-qPCR results, pregnant women, and those under 18 years of age were excluded, resulting in a total of 34,609 eligible individuals. The specific analysis of anosmia prevalence considered the 2,252 individuals who reported loss of smell among those eligible.

The data evaluated were the RT-qPCR test result and date; age, sex, and declared race/color; symptomatology and chronic diseases reported by the participants. The categorical variables were presented as absolute and relative frequencies for descriptive analysis. The comparisons between groups (positive and negative for Covid-19) were performed using the chi-square test and Fisher's exact test (when the count in the contingency table was less than 5), considering p-values <0.05 as significant. GraphPad Prism software version 5.0 (GraphPad Software, Inc. La Jolla, CA, USA) was used for statistical analyses.

This study was conducted in accordance with the ethical standards required in the Ministry of Health resolutions 466/2012, 510/2016, and 580/2018. The study was approved on September 14, 2020, by the Research Ethics Committee of the Universidade Federal de Santa Maria under Opinion number 5041431.

RESULTS

Among 34,609 eligible individuals, 2,252 or 6.5% participated in the study because they reported anosmia, and 1,228 had a positive molecular diagnosis for Covid-19 (Table 1). Using the chi-square test, it was observed that the number of positive individuals with anosmia was higher than expected for this population, demonstrating a significant *p-value*. Only individuals with anosmia were evaluated (*N*=2,252) in the present study.

Table 1. Frequency of individuals positive and negative for Covid-19 according to anosmia notification, North and Northwest regions of Rio Grande do Sul, 2020-2023.

Anosmia	Positive	Negative	Total	*p-value*
With	1228 (3.5)	1024 (3.0)	2252 (6.5)	<0.0001*
Without	10179 (29.4)	22178 (64.1)	32357 (93.5)	
Total	11407 (32.9)	23202 (67.1)	34609 (100)	

Abbreviations: *Indicates a significant association according to the chi-square test, considering $p< 0.05$.

Most participants with anosmia (90.1%) were adults between 18 and 59 years of age and female (61%). However, there was no association between age or sex and a positive Covid-19 test ($p>0.05$) (Table 2).

Among the participants with anosmia, 54.6% (*n*=1231) did not declare their race, 1.5% declared themselves Black or Brown, 3.6% Indigenous, and 40.3% White (Table 2). There was an association between Black/Brown and Indigenous race and a positive Covid-19 test ($p<0.05$). According to the chi-square test, the frequency of positive Black/Brown and Indigenous individuals was lower than expected for the studied population (Table 2). This condition may be related to the low rate of race self-declaration in the present study (only 45.4% of participants declared their race).

There was a significant association between the period of diagnosis and a positive Covid-19 test in individuals with anosmia ($p<0.05$), as according to the statistical test, there was a higher number of positive results than expected in both periods (Table 2). The number of individuals with anosmia was higher during the pandemic period up to February 2021.

Table 2. Frequency of individuals with anosmia who tested positive and negative for Covid-19 according to personal characteristics and RT-qPCR test period, North and Northwest regions of Rio Grande do Sul, 2020-2023.

	Positive (*n*=1228)	Negative (*n*=1024)	Total (*n*=2252)	*p-value*
Adults	1103 (49.0)	927 (41.2)	2030 (90.1)	0.5755
Older adults	125 (5.6)	97 (4.3)	222 (9.9)	
Female	766 (34.0)	607 (27.0)	1373 (61.0)	0.1331
Male	462 (20.5)	417 (18.5)	879 (39.0)	
Black/Brown	11 (0.5)	22 (1.0)	33 (1.5)	0.0138*
Others	1217 (54.0)	1002 (44.5)	1219 (54.1)	
Indigenous	25 (1.1)	55 (2.4)	80 (3.6)	<0.0001*
Others	1203 (53.4)	969 (27.7)	2172 (96.4)	
White	507 (22.5)	401 (17.8)	908 (40.3)	0.3057
Others	721 (32.0)	623 (27.7)	1344 (59.7)	
Tested until 02-2021	615 (27.3)	622 (27.6)	1237 (54.9)	<0.0001*
Tested from 03-2021	613 (27.2)	402 (17.9)	1015 (45.1)	

Abbreviations: *Indicates a significant association according to the chi-square test, considering $p<0.05$.

Regarding the clinical profile of patients with anosmia who tested for Covid-19 (Figure 1), hypertension was reported by 3.6% of individuals; diabetes by 1.0%; obesity by 0.5%; and asthma by 0.5%. Smoking was reported by 0.1% of patients. Of the hypertensive individuals with anosmia, 2.4% (*n*=53) tested positive, a higher number compared to those who tested negative (1.2%, *n*=28), which represented a statistically significant difference according to the chi-square test ($p=0.0447$). Similarly, the frequency of individuals with anosmia and diabetes who tested positive (0.8%, *n*=19) was higher than that of individuals who tested negative (0.1%, *n*=3), showing a significant association ($p=0.0026$).

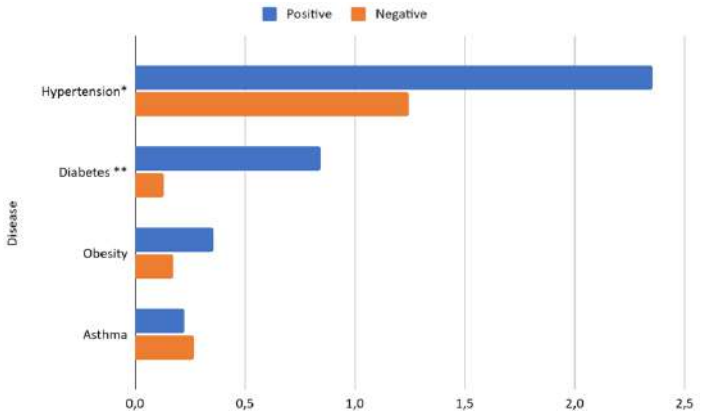

Figure 1. Percentual frequency of diseases in individuals with anosmia who tested for Covid-19 (n=2252), North and Northwest regions of Rio Grande do Sul, 2020-2023.
Abbreviations: *Indicates a significant association of the disease with the result of the Covid-19 test, according to the chi-square test (*p<0.05; **p<0.01).

The main symptoms reported by patients with anosmia who tested positive for Covid-19 were: dysgeusia 68.6%, headache 68.3%, and cough 63.2% (Figure 2). However, the symptoms that showed an association between anosmia and a positive Covid-19 test, according to the statistical test, were ageusia (2.7% positive vs 0.9% negative, *p*=0.0001), headache (37.5% vs 31.1%, *p*=0.0284), and cough (33.5% vs 29.8%, *p*=0.0483). The symptoms runny nose (13.4% positive vs 17.1% negative, *p*<0.0001), sore throat (27.3% vs 27.1% *p*<0.0001), dyspnea (7.3% vs 9.8%, *p*<0.0001), diarrhea (9.0% vs 9.9%, *p*=0.0019) and vomiting (1.5% vs 1.9%, *p*=0.0479) showed a lower frequency than expected for individuals who tested positive, showing an inversely significant association with anosmia associated with Covid-19.

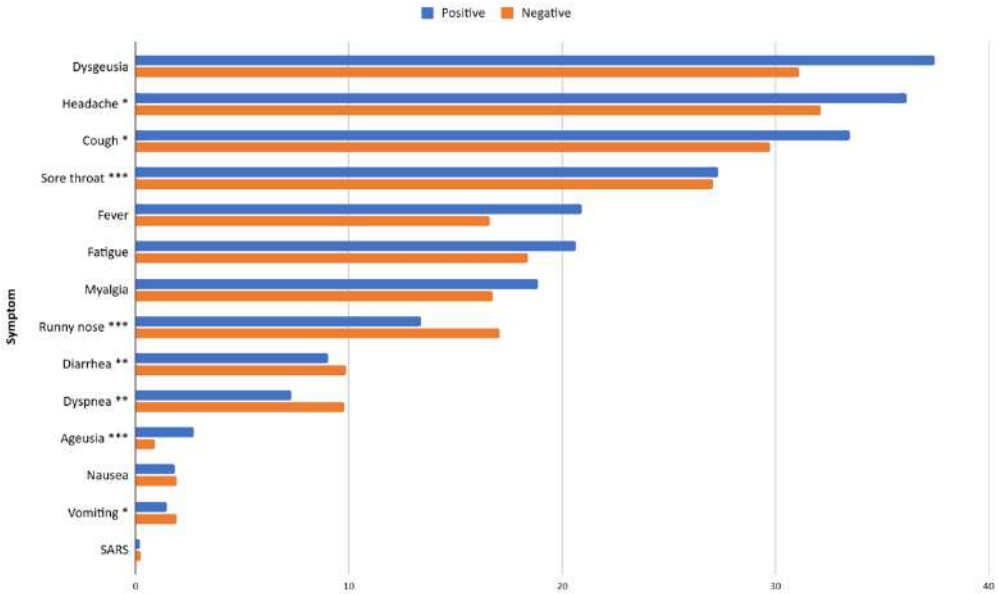

Figure 2. Percentage frequency of symptoms in individuals with anosmia who tested positive for Covid-19 (*n*=2252), North and Northwest region of Rio Grande do Sul, 2020-2023.
Abbreviations: *Indicates a significant association between the disease and the Covid-19 test result, according to the chi-square test (**p*<0.05; ***p*<0.01; ****p*<0.001).

Regarding anosmia as an isolated symptom, a frequency of 0.6% (*n*=10 for positive vs *n*=3 for negative) was obtained in individuals who reported the condition as the sole manifestation of the disease. Cases of anosmia in individuals associated only with dysgeusia accounted for 2% (*n*=24 for positive vs *n*=20 negative), and ageusia for 0.5% (*n*=12 for positive vs *n*=0 for negative).

DISCUSSION

Based on the results obtained in this study, we identified that 54.5% of individuals who reported anosmia were positive for Covid-19. In a retrospective cross-sectional study conducted with the Florida population seeking health services, the odds ratio for individuals with anosmia and dysgeusia to be positive for Covid-19 was 39.107.[12] In the same study, the prevalence of anosmia in Covid-19 positive patients was

12.88%. This result is close to the present study finding, in which 10.7% of individuals positive for Covid-19 reported anosmia (Table 1). In contrast, a literature review that evaluated studies from different countries and averaged all the results obtained a prevalence of 20.85% for anosmia in patients positive for Covid-19.[13] In Brazil, in one of the first studies, back in 2020, a prevalence of 4.51% of anosmia (self-reported) in patients positive for Covid-19 was found.[14]

Another finding demonstrated the regional variation in the incidence of anosmia in patients with Covid-19: East Asian countries presented a prevalence of 22.4% and Western countries of 48.4%. There was also a difference regarding taste alterations. While in East Asia a prevalence of dysgeusia was found in 16.2% of the individuals evaluated, in Western countries the prevalence was much higher, at 50.3%. The divergence in findings may result from different study designs, case definitions, and methods of monitoring the symptomatology of patients who self-reported their findings. The variability in the incidence of anosmia in different groups of individuals infected with Covid-19 highlights how challenging it is to consolidate information regarding the behavior of SARS-CoV-2 in the human body.[15]

In the current study, most Covid-19 positive individuals who reported anosmia were female (61%), in line with data found in another study conducted in Brazil (62%).[14] Regarding age frequency, 90.1% of patients with anosmia were adults, a close result to that observed in the same national study (86%).[14] However, most individuals referred by health services to the UFSM-Detecta program and who received a positive diagnosis for Covid-19 were adults (71%), and the incidence of anosmia in this group was approximately 11%. Although the statistical test indicated an association with Brown/Black and Indigenous individuals, this datum may have been influenced by the underreporting of race by the participants (Table 2).

The fact that the number of individuals with anosmia was higher during the pandemic period up to February 2021 may be related to the temporal profile of predominance of different SARS-CoV-2 variants in the region. During this period, until mid-2021, variants B.1.1, B.1.1.28, B.1.1.33, P.2, and Gamma predominated in Rio Grande do Sul. After July 2021, variants Delta and Omicron predominated in the sample region.[16] One study showed that patients with the Alpha variant B.1.1.7 reported a significantly higher proportion of olfactory abnormalities one month after infection compared to patients infected with the wild-type variant (D614G virus).[7] The Omicron variant, in turn, affected fewer patients with olfactory dysfunction when they were infected with the SARS-CoV-2 virus.[6] This finding may explain the results observed in the current study. After February 2021, the number of vaccinated individuals in the population gradually increased, which may also have influenced the olfactory symptomatology of SARS-CoV-2 infection. However, a study conducted in 2021 showed that symptoms of loss of smell and taste are also common findings in patients with symptomatic Covid-19 after complete vaccination.[17]

Regarding pre-existing comorbidities among patients who tested positive for anosmia, there was a higher rate of hypertension, followed by diabetes and obesity. However, a significant association was found only for hypertension and diabetes. In the literature, there are no reports of a relationship between hypertension and anosmia. This significant association may be related to the higher number of cases of these chronic diseases in the population. A study on diabetes revealed that reduced first-line nasal immune defense in type 2 patients increased susceptibility to SARS-CoV-2. This fragility in the nasal cavity, of still unknown cause, may explain the significant association of diabetes with anosmia in Covid-19.[18] An incidence of 0.2% of anosmia was also observed in patients who tested positive for asthma. Despite the absence of a physiological relationship between asthma and anosmia, patients with respiratory diseases are more susceptible to developing olfactory disorders.[15]

Among individuals with anosmia who tested positive for Covid-19, symptoms of ageusia, headache, and cough were directly associated with the diagnosis, corroborating the recurrence of these conditions observed in previous studies.[19] In another study, ageusia was reported by only 5% of the individuals evaluated, and dysgeusia was the most frequent symptom among patients. Due to the close relationship between taste and smell, a large part of gustatory dysfunctions stems from olfactory impairment, and not necessarily from alterations in the taste buds themselves.[20] Most patients with anosmia and dysgeusia resulting from Covid-19 recover within four weeks after infection, which is due to the short lifespan of olfactory sensory neurons. Although the origin and molecular mechanisms of these symptoms are not yet fully understood, the rapid recovery and concomitance of both suggest that the origin of the sensory loss caused by SARS-CoV-2 is neurosensory in nature. Literature suggests that the SARS-CoV-2 S protein adsorbs to ACE-2 receptors on olfactory sensory neurons, causing damage and even neural destruction, which explains anosmia in individuals with Covid-19.[15,21]

Headache, anosmia, ageusia, and hypogeusia are also among the main neurological symptoms manifested by Covid-19.[22] Among the patients evaluated, headache had a frequency of 68.3%, establishing itself as one of the main symptoms associated with anosmia. This condition manifests predominantly in young patients, and those with anosmia and dysgeusia are more likely to

develop it. This correlation suggests a possible intersection between the pathophysiological mechanisms that trigger these symptoms in Covid-19.[23]

In this study, the frequency of runny nose manifestation was lower among Covid-19-positive cases with anosmia. In this case, olfactory loss appears to be mainly related to damage to the olfactory neuroepithelium, rather than an obstructed olfactory cleft.[24] According to research in the literature, in Covid-19 cases, approximately 60% of individuals with anosmia did not present with nasal obstruction, rhinorrhea, or rhinitis symptoms, and those who manifested nasal congestion or rhinorrhea did not have significant mucosal edema in the nasal cleft or sinuses.[25] Anosmia can occur through conductive or sensorineural olfactory loss. Conductive loss results from mechanical obstruction and may be accompanied by nasal congestion or rhinitis, while sensorineural loss is a product of damage to the sensory neurons of the olfactory bulbs.[15] Viral infections that cause congestion, nasal obstruction, and rhinorrhea prevent odorant access to the sensory epithelium, preventing its binding to olfactory receptors.[15,25] In this sense, in the vast majority of individuals evaluated in this study, anosmia was not a consequence of mechanical obstruction generated by symptoms of runny nose and nasal congestion.

In addition to the runny nose, this study found inversely significant associations between dyspnea, sore throat, vomiting, and diarrhea with positive cases of Covid-19 who presented with anosmia. Studies have shown that patients with anosmia have a lower rate of disease progression and a better prognosis, which could explain this finding. A study showed that anosmia was significantly associated with mild chest infection and reflected in lower disease severity and less frequent admissions to intensive care units.[9] Although another study confirms that anosmia can be an indicator of good Covid-19 prognosis, it also showed an association between olfactory dysfunction and gastroenteritis symptoms, such as diarrhea, which differs from the findings in the current study.[19] The authors also highlighted that the presence of vomiting was significantly related to a longer duration of anosmia. This datum also differs from the findings of the present study, in which the frequency of vomiting was lower among those who tested positive compared to those who tested negative for Covid-19.

This study contributes to the understanding of the relationship between anosmia and the prognosis of Covid-19, as well as the factors associated with this characteristic symptom of SARS-CoV-2 infection. However, the use of secondary data from the health departments of the municipalities partnered with UFSM-Detecta should be considered a limitation.[11] The reliability of the information may be affected by the self-reported nature of the patients' accounts and by the variability in data collection during the anamnesis performed by health professionals.

According to the sample studied, the chronic diseases associated with anosmia in Covid-19 were hypertension and diabetes, and the symptoms directly associated with the condition were ageusia, headache, and cough. Symptoms such as runny nose, sore throat, dyspnea, diarrhea, and vomiting appeared less frequently than expected in individuals with anosmia who tested positive for Covid-19, suggesting less severe disease progression when this olfactory dysfunction is present, since dyspnea represents disease progression.

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AUTHORS' CONTRIBUTIONS

Fernanda Lopes Vilande contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics. **Terimar Facin Ruoso** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics. **Daniel Ângelo Sganzerla Graichen** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics. **Ângela Giovana Batista** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table preparation, conclusions, review, and statistics.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

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Original Article

Antimicrobial resistance: epidemiological profile of the city of Porto Alegre in 2021-2022

Resistência antimicrobiana: perfil epidemiológico do município de Porto Alegre em 2021-2022
Resistencia a los antimicrobianos: perfil epidemiológico de la ciudad de Porto Alegre en 2021-2022

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ABSTRACT

Background and Objectives: Monitoring multidrug-resistant microorganisms is crucial for containing their spread in healthcare settings. The aim of this study was to describe the main epidemiological characteristics of multidrug-resistant microorganisms identified and reported in Porto Alegre in 2021 and 2022. **Methods:** This quantitative, descriptive epidemiological study is based on an analysis of secondary data from the Porto Alegre Municipal Health Department. **Results:** During the analyzed period, 15,016 multidrug-resistant microorganisms were identified. Enterobacterales were the most frequently reported microorganisms. An increase in notifications was observed in 2021 and 2022, which was associated with the improvement and strengthening of the city's surveillance process. **Conclusion:** The significant increase in notifications may be related to improvements in epidemiological surveillance, reflecting enhanced monitoring and detection of multidrug-resistant microorganisms in Porto Alegre.

Keywords: *Public Health Surveillance. Drug Resistance. Carbapenems. Drug Resistance Microbial.*

RESUMO

Justificativa e Objetivos: A vigilância de microrganismos multirresistentes é essencial para o controle da disseminação dessas cepas nos serviços de saúde. Este estudo teve como objetivo descrever as principais características epidemiológicas dos microrganismos multirresistentes identificados e notificados em Porto Alegre nos anos de 2021 e 2022. **Métodos:** Trata-se de um estudo epidemiológico quantitativo e descritivo, baseado na análise de dados secundários provenientes da Secretaria Municipal de Saúde de Porto Alegre. **Resultados:** No período analisado, foram identificados 15.016 microrganismos multirresistentes. As Enterobacterales permaneceram como os principais microrganismos notificados. Observou-se um aumento no número de notificações nos anos de 2021 e 2022, associado ao fortalecimento e à qualificação do processo de vigilância no município. **Conclusão:** O aumento significativo das notificações pode estar relacionado à melhoria da vigilância epidemiológica, refletindo maior qualificação no monitoramento e detecção dos microrganismos multirresistentes em Porto Alegre.

Descritores: *Vigilância em Saúde Pública. Resistência a Medicamentos. Carbapenêmicos. Resistência Microbiana a Medicamentos.*

RESUMEN

Justificación y Objetivos: La vigilancia de los microorganismos multirresistentes es esencial para el control de la propagación de estas cepas en los servicios de salud. Este estudio tuvo como objetivo describir las principales características epidemiológicas de los microorganismos multirresistentes identificados y notificados en Porto Alegre en los años 2021 y 2022. **Métodos:** Se trata de un estudio epidemiológico cuantitativo y descriptivo, basado en el análisis de datos secundarios provenientes de la Secretaría Municipal de Salud de Porto Alegre. **Resultados:** En el período analizado, se identificaron 15.016 microorganismos multirresistentes. Las Enterobacterales siguieron siendo los principales microorganismos notificados. Se observó un aumento en el número de notificaciones en los años 2021 y 2022, asociado al fortalecimiento y a la cualificación del proceso de vigilancia en el municipio. **Conclusiones:** El aumento significativo de las notificaciones puede estar relacionado con la mejora de la vigilancia epidemiológica, lo que refleja una mayor cualificación en el monitoreo y la detección de los microorganismos multirresistentes en Porto Alegre.

Palabras Clave: *Vigilancia en Salud Pública. Resistencia a Medicamentos. Carbapenêmicos. Farmacorresistencia Microbiana a Medicamentos.*

INTRODUCTION

Antimicrobials represent one of the most important classes of drugs in the history of human health. They have the ability to inhibit or stop the growth of microorganisms, thus resulting in an effective option for treating various diseases. The first antimicrobial, penicillin, appeared in the late 1920s, discovered by physician Alexander Fleming. The importance of antimicrobials became clear during World War II, driving the expansion of research and the emergence of new classes of antimicrobials.[1,2]

Contemporary to their emergence is antimicrobial resistance (AMR). According to the WHO, AMR occurs when bacteria, viruses, fungi, or parasites can no longer be destroyed or have their growth limited by a drug to which they were previously sensitive, resulting in difficulties in treating and controlling infections, with prolonged hospitalizations, increasing disease transmission and the risk of death.[2,3] This resistance can result from several mechanisms: the presence of enzymes that degrade antimicrobials, genetic modification of the target site of the antimicrobial's binding to the microorganism, modification of the microorganism's structures hindering the entry of the antimicrobial, among others.[4,5]

AMR has been a constant cause for concern. Although it seems like a silent threat, in 2019 it was responsible for a higher mortality rate than other diseases of global concern, such as HIV/Aids or malaria.[6] Worldwide, in 2019, an estimated 4.5 million deaths were related to AMR. Of these, 1.27 million were directly attributed to resistance, while the other 3.23 million were deaths associated with it. This data shows how 1.27 million deaths could be prevented simply by using effective antimicrobials against microorganisms.[7]

In the city of Porto Alegre, there has been a significant increase in the number of reports related to the identification of multidrug-resistant microorganisms. Between 2009 and 2018, there was an average annual growth of 33.22% in the number of cases reported by hospitals, from 762 multidrug-resistant microorganisms in 2009 to 6,485 in 2018. Carbapenem-resistant *Klebsiella pneumoniae* accounted for 48.2% of all reported microorganisms, followed by *Acinetobacter* spp. (19.1%) and *Pseudomonas aeruginosa* (10.1%).[8]

In addition to the multidrug-resistant microorganisms reported in Porto Alegre, other examples of antimicrobial resistance have had a significant impact on the incidence of infections on a global scale. A notable case is that of vancomycin-resistant *Enterococcus* spp., which has prevailed in several regions of the world. In the United States, in 2017, approximately 54,500 hospital infections caused by *Enterococcus* spp. resistant to this drug were recorded, resulting in about 5,400 deaths, highlighting the seriousness of the problem.[9]

Given the emergence and spread of multidrug-resistant infections, it is important to understand the current epidemiological situation in the city of Porto Alegre, Rio Grande do Sul. Thus, the main objective of this study is to describe the main epidemiological characteristics of multidrug-resistant microorganisms identified and reported in Porto Alegre in 2021 and 2022. The current scenario reinforces the need for increased research and studies on the topic, so that standards can be established as a reference for mitigating and combating the occurrence of infections caused by multidrug-resistant microorganisms.

METHODS

This is a quantitative epidemiological study with a descriptive approach. Data collection was based on secondary sources, using official records of hospital notifications of multidrug-resistant microorganisms from the Municipal Health Department of Porto Alegre, referring to the period from 2021 to 2022.

The study scenario comprised all hospitals in the municipality of Porto Alegre capable of reporting MDR, totaling 30 institutions. This network includes hospitals of different sizes and care profiles (public, private, and philanthropic), thus covering the diversity of hospital care in the city, as determined by the municipal surveillance system.

All valid notification records contained in the official databases for the period analyzed were included in the study. As exclusion criteria, notifications that did not correspond to the 2021-2022 time window and duplicate records identified in the data checking and consolidation process were removed.

The databases used were obtained from two systems, since the municipality's notification flow underwent a change in the respective years. Thus, the 2021 data were collected from the Google Forms form provided by the State Health Surveillance Center (CEVS) and *Microsoft Excel*® spreadsheets in which the hospital institutions made the notifications. The 2022 data was collected from the SENTINELA® Platform. This platform compiles weekly notifications completed in 2022 with information on the detection of multidrug-resistant microorganisms in institutions.

The files were downloaded in Microsoft Excel® format and cleaned (a process of cleaning and standardization) according to predefined variables of interest, which included: Total number of notifications; Identified microorganisms, Identified enzymes (e.g., KPC, NDM, OXA-48, among others); Type of microbial resistance (resistant to carbapenems, etc.); Classification of the event (infection or colonization);

Biological material analyzed for identification of the microorganism (e.g., blood, urine, tracheal secretion); Hospital unit where the material was collected (e.g., ICU, clinic, emergency room).

The analyses were performed using Epi Info 7.2 software, focusing on the description of the absolute and relative frequencies of the variables analyzed. Comparisons between 2021 and 2022 were made based on the observed proportions.

The research was conducted in accordance with the legal precepts of the National Research Ethics Commission. The project was forwarded and submitted to the Ethics Committee of the Rio Grande do Sul School of Public Health and the SMS Research Ethics Committee, with CAEE number 69173323.7.0000. 5312, and was approved with opinion/protocol No. 6,142,337 on June 26, 2023.

RESULTS

In 2021, 7,700 notifications were recorded, in which 7,825 microorganisms with antimicrobial resistance were identified. In 2022, the total number of notifications was lower, with 7,191 notifications and 7,441 multidrug-resistant microorganisms (MDR) identified (Figure 1).

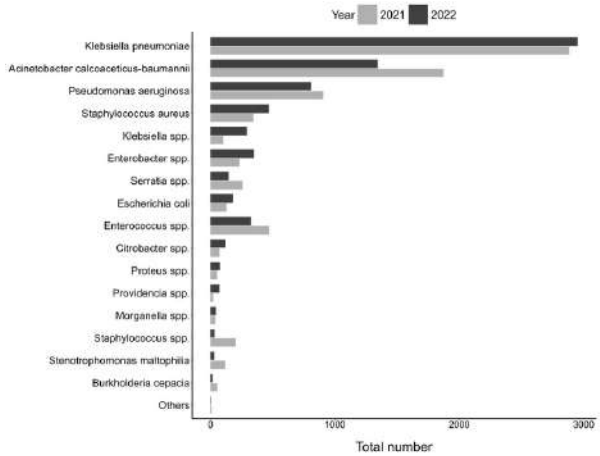

Figure 1. Multidrug-resistant microorganisms identified and reported in the city of Porto Alegre, RS, 2021 and 2022.

In 2021, Enterobacterales were predominant, accounting for 51.5% of notifications. Within this group, the *Klebsiella pneumoniae* complex was the most prevalent, with 36.89% of notifications. The *Acinetobacter calcoaceticus-baumannii* complex was the second most reported microorganism (23.93%), followed by *Pseudomonas aeruginosa* (11.62%) and *Enterococcus* spp. (5.99%) (Figure 1).

In 2022, *Klebsiella pneumoniae* continued to lead the notifications, with 39.65%, followed by the *Acinetobacter calcoaceticus-baumannii* complex (18.06%), *Pseudomonas aeruginosa* (10.87%), and *Staphylococcus aureus* (6.29%) (Figure 1).

Among the classes of antimicrobials analyzed, carbapenems had the highest resistance rates, accounting for 55.2% of notifications in 2021, with an increase to 66.7% in 2022. Resistance to third- and fourth-generation cephalosporins showed a statistically significant increase ($p < 0.001$), rising from 0.2% (2021) to 10.9% (2022). Additionally, in 2022, there were reports of resistance to sulfamethoxazole/trimethoprim, which had not been observed in the previous year (Figure 2).

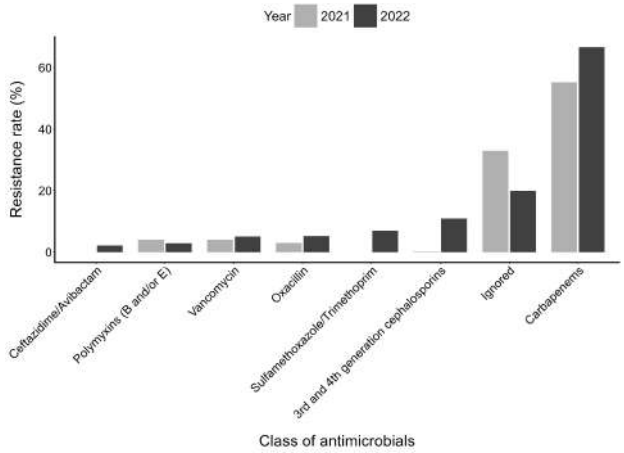

Figure 2. Distribution of antimicrobial resistance by antibiotic class in Porto Alegre, RS, 2021 and 2022.

It is worth noting that in 2021, in 33% of cases, the microbial resistance field was ignored, while in 2022 this omission fell to 19.92% (Figure 2).

In 2021, infections accounted for 31.90% of notifications, while colonizations accounted for 20.94%. In 47.16% of cases, this field was not filled in. In 2022, there was an increase in colonizations, which totaled 41.88%, while infections accounted for 38.2%. Only 19.92% of notifications did not have the classification reported (Table 1).

A

Table 1. Distribution of cases by final classification, material analyzed, hospital unit, and inhibitory enzyme (2021-2022), Porto Alegre, RS.

Variable	2021 N (%)[1]	2022 N (%)[1]	Total N (%)[2]	p-valor[3]
Final Classification				<0.001
Infection	2.496 (31.90)	2.842 (38.2)	5.338 (35.0)	
Colonization	1.638 (20.94)	3.116 (41.88)	4.754 (31.1)	
Unclassified	3.691 (47.16)	1.482 (19.92)	5.172 (33.9)	

Variable	2021 N (%)[1]	2022 N (%)[1]	Total N (%)[2]	p-valor[3]
Material Analyzed				<0.001
Surveillance swab	1.811 (23.15)	2.563 (34.45)	4.374 (28.7)	
Urine	1.217 (15.55)	1.490 (20.03)	2.707 (17.7)	
Tracheal aspirate	2.103 (26.88)	1.282 (17.23)	3.385 (22.2)	
Blood	1.289 (16.45)	740 (9.95)	2.027 (13.3)	
Sputum	504 (6.46)	369 (4.96)	873 (5.7)	
Surgical wound	69 (0.88)	159 (2.14)	228 (1.5)	
Bronchial Lavage	61 (0.78)	151 (2.03)	212 (1.4)	
Soft Tissues	0	99 (1.33)	99 (0.6)	
Cerebrospinal Fluid	7 (0.09)	12 (0.16)	19 (0.1)	
Others	764 (9.76)	575 (7.73)	1.339 (8.8)	
Hospital Unit				<0.001
Adult ICU	4.289 (54.8)	2.843 (38.21)	7.132 (43.9)	
Clinic	2.728 (34.8)	2.715 (36.49)	5.443 (33.5)	
Emergency Room	351 (4.49)	810 (10.89)	1.161 (7.1)	
Surgical	191 (2.4)	459 (5.4)	650 (4.0)	
Outpatient Clinic	169 (2.2)	1.168 (13.85)	1.337 (8.2)	
Pediatric ICU	0	136 (1.6)	136 (0.8)	
Pediatric Clinic	11 (0.1)	100 (1.2)	111 (0.7)	
Oncology	35 (0.4)	69 (0.8)	104 (0.6)	
Neonatal ICU	0	63 (0.7)	63 (0.4)	
Cardiology	2 (0.02)	24 (0.32)	26 (0.2)	
Obstetrics/Gynecology	6 (0.08)	13 (0.17)	19 (0.1)	
Neurology	0	010 (0.13)	10 (0.1)	
Hemodialysis	1 (0.01)	9 (0.12)	10 (0.1)	
Infectious Diseases	3 (0.04)	8 (0.11)	11 (0.1)	
Others	38 (0.76)	13 (0.17)	51 (0.3)	
Inhibitory Enzyme				<0.001[4]
KPC	1.591 (20.33)	1.979 (26.57)	3.570 (23.4)	
NDM	225 (2.87)	1.274 (17.12)	1.499 (9.8)	
OXA-48	0	20 (0.32)	20 (0.1)	
VIM	0	3 (0.04)	3 (0.0)	
IMP	0	2 (0.02)	2 (0.0)	
Other	0	272 (3.64)	272 (1.8)	
Unidentified	6.009 (76.79)	3.890 (52.28)	9.899 (64.8)	

Abbreviation: N: number of cases; 1: proportion in relation to the total for the year; 2: proportion in relation to the combined total for the two years (2021+2022); 3: Pearson's chi-square test for final classification, material analyzed, and hospital unit; 4: Fisher's exact test with Monte Carlo simulation (B= 10,000) for Inhibitory Enzyme. ICU: Intensive Care Unit. KPC: Klebsiella pneumoniae Carbapenemase; NDM: New Delhi Metallo-beta-lactamase; OXA-48: Oxacillinase-48; VIM: Verona imipenemase; IMP: Imipenemase.

Regarding enzymatic resistance mechanisms, *Klebsiella pneumoniae* carbapenemase (KPC) was the most prevalent enzyme in both years, accounting for 20.33% of notifications in 2021 and increasing to 26.57% in 2022. New Delhi Metallo-β-lactamase (NDM) showed a significant increase, from 2.87% in 2021 to 17.12% in 2022. IMP, OXA-48 Like, and VIM enzymes were reported in smaller proportions, all with frequencies below 1% (Table 1).

Regarding the clinical materials analyzed, in 2021, tracheal aspirate was the main material, representing 26.88% of the samples, followed by surveillance swabs (23.15%), blood (16.45%), and urine (15.55%). In 2022, surveillance swabs became the most analyzed material, corresponding to 34.45% of samples, followed by urine (20.03%) and tracheal aspirate (17.23%) (Table 1).

Intensive Care Units (ICUs) and Clinical Units were the hospital sectors that most identified multidrug-resistant microorganisms in 2021, with 54.8% and 34.8% of notifications, respectively. However, there was no distinction between the different types of ICUs this year. In 2022, due to changes in the reporting system, it was possible to differentiate between ICUs, with the Adult ICU accounting for 38.21% of reports and Clinical Units accounting for 36.49%. Other sectors, such as Emergency (10.89%) and Surgical Units (6.17%), were also reported (Table 1).

DISCUSSION

This study analyzed the dynamics of notifications of multidrug-resistant microorganisms (MDR) in the hospital network of Porto Alegre in 2021 and 2022. The results confirm a substantial and continuous burden of MDR in the municipality, with 7,700 notifications recorded in 2021 and 7,191 in 2022.

This scenario maintains the high level observed in previous years and continues the significant growth trend already documented in the city, which recorded an average increase of 35% per year between 2009 and 2018.[8] It is worth noting that the year 2020, marked by the onset of the Covid-19 pandemic, showed an atypical drop (5,011 notifications), suggesting possible underreporting or deprioritization of MDR surveillance during that period. Thus, the high number of notifications in 2021 (an increase of approximately 52% compared to 2020) may represent, in part, a resumption of surveillance capacity, in addition to the actual growth of the phenomenon. The slight reduction observed in 2022 (6.61% compared to 2021), while still maintaining a high level, indicates the endemic persistence of MDR as a critical challenge for local public health.[10]

The year 2021 marked the highest number of notifications in the history of MDR surveillance in Porto Alegre. This increase can be attributed to several factors, such as the strengthening of the notification process, changes in registration platforms, data qualification, and greater awareness of hospital units for the surveillance of antimicrobial resistance.[8]

During the period analyzed, the pattern of the main microorganisms reported remained consistent, with three pathogens standing out: the *Klebsiella pneumoniae* complex, the *Acinetobacter calcoaceticus-baumannii* complex, and *Pseudomonas aeruginosa*. The predominance of the *Klebsiella pneumoniae* complex in antimicrobial resistance is a global phenomenon. High resistance rates have been observed in several regions, such as South Africa (68.3%) and Equatorial Guinea (97.17%).[11] In Europe, rates vary significantly, with Greece presenting 60% of *K. pneumoniae* strains resistant to carbapenems, while in Italy this rate is 40%. 11 In the United States, *K. pneumoniae* is the most prevalent Enterobacterale in the country.[12]

The empirical use of antibiotics in clinical practice and the persistent exposure of *K. pneumoniae* to various antimicrobials are the main factors contributing to the development of resistant strains.[11] The mechanisms of co-resistance and co-selection are fundamental in this process. Co-resistance occurs when resistance genes are located on the same genetic element, such as plasmids, transposons, or integrons, facilitating the transmission of resistance between microorganisms. This linkage of genetic elements enables co-selection for other genes located on the same element, thus culminating in the transmission of resistance genes from one microorganism to another.[13]

Like *K. pneumoniae*, the *Acinetobacter calcoaceticus-baumannii* complex has been recognized as an emerging threat for nosocomial infections and antimicrobial resistance, with mortality rates ranging from 40% to 70%.[14] *Pseudomonas aeruginosa*, included in the list of priority pathogens for the development of new antimicrobials, stands out for its metabolic versatility and ability to adapt to different environments, causing acute and chronic infections.[14,15]

Carbapenems continue to be the class of antimicrobials with the highest resistance in the municipality, reflecting the scenario observed in other South American countries, where the growth of MDR is marked.[16] While in some countries, such as Australia, resistance to carbapenems is still rare, in others, such as Iran, it reached 56.3% in 2008, a figure close to that observed in Porto Alegre (55% in 2021 and 60% in 2022).[17]

It can be inferred from the data found in this study that the qualification of reported data is crucial, as evidenced by the significant reduction in microorganisms without identified resistance in 2022, compared to 2021. In addition, an increase in resistance to third- and fourth-generation cephalosporins was observed in 2022. Resistance to cephalosporins is particularly relevant in Neisseria gonorrhoeae infections, one of the most common community-acquired infections worldwide, highlighting the importance of continuous monitoring.[18]

K. pneumoniae resistance to carbapenems, mediated by carbapenemases, poses a global threat to public health due to its ability to inactivate most beta-lactams.[12,18] The most prevalent enzyme in Porto Alegre is *Klebsiella pneumoniae* Carbapenemase (KPC), whose presence is associated with up to a threefold increase in the hospital mortality rate.[19]

The New Delhi Metallo-β-lactamase (NDM) enzyme has also gained prominence, with its prevalence increasing significantly in the municipality ($p < 0.001$), from 2.9% in 2021 to 17.1% in 2022 (Table 1). First identified in India in 2010, NDM is known for its rapid spread among different species of Enterobacterales, and the growth observed in Porto Alegre reinforces its potential for expansion.[19,20]

Classifying the event as colonization or infection provides information that can be extremely useful in managing and monitoring cases, not only in terms of treatment but also prevention. In the United States, identifying patients colonized by vancomycin-resistant Enterococcus has been an effective strategy for preventing gastrointestinal infections, given that asymptomatic colonization of the intestine is a key factor in infection by gastrointestinal bacteria.[9,16] Thus, the importance of adequate monitoring of these aspects is understood, since it allows surveillance to be an

instrument for qualifying the process of preventing multidrug-resistant infections.[21]

The appropriate choice of materials collected for sensitivity testing is crucial, since the cut-off points for resistance vary according to the sample site (urinary tract, skin, blood, etc.).[22,23] In addition, an appropriate choice of sample origin is essential, as each pathogen may be more abundantly present in a particular sample. For example: for the detection of carbapenemase-producing Enterobacterales, rectal or perirectal swab collection is recommended; for Acinetobacter calcoaceticus-baumannii and Pseudomonas aeruginosa, oropharyngeal, endotracheal, or wound samples are indicated; while for Staphylococcus aureus, nasal swab collection is mandatory.[23]

The data presented in this article highlight the importance of a continuous process of qualification in MDR monitoring for establishing the epidemiological profile. Significant changes observed in 2022 highlight the impact of implementing a new reporting platform.

This study has some limitations that should be considered when interpreting the results. First, the use of secondary data from hospital notifications may be subject to underreporting or inconsistencies in data quality, since the completeness and accuracy of the information depend on proper completion by health professionals. In addition, the change in the reporting system between 2021 (Google Forms and Excel spreadsheets) and 2022 (SENTINELA® Platform) may have introduced variations in the way data were collected and recorded, making it difficult to directly compare the two years. Another limitation is the lack of detailed information on the clinical profile of patients, such as comorbidities, previous use of antimicrobials, and clinical outcomes, which could enrich the analysis of factors associated with antimicrobial resistance.

Nevertheless, the high rate of carbapenem resistance in the city of Porto Alegre underscores the urgent need to revise antibiotic prescribing guidelines, focusing on alternative treatments and more judicious use of broad-spectrum antimicrobials.

It is essential that further research evaluate the effectiveness of antibiotic management programs and new protocols for preventing hospital infections, with a view to containing the growth of antimicrobial resistance.

Finally, it is important to monitor multidrug-resistant microorganisms, given the significant increase in the number of notifications made by hospitals in the municipality, as well as endemic variations by microorganism species and their mechanisms of resistance to antimicrobials, which modify the epidemiological profile of MDR in the municipality. Surveillance of the information obtained through notification forms allows for the planning and implementation of effective strategies to mitigate the impacts of antimicrobial resistance.

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AUTHORS' CONTRIBUTIONS

Danilo Lucas Nunes Ribeiro contributed to the bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables and graphs, conclusions, review, and statistics. **Silvia Adriana Mayer Lentz** contributed to the writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, and review. **Raquel Cristine Barcella** contributed to the writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, and revision.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Original Article

Development and validation of a questionnaire on healthcare-associated infections for companions of hospitalized patients

Desenvolvimento e validação de um questionário sobre infecções relacionadas à assistência à saúde voltado a acompanhantes de pacientes internados

Desarrollo y validación de un cuestionario sobre infecciones relacionadas con la atención de la salud dirigido a acompañantes de pacientes hospitalizados

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ABSTRACT

Background and Objectives: Healthcare-Associated Infections (HAIs) represent a major challenge in hospital settings. Hospitalized patients, healthcare professionals, and patient companions are potential disseminators of pathogens, reinforcing the need for preventive and educational strategies. This study aimed to develop and validate a data collection instrument designed to assess the perceptions of companions of hospitalized patients regarding the transmission and prevention of HAIs. **Methods:** This was a qualitative–quantitative, descriptive, observational, and cross-sectional study conducted in four phases: (1) development of the data collection instrument; (2) content validation by experts using the Content Validity Index (CVI); (3) online validation; and (4) on-site validation in a hospital in the state of Minas Gerais, Brazil. **Results:** A questionnaire consisting of 30 objective items distributed across four thematic sections was developed. Expert evaluation demonstrated high CVI values (ranging from 0.76 to 1.0) for items related to hand hygiene, use of alcohol-based hand rub, respiratory etiquette, vaccination status, and understanding of contagious diseases. The online validation involved 83 participants from different regions of the country and resulted in suggestions for instrument improvement. The on-site validation, conducted with 140 companions in a hospital setting, allowed for adjustments in language, response time, and feasibility of questionnaire application. **Conclusion:** The instrument showed satisfactory evidence of content validity, clarity, and comprehension, indicating its suitability for subsequent phases of application and investigation of companions' perceptions regarding HAIs.

Keywords: *Health education. Hospital infection. Public health.*

RESUMO

Justificativa e Objetivos: As Infecções Relacionadas à Assistência à Saúde (IRAS) são um desafio nos hospitais. Pacientes internados, profissionais de saúde e acompanhantes são potenciais disseminadores de patógenos, o que reforça a necessidade de estratégias preventivas e educativas. Este estudo objetivou desenvolver e validar um instrumento de coleta de dados destinado à avaliação da percepção de acompanhantes de pacientes internados sobre a transmissão e prevenção das IRAS. **Métodos:** Estudo quali-quantitativo, descritivo, observacional e transversal, conduzido em quatro etapas: (1) elaboração do instrumento de coleta de dados; (2) validação de conteúdo por especialistas utilizando o Índice de Validade de Conteúdo - IVC; (3) validação on-line; (4) validação in loco em um hospital de Minas Gerais. **Resultados:** Foi desenvolvido um questionário com 30 questões objetivas, distribuídas em quatro blocos temáticos. A avaliação por especialistas evidenciou IVC elevado (entre 0,76 e 1,0) para itens relacionados à higienização das mãos, uso de álcool gel, etiqueta respiratória, situação vacinal e compreensão sobre doenças contagiosas. A validação on-line contou com 83 participantes de todo o país, resultando em sugestões de aprimoramento do instrumento. A validação in loco, realizada com 140 acompanhantes em ambiente hospitalar, permitiu ajustes na linguagem, no tempo de resposta e na viabilidade de aplicação do questionário. **Conclusão:** O instrumento apresentou evidências satisfatórias de validade de conteúdo, clareza e compreensão, indicando adequação para etapas posteriores de aplicação e investigação das percepções de acompanhantes sobre as IRAS.

Descritores: *Educação em saúde. Infecção hospitalar. Saúde pública.*

RESUMEN

Justificación y Objetivos: Las Infecciones Relacionadas con la Atención de la Salud (IRAS) constituyen un desafío en los hospitales. Los pacientes hospitalizados, los profesionales de la salud y los acompañantes son potenciales diseminadores de patógenos, lo que refuerza la necesidad de estrategias preventivas y educativas. Este estudio tuvo como objetivo desarrollar y validar un instrumento de recolección de datos destinado a evaluar la percepción de los acompañantes de pacientes hospitalizados sobre la transmisión y prevención de las IRAS. **Métodos:** Estudio cualitativo-cuantitativo, descriptivo, observacional y transversal, realizado en cuatro etapas: (1) elaboración del instrumento de recolección de datos; (2) validación de contenido por especialistas mediante el Índice de Validez de Contenido (IVC); (3) validación en línea; y (4) validación in loco en un hospital del estado de Minas Gerais, Brasil. **Resultados:** Se desarrolló un cuestionario con 30 ítems objetivos, distribuidos en cuatro bloques temáticos. La evaluación por especialistas evidenció valores elevados de IVC (entre 0,76 y 1,0) para los ítems relacionados con la higiene de manos, el uso de alcohol en gel, la etiqueta respiratoria, la situación vacunal y la comprensión sobre enfermedades contagiosas. La validación en línea contó con 83 participantes de todo el país y dio lugar a sugerencias de mejora del instrumento. La validación in loco, realizada con 140 acompañantes en un entorno hospitalario, permitió ajustes en el lenguaje, el tiempo de respuesta y la viabilidad de aplicación del cuestionario. **Conclusiones:** El instrumento presentó evidencias satisfactorias de validez de contenido, claridad y comprensión, lo que indica su adecuación para etapas posteriores de aplicación e investigación de las percepciones de los acompañantes sobre las IRAS.

Palabras Clave: *Educación para la salud. Infección hospitalaria. Salud pública.*

INTRODUCTION

According to the World Health Organization, Healthcare-Associated Infections (HAIs) are infections that occur during the care process in healthcare institutions and that were not present at the time of the patient's admission. These infections include clinical manifestations that appear after the third day of hospitalization or after medical procedures. Previously called hospital-acquired or nosocomial infections, they represent a serious public health problem, increasing morbidity, mortality, length of hospital stay, and related costs, in addition to compromising patient safety and the quality of health services.[1,2,3]

HAIs are frequently associated with critical environments, such as ICUs, and are especially serious for those with compromised immune systems or comorbidities.[4] Therefore, the need for effective prevention and control measures is even more evident. Literature suggests that by adopting appropriate practices, HAIs could be avoided, which reinforces the importance of effective control strategies and continuous awareness among all those involved in hospital care and patients.[5,6]

Analyzing risk factors and implementing control measures are essential to mitigate the impact of HAIs in the hospital environment.[7] Although prevention protocols focus primarily on healthcare professionals, there is recognition of the influence of other agents, such as caregivers of hospitalized individuals, on the dynamics of microorganism transmission. The absence of technical or educational barriers aimed at this group compromises the overall effectiveness of control strategies. Beyond reinforcing hygiene practices, it is necessary to integrate caregivers into institutional safety protocols, recognizing their active role in the healthcare environment and their shared responsibility in containing healthcare-associated infections (HAIs).[8]

Studies highlight that patient caregivers can act as vectors in the spread of pathogens.[9] Low adherence to hand hygiene among visitors is seen as a concern, as it contributes to an increased risk of HAIs.[10] Furthermore, the lack of specific guidance and adequate training for caregivers on infection prevention measures exacerbates this situation. The presence of caregivers, coupled with their mobility between different areas of the hospital and direct contact with patients, reinforces the need to include them in infection control strategies.[11]

Therefore, the objective of this study was to develop and validate a data collection instrument, as well as to evaluate its clarity, relevance, and applicability to investigate, in future contexts, the perception of caregivers of hospitalized patients regarding the transmission and prevention of HAIs.

METHODS

The study was characterized as qualitative-quantitative, descriptive, observational, and cross-sectional. This research took place between February and November 2024 and was divided into four phases: 1) Creation of a data collection instrument for caregivers; 2) Validation by experts; 3) Online validation; 4) On-site validation (Figure 1).

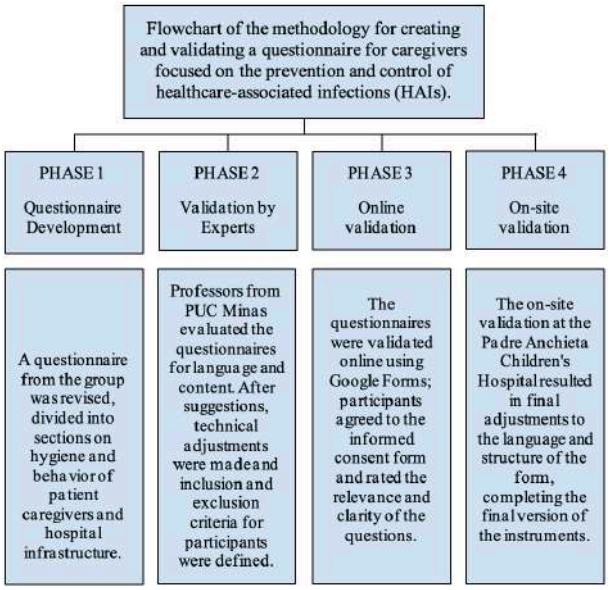

Figure 1. Schematic diagram of the questionnaire validation methodology.

In phase 1, carried out in February 2024, the data collection instrument was created based on a previous questionnaire model used with caregivers of patients hospitalized in a teaching hospital in the South of the country.[12] The reformulation considered recent scientific publications and the post-Covid-19 pandemic context, with necessary language adjustments and content insertion.[13,14,15]

The second phase, also held in February, involved the content validation of the questionnaire using the Content Validity Index (CVI) by 25 health experts from across the country, with at least a specialization, invited directly by email. The experts were selected for having training and/or experience in the areas of microbiology, infection control, public health or related fields. The professionals judged each item of the questionnaire regarding relevance, clarity and applicability, using a five-point Likert scale, ranging from 1 (“not relevant”) to 5 (“very relevant”). For the calculation of the CVI, responses with a score equal to or greater than 4 were considered valid, with the index obtained by the ratio between the number of responses 4 and 5 and the total number of respondents. In addition, at the end of each thematic section, participants evaluated the set of items through dichotomous questions ("yes"/"no"); for these, the CVI was calculated by assigning a value of 1 to positive responses and 0 to negative ones.

The online validation, the third phase of the research, took place between March and May 2024, where people with a profile similar to that of the target audience of the final questionnaire gave their opinions on the relevance of the topics covered and the language of the data collection instrument. Data collection was carried out using the simple random sampling technique, through the dissemination of an electronic form on the researchers' social networks.

Participants accessed the electronic address of the Google Forms Platform containing the Free and Informed Consent Form – TCLE, socioeconomic questions and the questionnaire to be evaluated. Participants rated the questions in each section as Relevant (R), Not Very Relevant (NVR), or Indifferent (I), evaluating the items as components of the instrument, as well as assessing the language and clarity of the questions. At the end of the online questionnaire, participants could suggest, add, or remove any question or topic. There was no time limit for answering the questionnaire; however, the "completion time" and "questionnaire size" were considered for the participants' evaluation.

The inclusion criteria for selecting participants in phase 3 were: being 18 years old or older, not working/having worked in the health field, or not pursuing/having pursued undergraduate or graduate studies in the health field, and signing the Informed Consent Form. Professionals and students in the health field were excluded from the study because they possessed prior knowledge that could interfere with the lay evaluation of the instrument, as well as those who did not agree with the Informed Consent Form or who did not complete the questionnaire in full.

The fourth phase of the research consisted of on-site validation of the instrument, conducted in person at the Padre Anchieta Children's Hospital (HIPA), located in Belo Horizonte - MG, between May and November 2024, with the objective of testing the clarity, comprehension, application time, and operational feasibility of the questionnaire. After explaining the research, obtaining agreement and signing the Informed Consent Form by companions of hospitalized patients, the questionnaires were applied in the form of an interview, focusing on evaluating the comprehension of the items and the dynamics of application, with the responses being recorded by the researchers. This phase aimed to evaluate the clarity, comprehension, and applicability of the instrument in a real-world context of use.

Descriptive statistical analysis was conducted systematically, with the data being tabulated and organized using Microsoft Office Excel and Graphpad Prism. For statistical purposes, in Tables 2, 3, and 4, the responses were quantified as follows: Relevant (R) received the value 2, Slightly Relevant (PR) the value 1, and Irrelevant (I) the value 0. This categorization allowed for the calculation of the mean and standard deviation, facilitating the visualization and interpretation of the results.

The research was approved under Opinion No. 6,497,920 and Certificate of Presentation for Ethical Appraisal (CAAE) No.: 73990023.00000.5137 issued on February 2, 2024. The conduct of the research fully complied with the ethical standards established by Resolutions No. 466/2012, No. 510/2016, and No. 580/2018 of the National Health Council/Ministry of Health, which regulate research involving human beings in Brazil.

RESULTS

As a result of phase 1 of the study, a questionnaire composed of 30 objective questions was developed, organized into four thematic sections: sociodemographic information, hygiene, practices and conduct, and hospital infrastructure.

Phase 2, validation by experts, showed high CVI (between 0.76 and 1.0) for items related to hand hygiene, use of alcohol gel, respiratory etiquette, vaccination status, and understanding of contagious diseases, indicating high clarity and relevance. In contrast, items that addressed non-compliance with hygiene practices, patient care during intestinal infection, the use of accessories in the hospital environment, and institutional guidance to the caregiver presented lower CVIs (0.36 to 0.56), possibly because they involved socially undesirable behaviors or reflected institutional variations. In general, the instrument demonstrated adequate content validity, with lower CVIs concentrated in potentially sensitive items, without compromising the representativeness of the construct evaluated.

Phase 3 involved 83 participants from all over Brazil who judged the relevance of the 30 questions in the instrument created in the previous phases. The majority of participants were between 18 and 28 years old (41%), female (67.5%), with incomplete undergraduate or postgraduate studies (44.6%), living in the Southeast region (83.1%). Approximately 80% of participants stated that they had previously accompanied an inpatient, with an average follow-up period of 1 to 3 days (56.5%) (Table 1).

Table 1. Sociodemographic Characteristics and Hospital Experience of Participants for the Online and On-site Phases.

Variable	Categories	N (%) 83 online
Age range (years)	18-27	34 (41.0)
	28-37	15 (18.1)
	>38	34 (41.0)
Gender	Female	56 (67.5)
	Male	27 (32.5)
Education	Incomplete undergraduate/postgraduate studies	21 (25.3)
	Complete High School	17 (20.5)
	Others	45 (54.2)
Region of residence	Southeast	72 (86.8)
	Others	11 (13.2)
Prior monitoring	Yes	66 (79.5)
	No	17 (20.5)
Duration of monitoring	1-3 days	39 (56.5)
	> 4 days	44 (43.5)

Abbreviation: NA: Not applicable.

The results of phase 3 were analyzed according to the sections containing questions designed to assess the clarity, pertinence, and relevance of the questionnaire items, aimed at understanding the participants' perception of: the importance of hygiene in the hospital context; practices and conduct of caregivers; hospital infrastructure; and the exchange of information between professionals and caregivers (Tables 2, 3, and 4, respectively).

The data regarding the relevance attributed by the participants to the questionnaire items that address hygiene practices show good indicators for handwashing, but contradictory rates for other hygiene practices. This fact is proven in the category "washing hands before and after entering the room or hospital," in which they obtained 92.7% and 96.3% responses in the "Relevant" category, respectively. The use of hand sanitizer before and after leaving the room/hospital was classified as “Relevant” by 90.3% and 89.1% of participants, respectively, while access to 70% alcohol whenever necessary received 74.6% responses as “Relevant”. Practices such as touching bodily fluids (57.8%) and caring for patients without washing hands (28.9%) showed a number below the average of responses considered “Relevant”, indicating less agreement regarding the adequacy of these items as questions in the instrument. Regarding behavior after returning home, 79.5% of participants indicated that the statement of washing clothes separately is “Relevant”. Other practices such as lending hygiene products (34.9%), removing shoes upon arriving home (42.1%), and sanitizing belongings (40.9%) showed a greater standard deviation from the mean, suggesting divergence in the assessment of the relevance of these items (Table 2).

Table 2. Results of the online validation on the relevance of items related to hand hygiene and biosecurity.

Statements	R (%)	NVR (%)	I (%)	ME	SD
I wash my hands before entering the room and/or hospital.	77 (92)	6 (7)	0 (0)	1.93	0.26
I wash my hands after leaving the room and/or hospital.	80 (96)	3 (4)	0 (0)	1.96	0.19
I use hand sanitizer before arriving at the room and/or hospital.	78 (94)	1 (1)	4 (5)	1.89	0.44
I use hand sanitizer after leaving the room and/or hospital.	75 (90)	4 (5)	4 (5)	1.61	0.71
I have access to 70% alcohol whenever I need it.	62 (75)	18 (22)	3 (4)	1.76	0.46
I have touched bodily fluids or contaminated objects.	40 (48)	30 (36)	13 (16)	1.33	0.73
I have had to care for more than one patient without washing my hands or using gloves.	29 (35)	50 (60)	4 (5)	0.87	0.76
I have helped care for other patients without washing my hands.	32 (38)	47 (57)	4 (5)	1.34	0.57
I arrive home after returning from the hospital and wash my clothes along with other clothes.	66 (79)	5 (6)	13 (16)	1.90	0.34
I borrow hygiene products from other patients or their respective companions.	29 (35)	54 (65)	0 (0)	1.35	0.48
When I arrive home, I leave my shoes outside.	35 (42)	17 (20)	31 (37)	1.29	0.86
I sanitize my belongings, taken to the hospital, when I arrive home.	34 (41)	31 (37)	18 (22)	1.19	0.77

Abbreviation: R: Relevant; NVR: Not Very Relevant; I: Indifferent; ME: Mean and SD: Standard Deviation.

Section 3 of the questionnaire refers to the assessment of the relevance of items regarding the practices and conduct of patient caregivers. Among the responses to this section, 55.4% of participants considered the question about accompanying someone to the hospital while they have the flu to be “Relevant,” and 30.1% reported the same in cases of intestinal infection. Regarding vaccination, 91.5% indicated that keeping vaccination records up-to-date was relevant, and 90.3% reported knowing what a contagious disease is. The use of jewelry was considered “Relevant” by 37.3% of participants, while 44.5% indicated the use of patients' bedsheets as “Relevant.” The items regarding the use of electronic devices and covering the mouth or nose when coughing or sneezing were indicated as “Relevant” by 53.0% and 86.7% of people, respectively (Table 3).

Table 3. Results of online validation regarding the relevance of items related to practices and conduct.

Statements	R (%)	NVR (%)	I (%)	ME	SD
I have accompanied someone to the hospital when I had the flu.	46 (55)	32 (38)	5 (7)	1.4	0.61
I have cared for patients while I had an intestinal infection.	25 (30)	52 (62)	6 (7)	1.23	0.57
My vaccination record is up to date.	76 (91)	7 (8)	0	1.92	0.28
I know what it means for a disease to be contagious.	75 (90)	7 (8)	1 (1)	1.89	0.35
I wear earrings and accessories while in the hospital environment.	31 (37)	30 (36)	22 (26)	1.11	0.79
I use the patient's sheets to cover myself in the hospital.	37 (44)	43 (52)	31 (37)	1.41	0.56
I use electronic devices, writing and reading materials during the visit.	44 (53)	20 (24)	19 (23)	1.30	0.82
I usually cover my mouth and nose when coughing or sneezing while accompanying a patient in the hospital.	72 (87)	6 (7)	5 (7)	1.81	0.53

Abbreviation: R: Relevant; NVR: Not Very Relevant; I: Indifferent; ME: Mean and SD: Standard Deviation.

Section 4 of the data collection instrument addresses the analysis of the relevance of items related to hospital infrastructure. Among the participants, 73.4% rated seeing posters teaching how to wash hands at sinks and in bathrooms as "Relevant". Regarding access to masks and gloves, 59.0% indicated it as "Relevant", 38.5% as "Somewhat Relevant", and 2.4% as "Indifferent". The statement about access to soap and water at handwashing sinks was considered "Relevant" by 77.1% of people, and receiving information about the correct way to contact patients was considered "Relevant" by 60.2% of people, while 32.5% rated it as "Somewhat Relevant" and 7.2% as "Indifferent". Regarding the information provided by the medical team about the patient's illness being contagious, 72.2% considered it "Relevant," 14.4% "Not very relevant," and 13.2% "Indifferent" (Table 4).

Table 4. Results of online validation regarding the relevance of items related to hospital infrastructure.

Statements	R (%)	NVR (%)	I (%)	ME	SD
I see posters teaching how to wash hands at the sinks and bathrooms.	61 (73)	11 (13)	11 (13)	1.60	0.71
I have access to masks and gloves whenever I need them.	49 (59)	32 (38)	2 (2)	1.57	0.54
I have access to soap and water at the handwashing sinks.	64 (77)	11 (13)	8 (10)	1.67	0.64
The hospital instructed me on the correct way to interact with the patient when I am a caregiver.	50 (60)	27 (32)	6 (7)	1.53	0.63
I received information from the medical team that the illness of the patient I am caring for is contagious.	60 (72)	12 (14)	11 (13)	1.59	0.71

Abbreviation: R: Relevant; NVR: Not Very Relevant; I: Indifferent; ME: Mean and SD: Standard Deviation.

Regarding satisfaction with the data collection instrument, 97% of participants stated that the questions were relevant and 88% stated that the language was clear and easy to understand, reinforcing the suitability of the instrument as a data collection tool. Suggestions were incorporated to change the language of some questions and to add new questions in sections 1 and 2.

Thus, after reformulation, the questionnaire had 35 questions with the answer options "yes", "no", "I don't know". It was used in phase 4, the on-site validation, carried out with 140 caregivers of patients hospitalized at HIPA. The results revealed that most participants were female (94.2%), aged between 28 and 37 years (42.8%), had completed high school (47.1%) and had a family income between 1 and 3 minimum wages (35%). In addition, 62.1% of caregivers accompanied children with respiratory diseases, mainly in the first days of hospitalization (66%). During on-site validation, it was observed that some questions needed reformulation because they had been misinterpreted, similar questions were causing bias in the answers, and terms were identified as "confusing" or "difficult to understand." The questionnaire response time was also evaluated and, in practice, exceeded expectations. Participant resistance was observed when interviews exceeded seven minutes. To address this issue, interviewers were trained for interactions of up to five minutes in duration.

Regarding sociodemographic information, new variables were added, including the caregiver's relationship with the patient, reason for hospitalization, and length of hospital stay. The reformulations aimed not only to improve the questionnaire's applicability but also to facilitate the statistical analysis of the data and ensure internal consistency between the thematic sections, providing a more intuitive response experience for participants.

DISCUSSION

The adequacy, clarity, and relevance of the instrument's items are discussed in light of the literature, as well as the judgment standards assigned by participants during the validation phases. It is observed

that even with prior contact with the hospital environment, the judgment of low relevance attributed to certain items highlights important informational gaps, reinforcing the need for educational strategies and interventions in the hospital context.[5]

Regarding the data from the online validation phase, it is observed that in the section dedicated to hand hygiene and biosafety practices, most questions were considered "Relevant," indicating agreement regarding the clarity and relevance of the items, especially with regard to hand washing and the use of alcohol in the hospital environment. However, items recognized as priorities by the Ministry of Health were classified as “Not Very Relevant” or “Indifferent,” suggesting challenges in understanding these practices by the evaluated population.[16]

For example, more than half of the participants considered the statements “I sanitize my belongings, taken to the hospital, when I get home” and “I have had to care for more than one patient without washing my hands or using gloves” to be irrelevant. In the context of validating the instrument, these findings justify maintaining these items, since they address critical practices for the prevention of HAIs, which can contribute to cross-contamination, that is, the transmission and dissemination of microorganisms between the hospital and home environments and between beds, spreading infections.[6]

In the section on practices and conduct, the low relevance attributed by participants to the item related to the use of jewellery in the hospital environment stands out, despite its importance according to the Ministry of Health.1[6] It is worth emphasizing that these jewellery can act as vehicles for the transmission of microorganisms, contributing to the spread of infections in the outpatient environment.[17] Similarly, the reduced judgment of relevance attributed to staying in the hospital while ill indicates weaknesses in the understanding of this risk, considering that clinically ill visitors should avoid frequenting health units because they are potential transmitters of HAIs.[18]

The results of the section on hospital infrastructure indicate that the community perceives the importance of the existence of informative posters about hand washing and the availability of resources for this practice. From a validation perspective, these findings confirm the clarity and relevance of the infrastructure-related items, since handwashing is a fundamental practice in controlling the spread of pathogens and depends on the adequate supply of water, soap, and hand sanitizer.[19,20] Studies have demonstrated that educational campaigns aimed at caregivers and family members increase awareness and improve adherence to hand hygiene practices, supporting the inclusion of these items in the questionnaire.[21,22]

The on-site validation phase was fundamental for understanding and practical functionality of the instrument in the hospital context. During this process, the adjustments made allowed for better management of response time and reinforced the methodological character of the study, centered on the validation of the instrument, with the elaboration of clearer and more accessible guidelines for the lay population.

The need for linguistic adjustments corroborates the literature, which highlights the importance of considering sociocultural variations when constructing texts and data collection instruments.[23] The use of technical terms without language adaptation can compromise the understanding and reliability of the responses, impacting the quality of the data obtained.[24] This difficulty is important in themes related to the prevention of HAIs, in which translating technical concepts into accessible language, without losing scientific rigor, becomes fundamental to ensure the understanding and effective participation of caregivers in infection control strategies.[12]

Another factor adjusted in the face-to-face application was the response time of the questionnaire by caregivers. In a hospital setting, the time available to caregivers is limited and impacted by the dynamics of care for hospitalized patients and by emotional factors.[14] Reformulating questions and standardizing response options reduced application time, increasing the instrument's viability in real-world scenarios and facilitating subsequent analyses.

Countries that have adopted rigorous health education protocols for caregivers have shown a reduction in cases of HAIs, reinforcing the effectiveness of these measures in containing the transmission of pathogens and improving hospital safety. This evidence reinforces the relevance of instruments that support structured educational actions. By recognizing the caregiver as a fundamental link in the care network, a more humanized, preventive care model aligned with the guidelines of a safety culture is created.[1,8,20] The developed instrument offers a consistent methodological basis for future investigations, in which the training of this individual can be explored as an essential component of infection prevention policies and the promotion of quality of health care.

The validation phases were fundamental to improving the instrument in terms of content, clarity, and language appropriateness, reinforcing the importance of systematic validation processes before its analytical application. However, limitations were identified, such as low adherence in the online validation, possibly associated with the initial length of the questionnaire, and the restriction of face-to-face validation to a single hospital context. To mitigate these limitations, the instrument was revised and optimized, with a reduction

in redundancies and simplification of sentences, aiming to increase its acceptability.

The results of this study contribute to strengthening continuing health education actions and the prevention of HAIs in the hospital environment. The instrument is validated in terms of content, clarity, and relevance, offering a structured basis for future investigations with caregivers of hospitalized patients and enabling its adaptation to different hospital settings, favoring the understanding of the role of caregivers in strategies for preventing healthcare-associated infections.

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AUTHORS' CONTRIBUTIONS

Arielle Teixeira Silva has contributed to project management, bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, table creation, conclusions, review, and statistics. **Rafaela Bergamini Resende Silveira** has contributed to project management, abstract writing, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics. **Fabrício Gomes Michel** has contributed to abstract writing, methodology, interpretation of results, conclusions, review, and statistics. **Evelyn Lívia Miranda da Silva** has worked remotely, contributing to the creation of the abstract, analysis and interpretation of online data, final text review, and support in the methodological organization of the study. **Tânia Elisabete Dias de Castro** has contributed to project management and data collection, as well as facilitating access to the research field and institutional information. **Thaimara Ribeiro Leite de Castro** has contributed to project management and data collection, as well as facilitating access to the research field and institutional information. **Sabrynna Brito Oliveira** was responsible for guiding the project, contributing to the methodological design, supervision of activities, critical review of the content, and final validation of the work.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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Perfil epidemiológico da dengue antes e durante a pandemia de Covid-19 em Mato Grosso
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ABSTRACT

Background and Objectives: The magnitude and severity of dengue may have been impacted by the Covid-19 pandemic. This study aimed to compare the incidence rate and the sociodemographic and clinical profile of suspected dengue cases reported in Mato Grosso (MT), Brazil, in the three-year period before and during the pandemic (2017–2022). **Methods:** This was a case series study based on secondary data from notification forms in the Notifiable Diseases Information System (SINAN) in MT 2017-2022. Incidence rates were analyzed across the state's 16 Health Regions, as well as sociodemographic and clinical characteristics. The chi-square test was used to compare the two trienniums, with a significance level of 5%. **Results:** A lower incidence rate was observed in the last triennium in the Baixada Cuiabana and Norte Araguaia regions, and a higher rate in the other regions during the pandemic triennium compared to the previous one — for instance, in Teles Pires, the rate increased from 806.5 to 7,161.7 cases per 100,000 inhabitants. In the 2020–2022 triennium, there was a higher proportion of cases among males, children aged 1 to 9 years, individuals of white race, those with higher education levels, and with laboratory confirmation. The proportion of cured cases was similar in both trienniums, and DENV-1 was the predominant serotype in both periods. **Conclusion:** The data indicate a higher cumulative incidence rate of dengue during the pandemic triennium compared to the previous period, with variations in sociodemographic and clinical profiles, which may have been influenced by the Covid-19 pandemic.

Keywords: *Dengue Virus. Arboviruses. Aedes aegypti. Covid-19. Public Health Surveillance.*

RESUMO

Justificativa e Objetivos: A magnitude e gravidade da dengue pode ter sido impactada pela pandemia de Covid-19. O estudo teve como objetivo comparar a taxa de incidência e o perfil sociodemográfico e clínico dos casos suspeitos de dengue notificados em Mato Grosso (MT) no triênio anterior e durante a pandemia (2017-2022). **Métodos:** Estudo de série de casos realizado a partir de dados de fonte secundária das fichas de notificação do Sistema de Informação de Agravos de Notificação (SINAN) de MT de 2017 a 2022. Foram avaliadas as taxas de incidência nas 16 Regiões de Saúde do estado e as características sociodemográficas e clínicas. Utilizou-se o teste qui-quadrado para comparação entre os triênios, com nível de significância de 5%. **Resultados:** Observou-se menor taxa de incidência no último triênio nas regiões da Baixada Cuiabana e Norte Araguaia, e maior taxa nas demais regiões no triênio da pandemia em comparação com o triênio anterior, Teles Pires, com 806,5 no primeiro para 7161,7 casos por 100.000 habitantes no segundo triênio. Foi maior a proporção de casos do sexo masculino, na faixa etária de 1 a 9 anos, cor branca, maior escolaridade e com confirmação laboratorial no triênio 2020-2022. A proporção de casos curados ocorreu de forma semelhante e DENV-1 foi o sorotipo predominante em ambos os triênios. **Conclusão:** Os dados indicam maior taxa de incidência acumulada de dengue no triênio de pandemia quando comparado ao período anterior, com diversidade no perfil sociodemográfico e clínico, que podem ter ocorrido por influência da pandemia de Covid-19.

Descritores: *Vírus da dengue. Infecções por Arbovirus. Aedes Aegypti. Covid-19. Vigilância em Saúde Pública.*

RESUMEN

Justificación y Objetivos: La magnitud y gravedad del dengue pueden haber sido impactadas por la pandemia de Covid-19. El estudio tuvo como objetivo comparar la tasa de incidencia y el perfil sociodemográfico y clínico de los casos sospechosos de dengue notificados en Mato Grosso (MT), Brasil, en el trienio anterior y durante la pandemia (2017–2022). **Método:** Se realizó un estudio de serie de casos a partir de datos secundarios provenientes de las fichas de notificación del Sistema de Información de Agravos de Notificación (SINAN) del estado de Mato Grosso, entre los años 2017 y 2022. Se evaluaron las tasas de incidencia en las 16 Regiones de Salud del estado, así como las características sociodemográficas y clínicas de los casos. Para la comparación entre los trienios se utilizó la prueba de chi-cuadrado, con un nivel de significancia del 5%. **Resultados:** Se observó una menor tasa de incidencia en el último trienio en las regiones de Baixada Cuiabana y Norte Araguaia, y una mayor tasa en las demás regiones durante el trienio pandémico en comparación con el anterior. En la región de Teles Pires, por ejemplo, la tasa aumentó de 806,5 a 7.161,7 casos por 100.000 habitantes. En el trienio 2020–2022 se registró una mayor proporción de casos en hombres, en el grupo de edad de 1 a 9 años, personas de raza blanca, con mayor nivel educativo y con confirmación de laboratorio. La proporción de casos curados fue similar en ambos trienios, y el DENV-1 fue el serotipo predominante en ambos períodos. **Conclusión:** Los datos indican una mayor tasa de incidencia acumulada de dengue durante el trienio pandémico en comparación con el período anterior, con variaciones en los perfiles sociodemográfico y clínico, las cuales podrían haber sido influenciadas por la pandemia de Covid-19.

Palabras Clave: *Virus del Dengue. Arbovirus. Aedes aegypti. Covid-19. Vigilancia en Salud.*

INTRODUCTION

Dengue is a growing concern, particularly in tropical regions. In Brazil, dengue epidemiological surveillance involves multiple levels of government, ranging from municipal health departments to the Ministry of Health.[1] Thus, preventing outbreaks relies heavily on surveillance through tracking previously diagnosed cases, as well as monitoring and controlling vectors.[2]

The range of the Aedes aegypti mosquito has expanded into new regions due to urbanization, globalization, human mobility, and climate change. Outbreaks of diseases transmitted by these mosquitoes are increasing in tropical areas and are now affecting subtropical and temperate regions.[2] These data underscore the ongoing importance of epidemiological surveillance and coordinated public health efforts to combat dengue, which remains a significant public health concern in Brazil.[3]

The declaration of a Public Health Emergency of International Concern due to the novel coronavirus (Covid-19) infection posed significant challenges to health systems globally. These challenges affected the diagnosis and management of other infectious diseases, including dengue.[4] During the pandemic, the initial symptoms of both diseases were similar, which posed diagnostic challenges and required adaptations in screening and diagnostic strategies.[5,6]

Another relevant point is that, in the early stages of the pandemic, access to diagnostic testing was limited and many private and university laboratories in Brazil were not equipped to perform large-scale testing. In this context, Central Public Health Laboratories (LACENs) emerged as key pillars in the response to the health crisis, playing a crucial role in early diagnosis and virus monitoring. Their operational capacity and technical expertise were essential for epidemiological surveillance, as evidenced by their contributions to the response to the health crisis. As the pandemic escalated, the LACENs significantly expanded their testing capacity and rapidly adapted their protocols to include diagnosing SARS-CoV-2, playing an essential role in guiding public health policies and control measures.[7]

Due to operational challenges such as reduced field teams and reallocated resources to combat the pandemic, the capacity to respond to dengue may have been affected. This includes the suspension of essential health services and difficulties screening and classifying suspected dengue cases, especially during periods when there is overlap with cases of the pandemic. These factors may indicate the impact of the pandemic on dengue control.[6]

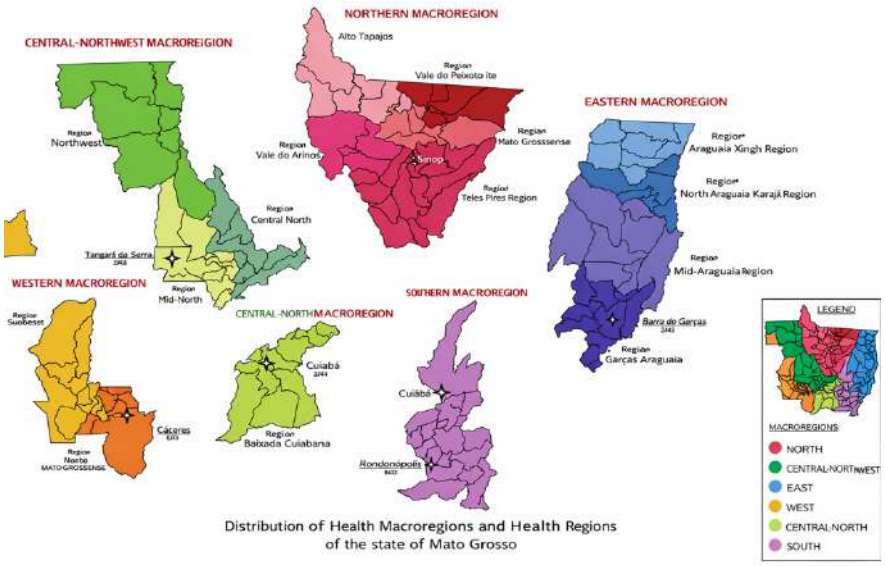
Due to the complexity of the pandemic period, comparing reported cases from 2017–2019 to 2020–2022 may reveal changes in the epidemiological profile due to disparities in access to health services, diagnosis, and dengue transmission. This comparison could contribute to integrating lessons learned during the pandemic into current dengue surveillance practices in Mato Grosso, Brazil. Thus, this study aimed to compare the incidence rate and sociodemographic and clinical profiles of suspected dengue cases reported in Mato Grosso (MT) during the three years prior to and during the pandemic (2017–2022).

METHODS

This ecological, cross-sectional study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist. Using secondary data obtained from dengue notification forms in the Information System for Notifiable Diseases (SINAN) from 2017 to 2022, the study compared disease incidence rates and sociodemographic and clinical characteristics across the 16 health regions of Mato Grosso during the triennia 2017–2019 and 2020–2022.

The study population comprised residents of the state of Mato Grosso, which is located in Brazil's Central-West region and has a population of 3,658,649.[8] The territory is organized into six health macroregions—North, Central-North, East, West, South, and Central-Northwest—which are subdivided into 16 health regions, as established by Resolution CIB/SES No. 57 of July 26, 2018 (Figure 1).[9]

Suspected dengue cases reported in Mato Grosso between 2017 and 2022 were analyzed according to sociodemographic and clinical profiles, with no exclusions.



Distribution of Health Macroregions and Health Regions of the state of Mato Grosso

Figure 1. Distribution of Health Macroregions and Health Regions in the State of Mato Grosso.

The sociodemographic variables analyzed were the following: health region of residence, sex (male or female), age group (1–9 years, 10–19 years, 20–59 years, or 60 years and older), race/skin color (white, black, yellow, brown, indigenous, or unknown), and educational level (illiterate, incomplete or complete elementary education, incomplete or complete secondary education, or incomplete or complete higher education).

The clinical variables included reported serotype (DENV-1, DENV-2, DENV-3, or DENV-4); serological test result (IgM positive, negative, inconclusive, or unknown); diagnostic criterion (laboratory, clinical-epidemiological, or unknown); PCR testing performance (performed or not performed); and case outcome (recovery, death due to dengue, or death due to other causes).

To calculate the incidence rates for 2017–2019, we considered the total number of reported cases during that period and the estimated resident population for 2017 by the Brazilian Institute of Geography and Statistics (IBGE), multiplied by 100,000 inhabitants. To calculate the incidence rates for 2020–2022, we used the IBGE's estimated population for 2020 and the cumulative number of cases during that period, multiplied by 100,000 inhabitants.

The data were imported and analyzed using Stata software. Descriptive statistical analyses were performed, including measures of central tendency and dispersion, as well as the absolute and relative frequencies of the reported suspected cases. The chi-square test was used to compare analyzed sociodemographic and diagnostic-related variables between the 2017–2019 and 2020–2022 periods, adopting a 5% significance level.

The Research Ethics Committee of the State University of Mato Grosso (UNEMAT) approved this study, which was conducted using publicly available data (CAEE: 65072322.3.0000.5166; Opinion No. 5,823,767).

RESULTS

Between 2017 and 2022, a total of 120,816 suspected dengue cases were reported in Mato Grosso, 27,860 of which occurred in the pre-pandemic triennium and 92,956 of which occurred during the pandemic triennium. The Teles Pires health region had an incidence rate of 7,161.7 cases per 100,000 people from 2020 to 2022, compared to an incidence rate of 806.5 cases per 100,000 people from 2017 to 2019. In the Baixada Cuiabana health region, where the state capital is located, the incidence rate was 1,032.8 cases per 100,000 people in the 2017–2019 period and 551.9 cases per 100,000 people in the 2020–2022 period (Figure 2).

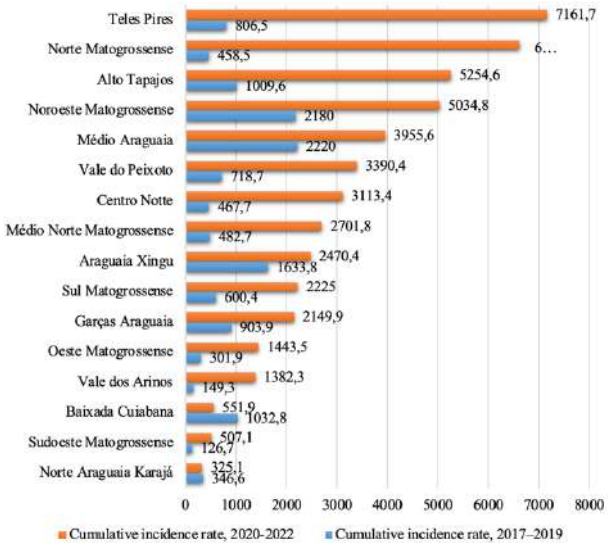


Figure 2. Dengue incidence rate (per 100,000 people) by health region in Mato Grosso during the triennia of 2017–2019 and 2020–2022.

A significant difference in the distribution of cases by sex was observed between the two analyzed triennia (p<0.01). From 2020 to 2022, the proportion of male cases increased from 46.10% to 48.54%, compared to the previous triennium. There was also significant variation in age group (p<0.01), particularly in the 1–9 age group, which increased proportionally from 11.65% to 14.45%.

Regarding race/skin color, the proportion of notifications increased among individuals classified as white during the pandemic (30.79%) compared to the previous period (25.56%), while the proportion of individuals classified as brown decreased. This pattern was reflected in the educational level variable as well, with a significant increase in the proportion of cases among individuals who had completed secondary education (Table 1).

Table 1. Sociodemographic Characteristics of Suspected Dengue Cases Reported in Mato Grosso, Brazil During the 2017–2019 and 2020–2022 Triennia.

	2017-2019 N (%)	2020-2022 N (%)	p-value*
Sex			<0.01
Male	12,838 (46.10)	45,097 (48.54)	
Female	15,011 (53.90)	47,810 (51.46)	
Age group (in Years)			
Under 1 year old	612 (2.20)	1,950 (2.14)	
1-9	3,247 (11.65)	13,429 (14.45)	
10-19	5,150 (18.49)	16,675 (17.94)	
20-59	16,485 (59.17)	53,513 (57.57)	
60 or older	2,365 (8.49)	7,352 (7.91)	
Race/skin color			<0.01
White	7,122 (25.56)	28,622 (30.79)	
Black	1,274 (4.57)	3,520 (3.79)	
Yellow	213 (0.76)	956 (1.03)	
Brown	16,488 (59.18)	49,568 (53.32)	
Indigenous	114 (0.41)	383 (0.41)	
Unknown	2,648 (9.51)	9,906 (10.66)	
Education			<0.01
Illiterate; incomplete elementary education	4,988 (34.09)	16,732 (32.15)	
Complete elementary education	3,814 (26.07)	12,889 (24.77)	
Incomplete/complete secondary education	4,686 (32.03)	17,937 (34.47)	
incomplete/complete higher education	1,144 (7.82)	4,479 (8.61)	
Ignored	13,228 (47.48)	40,919 (44.02)	

Abbreviation: *p-value of the chi-square test.

An increase in the proportion of cases confirmed by laboratory criteria was observed when the diagnostic confirmation criterion was evaluated between the two analyzed triennia, rising from 35.4% to 57.2% (p < 0.01). While the proportion of PCR testing remained stable, the number of PCR tests performed increased from 271 to 856, reflecting an expansion of diagnostic capacity in the state during the pandemic. There was also an increase in the proportion of positive IgM results (from 24.92% to 32.96%) and in the predominance of the DENV-1 serotype (from 64.46% to 83.85%) between the two periods (Table 2).

Table 2. Diagnostic-related aspects of suspected dengue cases reported during the 2017–2019 and 2020–2022 triennia in Mato Grosso.

	2017-2019 N (%)	2020-2022 N (%)	p-value*
Diagnostic criterion	-	-	<0,01
Laboratory	9,859 (35.4)	53,171 (57.2)	
Clínical-epidemiological	14,672 (52.7)	29,046 (31.2)	
Unkown	3,329 (11.9)	10,739 (11.5)	
p-value			
PCR testing			<0.01
Performed	271 (0.97)	856 (0.92)	
Not performed	19,830 (71.18)	52,963 (56.98)	
Unkown/blank	7,759 (27.85)	39,137 (42.10)	
p-value			
IgM para dengue			
Positive	6,943 (24.92)	30,640 (32.96)	<0.01
Negative	1,160 (4.16)	5,102 (5.49)	
Inconcluive	106 (0.38)	295 (0.32)	
Unkown	19,651 (70.53)	76,570 (61.23)	
p-value			<0.01

continue

	2017-2019 N (%)	2020-2022 N (%)	p-value*
Sorotiype			
DENV-1	107 (64.46)	457 (83.85)	
DENV-2	39 (23.49)	84 (15.41)	
DENV-4	20 (12.05)	4 (0.73)	
p-value			
Outcome			<0.01
Recovery	23,710 (85.10)	77,509 (83.38)	
Death due dengue	13 (0.05)	51 (0.05)	
Death due other causes	21 (0.08)	56 (0.06)	
Unkown	4,116 (14.77)	15,340 (16.50)	

Abbreviation: *p-value of the chi-square test.

DISCUSSION

This study significantly contributes to our understanding of dengue epidemiological dynamics in the state of Mato Grosso. It accomplishes this by comparing two distinct periods: before and during the Covid-19 pandemic. The study demonstrates how this context influenced not only disease incidence, but also the sociodemographic profile of reported cases and diagnostic patterns. The analysis, which is based on SINAN data, identifies changes that may have been driven by shifts in population behavior, reorganization of health services, the impact of social distancing measures, and the prioritization of resources to address the pandemic. Understanding these changes is essential for guiding future strategies for integrated surveillance and responses to endemic diseases in public health emergency scenarios. The findings presented here may inform more effective public policies and encourage similar studies in other regions of the country.

When analyzing incidence rates across Mato Grosso's health regions, the vast majority showed an increase in rates during the second triennium. However, Baixada Cuiabana and North Araguaia Karajá health regions showed a slight reduction.

The higher incidence rates observed during the pandemic were consistent with national trends. Bulletins from the Ministry of Health revealed that dengue incidence increased throughout the country during the 2020–2022 period.[7] However, the reduction observed in regions such as Baixada Cuiabana and North Araguaia-Karajá suggests different hypotheses. One possibility is underreporting of cases during the pandemic, particularly in regions with a higher concentration of health facilities dedicated to treating patients with Covid-19. Another hypothesis is that social isolation imposed during the outbreaks reduced urban mobility and consequently exposure to the vector in densely populated areas. Additionally, these regions may have implemented more effective vector control measures, which had a localized impact on viral transmission.[10] Such regional variations underscore the necessity of ongoing territorial analyses sensitive to local contexts, especially in scenarios involving overlapping health crises.

Upon evaluating the sociodemographic characteristics, it was observed that, although women accounted for the majority of reported suspected cases, the proportion of male cases increased from 46.1% during the 2017–2019 period to 48.54% during the 2020–2022 period. Changes in the distribution of cases by age group were also noted, including a proportional increase in the 1–9 age group, which increased from 11.65% in the first triennium to 14.45% in the second. This increase among children may be due to their greater immunological susceptibility, resulting from lower prior exposure to the dengue virus and reduced acquired immunity against different circulating serotypes. Changes in patterns of household and recreational exposure during social isolation may also be a factor. The suspension of in-person school activities and increased time spent at home may have expanded contact with vector breeding sites in residential environments. The increase in notifications among white individuals and those with higher educational attainment may reflect historical inequalities in access to diagnosis, with more advantaged groups being more likely to access health services and undergo testing.[11] The reduction in the 20–59 age group may indicate lower healthcare-seeking behavior in this group during the pandemic due to fear of contracting Covid-19 or prioritizing care for more vulnerable groups.

At the aggregate level, the literature has shown that income and race/skin color impact incidence rate ratios within a territory, with higher risks among those who self-identify as Black or Brown.[12] However, analysis of the race/skin color variable revealed a proportional increase in notifications among those classified as White from 2020 to 2022 compared with the previous period (increasing from 25.56% to 30.79%), while the proportion of notifications among those who self-identify as Brown decreased (decreasing from 59.18% to 53.32%). The results of the present study should be interpreted with caution, as previous studies have indicated that the distribution of reported dengue cases by race/skin color often reflects inequalities in access to health services, patterns of health system use, and the quality of notification form completion.[13]

Regarding educational level, the proportion of cases among individuals with complete secondary education increased from 32.03% in 2017–2019 to 34.47% in 2020–2022. However, as previously

described in the literature, the high level of incompleteness of these variable limits more robust inferences about the educational profile of cases in the state.[14] In this sense, the findings reinforce the need to improve the quality of notification form completion, which is essential for more accurate epidemiological analyses and for planning surveillance and control actions.

A substantial increase in laboratory confirmation was noted regarding diagnostic criteria in the 2020–2022 period compared with the previous triennium. This may indicate improved access to or greater availability of laboratory testing during this period, which may be associated with the enhanced capacity and technology that laboratories implemented to confront the Covid-19 pandemic. Laboratory diagnosis of dengue is essential for confirming infection and ensuring the appropriate clinical management of patients.[15] During the pandemic, the Central Public Health Laboratory (LACEN) of Mato Grosso rapidly adapted to implement and expand testing. This laboratory played a crucial role in identifying cases of SARS-CoV-2 while simultaneously continuing to diagnose other endemic diseases, such as dengue.[16] This growth may indicate an increase in the operational capacity of state public laboratories, driven by investments made for SARS-CoV-2 testing. The expansion of equipment, supplies, and laboratory teams during the pandemic may indirectly benefit the diagnosis of endemic diseases, such as dengue.

PCR testing and IgM detection for dengue revealed significant differences between the two time periods. The increase in IgM detection indicates greater viral circulation in the more recent period. It may also be related to intensified laboratory surveillance and sustained viral circulation in the state. These results highlight the importance of monitoring collective immunity dynamics, particularly in populations with prior exposure to different serotypes, as this can elevate the risk of severe dengue through cross-reactive immune responses.[17]

The distribution of dengue serotypes changed significantly between the analyzed periods. Although DENV-1 predominated in both periods, its proportion increased markedly in the second period, while the proportion of DENV-2 decreased. This dynamic may reflect cycles of serotype replacement, a widely described phenomenon in the literature associated with the interaction between viral circulation and the population's collective immunity profile.[17] The reemergence or intensification of a given serotype's circulation tends to occur when population-specific immunity declines, favoring its spread in endemic contexts. Additionally, shifts in serotype predominance have significant implications for disease severity because secondary infections with different serotypes are associated with a higher risk of severe dengue mediated by immunological mechanisms, such as antibody-dependent enhancement.[17]

The increase in cases with unknown outcomes during the second triennium (from 14.77% to 16.50%) suggests that there were weaknesses in the timely closure of notifications during the pandemic. This may be due to an overload of epidemiological surveillance teams, reassignment of professionals to the response to the pandemic, and prioritization of respiratory conditions in care flows. In many municipalities, the pandemic caused disorganization in record systems, hindering monitoring of the clinical outcomes of suspected cases. Studies indicate that public health emergency contexts tend to generate discontinuity in endemic disease follow-up processes, especially when conditions with similar symptoms overlap, such as dengue and Covid-19.[18] These findings reinforce the importance of maintaining resilient health surveillance structures capable of responding simultaneously to different threats.

The present study revealed significant changes in the sociodemographic and clinical profiles of dengue cases in Mato Grosso between 2017 and 2022, suggesting a potential shift in access to diagnosis and disease notification. This shift was likely influenced by the Covid-19 pandemic. The need to allocate resources and attention to combating the virus may have compromised dengue epidemiological confirmation and surveillance. However, there was also increased access to laboratory confirmation of cases. This increase may reflect a greater emphasis on diagnostic accuracy, which contributes to differentiation and provides a more precise and critically important response. During the pandemic, distinguishing dengue symptoms from those of Covid-19 was more difficult due to health system overload.[19]

Although a higher number of notifications were recorded during the pandemic triennium, diagnostic delays or underreporting cannot be ruled out, as most medical and laboratory resources were directed toward addressing the pandemic. This situation underscores the complexity of the challenges that health systems face when managing two public health crises simultaneously.

This study has limitations inherent to the use of secondary data from SINAN, including underreporting, incomplete records, and possible inconsistencies in the outcome and final classification fields. There is a particular emphasis on the incompleteness of the educational level variable. These limitations may have affected the accuracy of certain variables, particularly during periods of greater health system overload. The absence of detailed clinical data and complete laboratory information also limited the analysis of specific clinical outcomes.

This study revealed significant changes in the epidemiological and laboratory profiles of dengue in

Mato Grosso when comparing the pre- and pandemic periods of the Covid-19 pandemic. There was an increase in the cumulative incidence rate, a shift in the most affected age groups, a change in the sociodemographic profile of reported cases, and an increase in laboratory confirmations. These variations suggest the pandemic directly influenced epidemiological surveillance through service reorganization and increased laboratory testing availability. These findings address the objective of analyzing the impact of the pandemic on dengue notifications and diagnoses, emphasizing the need for resilient health systems that can address multiple diseases simultaneously. Understanding these transformations is essential to improving dengue control and prevention strategies, particularly in the event of future overlapping public health emergencies.

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AUTHORS' CONTRIBUTIONS

Michelly Lustri Fabre de Figueiredo contributed to drafting the abstract and methods, interpreting the results, drawing conclusions, reviewing the manuscript, and performing statistical analyses. **Elaine Cristina de Oliveira** provided and

coordinated access to the data, supporting the understanding of the database. **Ana Cláudia Pereira Terças Trettel** contributed to the review of the manuscript and the interpretation of the results. **Ana Paula Muraro** contributed to the drafting of the abstract and methods, the interpretation of the results, the conclusions, the manuscript review, and the statistical analyses.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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PUBLICAÇÃO OFICIAL DO NÚCLEO HOSPITALAR DE EPIDEMIOLOGIA DO HOSPITAL SANTA CRUZ E PROGRAMA DE PÓS GRADUAÇÃO EM PROMOÇÃO DA SAÚDE - DEPARTAMENTO DE BIOLOGIA E FARMÁCIA DA UNISC

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Original Article

Free and nanoemulsified Cymbopogon flexuosus essential oil: antifungal effect on Candida spp. in vitro

Óleo essencial de Cymbopogon flexuosus livre e nanoemulsionado: efeito antifúngico sobre Candida spp. in vitro
Aceite esencial de Cymbopogon flexuosus libre y nanoemulsionado: efecto antifúngico sobre Candida spp. in vitro

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ABSTRACT

Background and Objectives: The *Cymbopogon* genus has attracted interest due to its bioactive compounds with antifungal and antimicrobial potential. This study investigated the *in vitro* antifungal activity of free and nanoemulsified essential oil of *Cymbopogon flexuosus* against ATCC standard strains of *Candida* spp. **Methods:** The strains used in the assay were *Candida albicans*, *Candida tropicalis*, *Candida krusei*, and *Candida glabrata*, tested alongside a positive control (Fluconazole and Amphotericin B) and a negative control (distilled water + Tween 80 at 2%). The agar diffusion technique was employed. After treatment, the assays were incubated at 36 °C for 48 hours and performed in six replicates. **Results:** Antifungal activity was observed against all ATCC strains tested. The free oil at concentrations of 10%, 15%, and 70% showed activity similar to the positive control for *Candida tropicalis*. The nanoemulsified oil at a concentration of 5% presented results comparable to the positive control for *Candida glabrata*. **Conclusion:** Among the species tested, *Candida albicans* proved to be the most sensitive at all concentrations, whereas *Candida krusei* was the most resistant to essential oil treatment. Further toxicological and clinical studies are needed to complement our findings.

Keywords: *Cymbopogon. Nanoparticles. Phytochemicals.*

RESUMO

Justificativa e Objetivos: O gênero *Cymbopogon* sp. tem despertado interesse devido aos seus compostos bioativos com potencial antifúngico e antimicrobiano. Este estudo investigou a atividade antifúngica *in vitro* do óleo essencial de *Cymbopogon flexuosus* livre e nanoemulsionado contra cepas padrão ATCC de *Candida* spp. **Métodos:** Foram utilizadas no ensaio as cepas de: *Candida albicans*, *Candida tropicalis*, *Candida Krusei* e *Candida glabrata*, comparadas a um controle positivo (Fluconazol e Anfotericina B) e controle negativo (água destilada+Tween 80 a 2%). A técnica utilizada foi de difusão em ágar. Após o tratamento, os ensaios foram incubados a 36°C, por 48 horas, sendo realizados com seis repetições. **Resultados:** No ensaio foi observada atividade antifúngica para todas as cepas ATCC testadas. O óleo livre nas concentrações de 10, 15 e 70% foi semelhante ao controle positivo para *Candida tropicalis*. A concentração de 5% do óleo nanoemulsionado apresentou resultado semelhante ao controle positivo para *Candida glabrata*. **Conclusão:** Entre as espécies testadas, a *Candida albicans* mostrou ser mais sensível em todas as concentrações; a *Candida krusei* foi a cepa mais resistente para o uso de óleo essencial. Novos estudos, de cunho toxicológico e clínico, são necessários para complementar nossos achados.

Descritores: *Cymbopogon. Nanopartículas. Compostos Fitoquímicos.*

RESUMEN

Justificación y Objetivos: El género *Cymbopogon* ha despertado interés debido a sus compuestos bioactivos con potencial antifúngico y antimicrobiano. Este estudio evaluó la actividad antifúngica *in vitro* del aceite esencial de *Cymbopogon flexuosus* libre y nanoemulsionado contra cepas estándar ATCC de *Candida* spp. **Método:** En el ensayo se utilizaron las cepas *Candida albicans*, *Candida tropicalis*, *Candida krusei* y *Candida glabrata* comparadas con un control positivo (Fluconazol y Anfotericina B) y un control negativo (agua destilada + Tween 80 al 2%). Se empleó la técnica de difusión en agar. Tras el tratamiento, los ensayos fueron incubados a 36°C durante 48 horas y realizados con seis repeticiones. **Resultados:** En el ensayo se observó actividad antifúngica para todas las cepas ATCC evaluadas. El aceite libre en concentraciones del 10%, 15% y 70% mostró actividad similar al control positivo para *Candida tropicalis*. La concentración del 5% del aceite nanoemulsionado presentó resultados comparables al control positivo para *Candida glabrata.* **Conclusión:** Entre las especies analizadas, *Candida albicans* demostró ser la más sensible en todas las concentraciones, mientras que *Candida krusei* fue la cepa más resistente al uso del aceite esencial. Se requieren nuevos estudios, de carácter toxicológico y clínico, para complementar nuestros hallazgos.

Palabras Clave: *Cymbopogon. Nanopartículas. Fitoquímicos.*

INTRODUCTION

Yeasts can colonize humans and loss of the parasite-host balance cause localized or disseminated infectious, conditions that have shown increasing incidence. Among yeasts, the genus *Candida* sp. is greatly relevant due to its high colonization and infection in human hosts.[1] *Candida albicans* is the species most frequently isolated from superficial infections, followed by *Candida tropicalis*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, and *Candida lusitaniae*.[2]

The treatment for *Candida* sp. pathogenicity involves antifungals, drugs that are often ineffective due to fungal resistance.[3] *Candida* sp. resistance to antifungal treatment has been attributed to recurrent infections and intermittent and continuous exposure to antifungals.[4] Thus, the decrease in yeast sensitivity to conventional antifungals has increased the interest in natural antifungal products to find new alternatives to treatment with good efficacy, spectrum of action, and tolerability.[3]

Essential oils (EOs) stand out among the novel alternatives for their phytochemical pharmacological properties in in vitro models and antibacterial and antifungal action.[5] Studies with EOs show that these oils have *in vitro* antifungal activity in *Candida* spp. strains.[6]

Of the plants producing OEs, the genus *Cymbopogon* sp. and the species *Cymbopogon flexuosus* (Nees ex Steud) Will Watson (popularly known as lemongrass) stands out. The main constituent in its EO is (3,7-dimethyl-2,6-octadienal), followed by geraniol, citronellol, and citral.[5,7] The encapsulation of bioactive compounds such as EOs aims to protect them against degradation and improve their stability to increase their durability up to fungal death.[8] Nanoemulsions (nanometric emulsions of green synthesis mediated by plants) are among the most advantageous alternatives for encapsulating EOs compared with other chemical and physical methods due to their relatively small droplet sizes, with average radii of up to 200nm.[9]

Thus, natural products have a promising potential in the development of new antifungal options. Thus, this study aims to evaluate the antifungal activity of free and nanoemulsified EOs of *C. flexuosus* against *C. albicans*, *C. glabrata*, *C. krusei*, and *C. tropicalis*.

METHODS

The EO was extracted from fresh *C. flexuosus* leaves at the Unijuí Oleochemical Complex in Três Passos/RS (27°26'02.4" latitude S and 53°57'06.7" longitude W). A modified D20 Clevenger, manufactured by LINAX, was used for 1 h 30 min for hydrodistillation. The plant was identified in the Botany Laboratory of the Universidade Regional do Noroeste do Estado do Rio Grande do Sul. The species was cataloged and registered in the Rogério Bueno University Herbarium under number 8113 (*C. flexuosus*) according to Flora do Brasil.[10]

The nanoemulsions were developed at the Nanotechnology Laboratory of Universidade Francisca in Santa Maria/RS by a high-energy method without organic solvents and with temperature control.[11] The formulations (n=3) were obtained after an injection of an oily phase (5% oil) and 2% sorbitan monooleate (Span 80®) in the aqueous phase (2% polysorbate 80 - Tween 80® - and ultrapure water) under high agitation in an T18 Ultra-Turrax® (IKA®, Germany at 10,000 rpm). After mixing, the mixture was agitated at 17,000 rpm for 45 minutes. During the obtention of the nanoemulsions, a temperature control (ice bath) was carried out to prevent volatilization and/or the degradation of the oil constituents. For comparisons, negative control formulations were prepared (n=3) using capric/caprylic triglyceride mixture. All formulations were prepared in triplicates and stored in the dark. The final concentration of the nanoemulsified EO totaled 5%.

Antifungal activity was evaluated by agar diffusion with ATCC strains of *C. albicans* (CAMT05), *C. tropicalis* (CTMT16), *C. krusei* (ATCC6258), and *C. glabrata* (CGMT01) strains that were donated by the Applied Mycology Research Laboratory at Universidade Federal do Rio Grande do Sul. The strains were seeded in sterile plates with a Sabouraud agar medium by loop sowing. Cell density was adjusted with a spectrophotometer, adding enough saline solution up to a standard solution equivalent to the 0.5 McFarland scale at a 625-nm wavelength. After being seeded with the fungus, the surface of the plates was drilled at different points, forming holes with about 5 mm in diameter.

For the antimicrobial susceptibility tests, the concentrations were prepared from free and nanoemulsified EO, which were diluted in water and emulsified in 2% polysorbate 80 (Tween™ 80) (Table 1).

Table 1. Concentrations (%) of free and nanoemulsified essential oils prepared for testing.

	Tested concentrations (µL mL⁻¹)	Concentration OE in %	Description
Treatment 1 - Free EO	25; 50; 100; 300; 700; 1000µL	2.5, 5, 10, 15, 30, 70, 100%	Free *Cymbopogon flexuosus* + sterile distilled water
Treatment 2 – Nanoemulsified EO b*	15; 30; 60; 125; 1000µL	0.3125, 0.625, 1.25, 2.5, 5%	Nanoemulsified *Cymbopogon flexuosus* + sterile distilled water
Positive control	-	-	Fluconazole and Amphotericin B
Negative Control	-	-	Sterile distilled water with Tween 80 at 2%

Abbreviation: b* At the end of the emulsification, the nanoemulsified essential oil had a 5% concentration.

The concentrations were prepared in sterile Eppendorf microtubes in sufficient quantities for 1mL. After adding the components, the microtubes were subjected to a mechanical vortex agitator for two minutes; an operation that was immediately repeated before each experiment.

In the plates, 20-µL (microliter) aliquots of essential oil from each solution concentration were applied to each orifice. After preparing the plates with the treatments, the plates were incubated at 36°C for 48 hours. Then, the diameters of the inhibition halos were measured in mm. In total, two positive controls were used: a) The results were evaluated by measuring the diameters of the growth inhibition halos (mm). The assay was performed in six replicates.

The results were tabulated on Microsoft Office Excel® and analyzed on the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA), version 23.0. The data are shown as means and standard deviations. For each tested fungus, all concentrations were compared by the one-way analysis of variance and the Tukey's post-hoc tests.

Based on the project description, this research required no consideration by the Ethics Committee for Research with Human Beings or by the Ethics Committee for the Use of Animals since no human beings or vertebrate animals were used in the experimental stages of this research.

RESULTS

This study obtained positive results (Table 2). The 24-hour results for *C. glabrata* and *C. tropicalis* strains and the 10, 15, 30, and 70% of free EO concentrations did not statistically differ from the positive control. For *Candida albicans*, the 10 and 70% doses showed efficacy but with no differences from the positive control. *C. krusei* showed no inhibition halo in any free EO concentration. At the 100% free EO concentration, the plates showed no fungal growth for any tested species 24 hours after incubation since such EO concentration inhibited any growth on the entire plate in the test, making it impossible to read the halo.

The mean free EO 10, 15, 30, and 70% concentrations show no mean differences for *C. albicans*, *C. glabrata*, and *C. tropicalis* 48 hours after incubation when compared with the positive control, which showed a 29.17-mm inhibition halo, indicating good antifungal activity.

Table 2. Inhibition halos (mm) formed by the antifungal action of free *C. flexuosus* essential oil on C. spp. strains after 24 and 48 hours.

	Candida albicans CAMT05						*Candida glabrata* CGMT01					
	24h			48h			24h			48h		
Concentration in %	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2
2.5	13.17	1.47	B	21.50	4.37	B	14.83	1.83	B	18.83	0.98	B
5	19.00	0.89	B	20.50	2.17	B	18.67	1.21	B	20.33	1.86	B
10	27.17	1.17	A	29.67	1.51	A	27.83	1.47	A	26.83	3.13	A
15	22.67	1.75	B	28.67	3.01	A	24	3.01	A	23.83	1.94	A
30	19.67	1.51	B	28.33	2.66	A	25.83	3.92	A	25.83	3.92	A
70	25.83	2.99	A	26.83	2.40	A	25.33	4.18	A	27.17	3.13	A
100	0	0		0	0		0	0		0	0	
C+	28.33	1.21	A	29.17	1	A	26.67	4.32	A	28.17	3.43	A
C-	0	0	B	0	0	B	0	0	B	0	0	B
p1	<0.001			<0.001			<0.001			<0.001		
	Candida krusei ATCC6258						*Candida tropicalis* CTMT16					
	24h			48h			24h			48h		
Concentration In %	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2
2.5	0	0	B	0	0	B	18.67	2.73	B	16.83	2.23	B
5	0	0	B	0	0	B	20.33	1.97	B	16.67	2.07	B
10	0	0	B	0	0	B	32.67	2.42	A	24.69	1.79	A
15	0	0	B	0	0	B	31.33	1.63	A	29.83	2.71	A
30	0	0	B	0	0	B	27.84	2.34	A	28.67	3.27	A
70	0	0	B	0	0	B	28.50	2.81	A	23.17	3.13	A
100	0	0	B	0	0	B	0	0	B	0	0	B
C+	21.67	2.34	A	25.33	3.01	A	29.00	3.52	A	29.33	3.50	A
C-	0	0	B	0	0	B	0	0	B	4.67	11.43	B
p1	<0.001			<0.001			<0.001			<0.001		

Abbreviation: c+ = positive control; c−= negative control; SD=standard deviation; p1=1-way analysis of variance. P2=post hoc test to compare each concentration and c+; A (no significant difference between concentrations and c+; b (value significantly lower than c+).

The nanoemulsified EO showed inhibition halos at 1.2–-5% concentrations for all strains. For *C. tropicalis*, 24h after the incubation, only the 5% concentration had an effect equal to that of the positive control (Table 3); the 2.5 and 5% doses stood out at 48 hours. For *C. krusei*, at 48h, the 1.25, 2.5, and 5% concentrations showed inhibition halos equal to the control group, as in *C. albicans* at 24h and 48h. The 0.3% concentration showed no inhibition halos in the tested strains, except in *C. glabrata*, which averaged 12±14mm. *C. krusei* and *C. tropicalis* better resisted the 0.325 and 0.625% concentrations of the nanoemulsified oil.

Table 3. Nanoemulsified EO data. Inhibition halos (mm) formed by the antifungal action of nanoemulsified *C. flexuosus* essential oil on strains *Candida* spp. after 24 and 48 hours.

	Candida albicans CAMT05						*Candida glabrata* CGMT01					
	24h			48h			24h			48h		
Concentration in %	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2
0.31	0	0	B	0	0	B	12.333	1.5055	B	14.667	3.7238	B
0.63	15.33	3.93	B	19.67	1.97	B	13.67	2.66	B	16.33	4.46	B
1.25	21.67	4.63	A	25.33	4.84	A	25.17	3.82	A	25.50	3.78	A
2.5	19.50	2.66	B	24	3.88	A	17.33	3.72	A	21.67	3.67	A
5	20.33	5.28	A	20.33	7.20	B	25.67	3.44	A	29.67	3.20	A
C+	26.00	3.10	A	28.00	4.56	A	23.17	4.92	A	27.00	4.52	A
C-	0	0	B	0	0	B	0	0	b	0	0	B
p1	<0.001			<0.001			<0.001			<0.001		

	Candida krusei ATCC6258						*Candida tropicalis* CTMT16					
	24h			48h			24h			48h		
Concentration in %	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2	Mean	SD	p2
0.31	0	0	B	0	0	B	0	0	B	0	0	B
0.63	0	0	B	7.33	5.75	B	0	0	B	0	0	B
1.25	21.67	2.34	B	23.17	3.92	A	20.33	1.97	B	21.67	2.34	B
2.5	22.67	1.63	A	22.33	1.51	A	25.67	3.44	B	28.67	2.73	A
5	27.33	6.15	A	23.33	7.45	A	29.33	3.01	A	26.00	3.10	A
C-	27.00	3.29	A	29.00	2.76	A	30.33	3.44	A	32.00	1.79	A
C-	0	0	B	0	0	B	0	0	B	0	0	B
p1	<0.001			<0.001			<0.001			<0.001		

Abbreviation: c+ = positive control; c-= negative control; SD= standard deviation; p1=1-way analysis of variance. P2=post hoc test to compare each concentration and C+; A (no significant difference between concentrations and c+; b (value significantly lower than c+). Source: developed by the author, 2024.

DISCUSSION

The antifungal biological activity of the free and nanoemulsified EOs in this study inhibited fungal growth. This effect is related to their complex phytochemical composition, which includes citral, pinene, cineole, caryophyllene, elemene, furanodiene, limonene, eugenol, eucalyptol, carvacrol, and others. Such constituents have antiseptic, antibacterial, antifungal, and antiparasitic properties.[12]

Similar research has evaluated the antifungal activity of the *Cymbopogon winterianus* and *Cymbopogon martinii* OEs in *C. albicans* strains. It observed that at a 15% concentration, both oils showed growth inhibition halos that averaged above 32mm, corroborating this study, which found that free *C. flexuosus* at 10 and 15% concentrations showed similar results for *C. albicans*, averaging 29mm. In our assays, the *C.* spp. strains, except *C. krusei*, showed inhibition due to low *C. flexuosus* concentrations, just as in a study on *Cymbopogon citratus* EO in isolated strains of *C. albicans* and *C. tropicalis* in 10, 15, 25, 35, 50, and 60% concentrations.[13] It observed that, at the 15% concentration, the EO showed halos averaging 21mm in *C. albicans*, similar to the results in our study, which, at this concentration, showed a 22-mm mean halo.

A study evaluated the fungicidal effect of *Rosmarinus officinalis* Linn EO in an agar diffusion in *C. dubliniensis*, *C. albicans*, *C. parapsilosis*, and *C. krusei* strains.[14] Its results showed inhibition halos ranging from 39 to 47mm due to its free essential oil. Those authors also observed an inhibition halo for *C. krusei*, unlike our study. *R. officinalis* EO has α-Pinene and 1,8-Cineole (cineole) in its phytochemical composition, which may be responsible for the antifungal effect against this strain. Note the divergent methodologies between that study and ours, which may contribute to such findings due to the absence of standardized techniques to evaluate antifungal activity (unlike the evaluation of antifungal drugs, which was standardized by the Clinical and Laboratory Standards Institute M27-A3 methodology).

C. krusei, responsible for invasive infections, differs from other species due to its intrinsic resistance to the antifungal fluconazole stemming from its morphological and metabolic characteristics. Such information may influence the therapeutic approach and pathogenicity of this species when compared to others, which may explain our findings, in which *C. krusei* showed no fungal growth for free EO, only halo formation at 1.25, 2.5, and 5% concentrations of the nanoemulsified EO.[15] Free EOs are volatile, have a low molecular weight, and

enter a gaseous state when exposed to the environment. On the other hand, nanoemulsions protect EOs against degradation in harsh environments, providing sufficient stability, persistence, and permeability over time.[16] This may justify the results of this study, indicating a potential use of nanoemulsified *C. flexuosus* EO on *C.* spp.

Researchers have conducted a similar investigation on the effect of free and nanoemulsified *Origanum vulgari* L., (oregano) EO in a 5% concentration by oil mass.[17] They found that free and nanoemulsified OEs showed effective activity against the tested strains, especially for *C. albicans*. These results corroborate this research, in which the free and nanoemulsified *C. flexuosus* EOs also showed antifungal effects against *C. albicans*. Although these above used different EOs, both have terpenes, which may be responsible for the observed effect.

Researchers have also evaluated the effect of the antifungal activity of EOs, including of *Laurus nobilis*, *Thymus vulgaris*, *Mentha piperita*, *Cymbopogon citratus*, and *Lippia junellian* on clinical *C. krusei*, *C. albicans*, *C. glabrata*, and *C. parapsilosis* strains.[18] Among the tested oils, the one with the greatest activity on these strains was that of *C. citratus* and *L. nobilis*. Of the tested strains, *Candida albicans* showed the greatest sensitivity to these EOs. Both EOs showed efficacy against the tested strains, obtaining antifungal effects at low concentrations. The phenolic compounds responsible for the antifungal activity of EOs can be evalulated at the macromorphological and cellular levels.[8] Macromorphological changes include lack of sporulation or pigmentation, change in the number of conidia, increase in the branching of the hyphae, or change in their size.[19] EOs can inhibit the synthesis of DNA, RNA, proteins, and polysaccharides in fungi and bacterial cells, which can cause similar changes to the mechanism of antibiotic activity.[19,20]

The findings evince that the tested free and nanoemulsified EO showed significant fungal activity in the tested species and that the 10, 15, and 70% concentrations obtained similar results to the positive control. The free EO 100% concentration failed to inhibit the halos of all tested strains. The nanoemulsified EO at 1.25, 2.5, and 5% showed inhibition halos for all tested strains; its 5% concentration showed a result similar to the positive control. *C. albicans* showed greater inhibition halos. Comparing the means of the free and nanoemulsified EO inhibition halos obtained positive results.

Despite its promising results, this study has some limitations that require consideration. It only carried out *in vitro* tests, which limits the extrapolation of its data to clinical applications as it ignored issues such as toxicity, safety, and efficacy in more complex biological models. It also neither investigated the mechanisms of action of the active compounds in the EOs nor the stability of the nanoemulsions over time.

Free and nanoemulsified *C. flexuosus* EOs showed antifungal activity against the tested strains. However, it is crucial to carry out more studies to better understand the mechanisms of action of EOs and to consider safety and toxicity issues to develop formulations that guarantee stable compounds. Ultimately, research on EOs offers promising prospects for the development of new therapeutic strategies to combat fungal infections. We emphasize the need for clinical studies to evaluate its effectiveness.

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AUTHORS' CONTRIBUTIONS

Dara Monize Pazze and **Christiane de Fátima Colet** contributed to the bibliographic research, writing of the abstract, introduction, methodology, and discussion, interpretation and description of the results, preparation of tables, conclusions, review, and statistics. **Kétlin Luiza Strada** and **Karine Raquel Uhdich Kleibert** contributed to project management, bibliographic research, writing of the abstract, introduction, methodology, and discussion, interpretation and description of results, conclusions, review, and statistics. **Gabriela Matte Bertoldi**, **Ivan Ricardo Carvalho** and **José Antônio Gonzalez da Silva** contributed to the writing of the abstract, and methodology, interpretation of results, conclusions, review, and statistics. **Fernanda Wagner Boz** contributed to the writing of the abstract, review, and statistics. **Patrícia Gomes** and **Giane Engel Montagner** contributed to project administration, fund acquisition, literature research, proofreading, and statistics. **Dara Monize Pazze** and **Christiane de Fátima Colet** contributed to project management, bibliographic research, writing of the abstract, introduction, methodology, and discussion, interpretation and description of results, conclusions, review, and statistics.

All authors approved the final version to be published and are accountable for all aspects of this study, including ensuring its accuracy and integrity.

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Review Article

Healthcare-associated infections and mechanisms of microorganism resistance: a scoping review

Infecções relacionadas à assistência à saúde e os mecanismos de resistência de microrganismos: revisão de escopo

Infecciones asociadas a la atención sanitaria y los mecanismos de resistencia de los microorganismos: revisión del alcance

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ABSTRACT

Background and Objectives: healthcare-associated infections are preventable adverse events that contribute to microbial resistance and constitute a public health problem. Thus, this study aims to evaluate the profile of healthcare-associated infections and resistance mechanisms of microorganisms from 2019 to 2024. **Methods:** this scoping review was prepared according to the PRISMA Extension for Scoping Reviews checklist. The acronym "participants, concept, and context" was used as the search strategy. The participants in this study were patients with nosocomial healthcare-associated infections who were aged 18 years or older. The concept included studies on nosocomial infections, epidemiology, and mechanisms of microorganism resistance. Randomized and non-randomized clinical trials, observational studies, and reviews with and without meta-analysis that were published in English, Portuguese, and Spanish and carried out from January 2019 to August 2024, were considered. The sources of evidence used were the Virtual Health Library, the National Library of Medicine, Scopus, and Google Scholar. **Results:** the incidence of healthcare-associated infections in Brazil and worldwide has increased, with the main sites of infection referring to the bloodstream, urinary tract, and respiratory tract. The predominant microorganisms were Gram-negative, with the following main resistance mechanisms: oxacillinases, carbapenemase-producing Klebsiella, New Delhi metallo-β-lactamases, and Verona integron. **Conclusion:** knowledge about the epidemiology of healthcare infections can help promote health actions and control and prevent infections.

Keywords: *Cross Infection. Health care. Health care delivery. Anti-infectives. Microbial drug resistance.*

RESUMO

Justificativa e Objetivos: as infecções relacionadas à assistência à saúde são eventos adversos evitáveis, que contribuem para a resistência microbiana, constituindo-se um problema de saúde pública. Assim, o estudo objetiva avaliar o perfil de infecções relacionadas à assistência à saúde e os mecanismos de resistência dos microrganismos no período de 2019 a 2024. **Métodos:** trata-se de uma revisão de escopo, elaborada de acordo com o checklist PRISMA *Extension for Scoping Reviews*. Foi empregado como estratégia de busca o acrônimo *participants, concept* e *context*. Os participantes desse estudo foram pacientes com infecções relacionadas à assistência à saúde nosocomiais com 18 anos ou mais. Foram incluídos como conceito estudos sobre infecções nosocomiais, epidemiologia e mecanismo de resistências de microrganismos. Foram considerados como base deste artigo ensaio clínico randomizado e não randomizado, estudos observacionais e revisão com e sem metanálise publicados em inglês, português e espanhol, realizadas entre janeiro de 2019 a agosto de 2024. As fontes de evidências utilizadas foram a Biblioteca Virtual em Saúde (BVS - Lilacs), National Library of Medicine, Scopus e Google acadêmico. **Resultados:** destaca-se o aumento da incidência de infecções relacionadas à assistência à saúde no Brasil e no mundo, tendo como principais sítios de infecção a corrente sanguínea, o trato urinário e o trato respiratório. Os microrganismos predominantes foram os gram-negativos, e como principais mecanismos de resistências: as oxacilinases, *Klebsiella* Produtora de Carbapenemase, metalo-β-lactamases de Nova Délhi e Intergron de Verona. **Conclusão:** o conhecimento acerca da epidemiologia das infecções em saúde pode auxiliar na promoção de ações em saúde e no controle e prevenção de infecções.

Descritores: *Infecção Hospitalar. Assistência em saúde. Prestação de cuidados de saúde. Anti-infecciosos. Resistência microbiana a medicamentos.*

RESUMEN

Justificación y Objetivos: las infecciones relacionadas con la atención sanitaria son eventos adversos prevenibles y contribuyen a la resistencia microbiana, lo cual es un problema de salud pública. Así, este estudio tiene como objetivo evaluar el perfil de las infecciones relacionadas con la atención sanitaria y los mecanismos de resistencia de los microorganismos de 2019 a 2024. **Método:** esta es una revisión del alcance, preparada de acuerdo con la lista de verificación de PRISMA *Extension for Scoping Reviews*. Se utilizó como estrategia de búsqueda los términos *participants*, *concept* y *context*. Los participantes en este estudio fueron pacientes con infecciones nosocomiales asociadas a la atención médica, con edades de 18 años o más. El concepto incluía estudios sobre infecciones nosocomiales, epidemiología y mecanismos de resistencia de los microorganismos. Se consideraron ensayos clínicos aleatorios y no aleatorios, estudios observacionales y revisiones con y sin metaanálisis publicados en inglés, portugués y español, realizados entre enero de 2019 y agosto de 2024. Las fuentes de evidencia utilizadas fueron la Biblioteca Virtual en Salud (BVS - Lilacs), Biblioteca Nacional de Medicina, Scopus y Google Scholar. **Resultados:** se destaca el aumento de la incidencia de infecciones relacionadas con la atención sanitaria en Brasil y en el mundo, y los principales sitios de infección son el torrente sanguíneo, las vías urinarias y las vías respiratorias. Los microorganismos predominantes fueron gran-negativos; y los principales mecanismos de resistencia, oxacilinasas, *Klebsiella* productora de carbapenemasas, metalo-β-lactamasas de Nueva Delhi e Intergron de Verona. **Conclusión:** el conocimiento sobre la epidemiología de las infecciones sanitarias puede ayudar a promover acciones sanitarias y a controlar y prevenir infecciones.

Palabras Clave: *Infección hospitalaria. Asistencia sanitaria. Prestación de asistencia sanitaria. Antiinfecciosos. Farmacorresistencia microbiana.*

INTRODUCTION

Healthcare-associated infections (HAIs) are considered avoidable adverse events, as correctly adopting prevention and control measures nullify the emergence of these diseases.[1,2] For health services, HAIs configure a public health problem as their prevalence is related to high rates of morbidity and mortality, longer hospitalization stays, and increased health costs that negatively affect quality of care and favor the selection and dissemination of multidrug-resistant microorganisms.[3,4]

Epidemiology estimates a 10% global prevalence of HAIs cases (developed countries show a 15% incidence).[5] The United States diagnoses about 1.7 million patients a year (of whom almost 100,000 die) and averages US$ 35 to 45 billion dollars in hospitalizations a year.[3,6] On the other hand, Brazil shows a 15.5%, incidence; daily hospitalization costs 55% more in patients with HAIs.[3,4]

HAIs can be defined as a clinical nosocomial condition patients acquire after 48 hours of hospitalization that were absent or in incubation at the time of admission.[7,8] The main risk factors include invasive devices, prolonged hospitalizations, antibiotics and immunosuppressants, age > 60 years, multiple comorbidities, and previous surgical history.[9] Urinary tract (UTI), primary bloodstream (PBSI), surgical site (SSI), and lower respiratory tract infections (lRTI) stand out among the most common conditions.[4] However, it is of paramount importance to know the origin, the focus, and the main involved microorganisms of these infections to guide the choice of appropriate antibiotic therapy.

This perspective considers antimicrobial resistance as a global threat since it restricts the available therapeutic options and increases the risk of in-hospital mortality due to lack of treatment.[10,11] However, the indiscriminate use of empirical antibiotics and the low rate of de-escalation are associated with multidrug-resistant microorganisms, as per a study in Serbia, which found a 12.8% pan-drug resistant profile, i.e., no susceptibility to the tested antimicrobials. [12,13]

In line with this, the World Health Organization updated, in May 2024, the list of bacteria with a multidrug-resistant profile in need of research into new antimicrobials to reduce morbidity and mortality. The list classifies these bacteria into three groups: critical, medium, and high. The carbapenem-resistant *Acinetobacter baumannii*, third-generation cephalosporin-resistant *Enterobacteriaceae*, and carbapenem-resistant *Enterobacteriaceae* deserve critical priority.[14] This scenario further evinces the need to strengthen evidence-based practices to prevent and control HAIs by implementing hospital infection control programs that emphasize adherence to standardized protocols, multiprofessional teams' continuous training, and care indicator monitoring.[7]

Thus, this study aims to evaluate the profile of HAIs and the resistance mechanisms of microorganisms from 2019 to 2024.

METHODS

This scoping review was prepared in accordance with the recommendations of the international checklist Preferred Reporting Items for Systematic Reviews and Meta-analyses for Scoping Review. to retrieve, investigate, and synthesize information on the subject from databases and portals.[15] The protocol of this review was registered on the Open Science Framework according to DOI 10.17605/OSF. IO/P6AXG under public disclosure. The following guiding question was used: What is the scientific evidence about the profile of HAIs and the mechanisms of resistance of their related microorganisms from 2019 to 2024?

The acronym "participants, concept, and context" was used as the search strategy. Hospitalized patients with HAIs who were aged 18 years or older were included in this study. Studies on nosocomial infections, epidemiology, and mechanisms of microbial resistance were included as the concept. Quantitative and experimental studies, randomized and non-randomized clinical trials, observational studies, and reviews with and without meta-analysis that were published in English, Portuguese, and Spanish from January 2019 to August 2024 were considered as context. Animal studies, letter to the author, reviews, and articles unavailable in full were excluded.

The literature was evaluated in August 2024 on the following portals: Virtual Health Library (VHL – Lilacs), National Library of Medicine (PubMed), Scopus, and Google scholar (gray literature). Medical subject headings the Boolean operators "AND" and "OR" were used to find the area terms and subjects. The concepts "*infecção hospitalar*" and "*assistência à saúde*" were translated as "cross infection" and "delivery of health care," respectively. Note the use of entry terms (synonymous with the terms in question) for the search strategy.

In this context, the following general search strategy was used: *("Cross Infection" OR "cross infections" OR "Healthcare Associated Infections" OR "Healthcare Associated Infection" OR "Health Care Associated Infection" OR "Health Care Associated Infections" OR "Hospital Infection" OR "Nosocomial Infection" OR "Nosocomial Infections" OR "Hospital Infections")* AND *("Delivery of Health Care" OR "Delivery of Healthcare" OR "Healthcare Deliveries" OR "Healthcare Delivery" OR "Health Care Delivery" OR "Delivery, Health Care" OR "Health Care" OR "Care, Health" OR "Healthcare" OR "Health Care Systems"*

OR "Health Care System"). However, some adaptations were made to the PubMed database. The term MESH followed only the keywords cross infection and delivery of health care, whereas "text word" succeeded all entry terms. However, these words were removed from the explicit strategy, which preserved the remaining terms.

To select articles, the Rayyan-Intelligent Systematic Review was used, a software to assist the identification, selection, and organization of publications to be included in literature reviews. The articles were evaluated in pairs by independent reviewers. Any conflict was solved by consensus without the need for a third author in the following order: I – titles and the respective abstracts of the retrieved studies by the search strategy, II – complete reading of the articles after the first phase.

The following data were extracted from the eligible articles: journal, authors, country, study design, year of publication, participants, and sample. From the results of the articles, information was extracted on the prevalence and incidence of HAIs, the main involved microorganisms, the site of infections, and antimicrobial resistance profiles. This research performed a pilot study to evaluate its chosen tool in 10 articles to standardize result extraction. These articles were included in this review.

RESULTS AND DISCUSSION

This research found 457 results in the searched databases. Its first phase, after reading the titles and abstracts of the chosen studies, excluded 379 articles following its inclusion/exclusion criteria and one duplicate. Its second phase excluded 39 articles according to its eligibility criteria after reading them in full text, rendering 38 studies and one dissertation as its final sample (Figure 1).

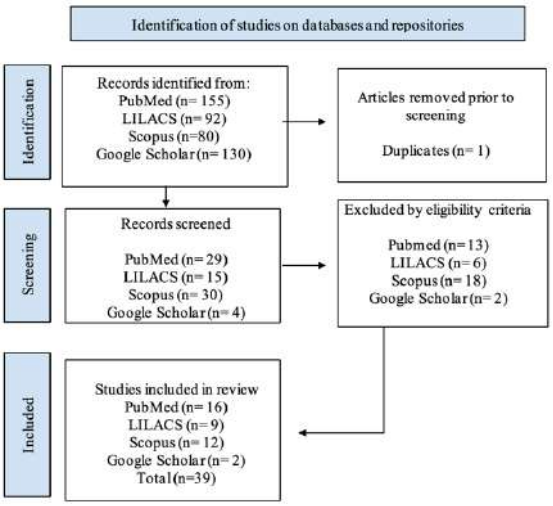

Figure 1. Flowchart referring to the selection process of the studies in this scoping review, adapted from Systematic Reviews and Meta-analyses for Scoping Review, Bahia, Brazil, 2024.

The 39 eligible articles included six studies that had been conducted in Brazil and 33 in other countries. Regarding study design, the sample included two systematic reviews with meta-analysis, two narrative revisions, and 34 cross-sectional and one cohort observational studies (Chart 1).

The eligible studies found the following the risk factors for the development of HAIs: age > 60 years, the male gender, length of hospital stay > 7 days, previous use of antibiotics, surgical procedures, and invasive devices such as mechanical ventilation (MV), probes, orotracheal tubes, central venous catheters (CVC), and hemodialysis.[8,9,12,21,27,29,32,34,46]

The most mentioned microorganisms referred to Gram-negative bacilli, especially Pseudomonas aeruginosa, *A. baumanni*, *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, *Serratia marcescens*, and *Stenotrophomonas, Malthophilia*.[1,2,13,18,19,2,23,24,25,26,27,29,30,31,32,33,34,36,37,39,42,44,45,46,49] Some species of Gram-positive bacteria received fewer mentions, such as *Staphylococcus aureus*, *Enterorococcus faecalis*, and *Enterococcus faecium*.[12,13,17,18,19,24,25,27,33,35,39,49] Class B metallo-β-lactamases (MβLS) configured the most frequent resistance mechanisms: K. pneumoniae carbapenemase (KPC), imipenemase (IMP), New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), followed by class D oxacillinase-23 (OXA-23), oxacillinase-48 (OXA-48), oxacillinase-51 (OXA-51), oxacillinase-58 (OXA-58) oxacillinases and class A extended-spectrum β-lactamase (ESBL).[16,20,21,23,28,29,36]

Year	Journal	Authors	Country	Study design	Number of participants	Epidemiology/Risk factors/HAI sites of infection	Prevalence of microorganisms	Microorganism resistance mechanisms
2022	CAMbios Rev Med	Trujillo T, et al.[16]	Ecuador	Review	-	-	-	*K. pneumoniae*: KPC, IMP, NDM, VIM, OXA-48; *E. coli*: KPC, NDM, OXA-48; *E. cloacea*: KPC, NDM, IMP, OXA-48; *S. marcensens*: KPC, NDM, OXA-48; *E. Aerogens:* KPC, NDM, OXA-48; *P. mirabilis*: KPC, NDM; *P. aeruginosa*: KPC, NDM, IMP, VIM; *A. baumannii*: IMP, OXA-48, OXA-51, OXA-24, OXA-24, OXA-143, OXA-58; *Enterobactereacea:* ESBL
2022	Repert Med Cir	Sendoya Vargas JD, et al.[17]	Colombia	Observational Cross-sectional	100	TI%: (57%) HAIs P: 0.154%	GP: *E. faecalis* (72%), *E. faecium* (28%)	-
2021	Rev Cuba Angiol Cir Vasc	Rodríguez Álvarez V, Hernández Seara A[18]	Cuba	Observational Cross-sectional	89	TI%: (49.4%) SI: (43%) SSI, (25%) PNM, (1%) UTI, (18%) skin and mucous membranes, (2%) associated with device	GN: *P. aeruginosa* (13.5%), *A. baumanni* (9%). GP: *S. aureus*	-
2021	Rev Soc Bras MedTrop	Gaspar G, et al.[19]	Brazil	Observational Cross-sectional	466	-	GN: *K. pneumoniae* (53%), *A. baumanni* (37%). GP: *S. aureus* (10%)	-
2020	Cuban Med Trop Review	Pérez DQ, et al.[59]	Cuba	Cross-sectional observational	119	-	-	*E. coli*: ESBL (43.7%), cAMP (92.4%), MβL (99.2%)
2020	Braz J Cardiovasc Surg	Ferreira GB, et al.[8]	Brazil	Observational Cross-sectional	195	TI%: (22.6%) SI: SSI (45.5%), pulmonary (45.5%), UTI (11.4%), and others (11.4%). FR: female gender (56.8%), (p=0.015); LHS>9 days: (15%), (p= <0.001)	-	-
2020	Rev Soc Bras MedTrop	Kurihara M, et al.[21]	-	Literature Review	-	RF for Infection *A. baumanni* in the ICU: CVC use, MV use, previous ATB use, previous hospitalization, ICU stay >3 days, surgical procedures	-	blaOXA-23, blaOXA-51, blaOXA-58, blaOXA-65
2019	HU Rev	Dias V, *et al.,* [22]	Brazil	Observational Cross-sectional	39,547	SI: Pulmonary (70.6%), BSI (15.5%), tissue (3.5%), other (10.4%)	GN: 14% isolated *S. maltophilia*	
2019	Rev Esc Enferm USP	Alvim A, et al.[2]	Brazil	Observational Cross-sectional	82	SI: PBSI 30%, CAUTI 22%, lRTI except pneumonia 20%, SSI 17%, VAP 7%, other: 4	GN: *K. pneumoniae* 68% *S. marcescens* 2% *E. Cloacea* 9%	blaKPC gene 100% of the samples.
2022	Int J Infect Dis	Ergonul O, et al.[23]	Türkiye	Observational Cross-sectional	59	TI%: (49%) HAIs	GN: *A. baumanni* (49%)	(76%) of the isolates produced OXA-23 carbapenemase
2023	J Hosp Infect	Liu X, et al.[9]	China	Systematic review with meta-analysis	-	RF: age > 60 years, the male gender, arteriovenous cannula, catheterization, IUC, intravenous infusion, MV, Surgery, TCT, ventilator, Coma, DM, bed restriction, chemotherapy, HD, hormonal therapy, use of immunosuppressants, use of ATB, and LHS>15 days. All FR with (p-value=<0.001)	-	-
2023	J Hosp Infect	Gajic I, et al.[13]	Serbia	Observational Cross-sectional	6,478	TI%: (12.5%) HAIs SI: PNM (n: 240), BSI (n: 268), UTI (n: 169), gastroenteritis (n: 103), skin and soft tissues (n: 29).	GN: (69.3%); *K. pneumoniae* (24.9%), *A. baumanni* (24.5%), *C. difficile* (9%) *P. aeruginosas* (5%), *P. mirabilis* (3.7%), *E. coli* (1.2%) GP: 30.7 *S. aureus* (1.2%)	-
2023	BMC Infect Dis	Aiesh BM, et al.[24]	Palestine	Observational Cross-sectional	157	TI%: (61%) HAIs SI: Skin and soft tissue infections (35.8%), UTI (33.7%), pneumonia (36.8%), intra-abdominal infection (20%), BSI (27.4%)	GN: *P. aeruginosa* (26.3%), *A. baumanni* (25.3%), *E. coli* ESBL (23.2%), *K. pneumoniae* ESBL (15.8%). GP: *S. epidemidis* (17.9%), *E. facium* (17.7%), *E. faecalis* (7.4%). Fungi: *C. albicans* (17.9%)	-

continue

Year	Journal	Authors	Country	Study design	Number of participants	Epidemiology/Risk factors/HAI sites of infection	Prevalence of microorganisms	Microorganism resistance mechanisms
2021	J Hosp Infect	Stewart S, et al.[25]	Scotland	Observational Cross-sectional	99,018	SI: UTI, BSI, lRTI, SSI, and PNM	GN: (40.7%), *E. coli* (18.4%), *K. pneumoniae* (4.34%), *P. mirabilis* (2.74%), *S. marcescens* (1.67) GP: (36%) *S. aureus* (10.8%), *E. faecalis* (5%), *E. faecium* (4.3%), *C. difficile* (2.8%) Fungi (7.31%) *C. albicans* (1.98%)	-
2021	Crit Care	He Q, et al.[26]	China	Observational Cross-sectional	22,343	SI (2.9%) VAP	GN: *A. baumanni* (42%), *K. pneumoniae* (18%), *P. aeruginosa* (15%), *Enterobacteria spp.* (9%), *S. maltophilia* (7%), *B. cepecia* (7%) GP: *A. aureus* (5%)	-
2023	Ann Ig	Damico V, et al.[27]	Italy	Observational Cross-sectional	118	TI%: 33.1% SI: UTI (36.8%), BSI (20.6%), PNM (13.2%), skin (5.9%), associated device (2.9%), CNSI (1.5%) RF: length of stay > 7 days (OR: 2.6, 95% CI: 1.19-3.54, p=0.002), type II DM (OR: 1.8, 95% CI: 1.07-2.29, p=0.019), cardiovascular disease use, MV, surgery, prolonged hospitalization, tracheostomy wound and devices. (OR: 1.4; 95%CI: 1.05-2.29, p=0.021), CVC (OR: 4.9; 95%CI: 1.56-11.52 p=0.014, MV >48h (OR: 4.2; 95%CI: 1.49-11.51, p=0.003.	GN: *Klebsiella spp.* (15.9%), *A. baumanni* (13.8%), *Enterococcus spp.* (13.8%), *P. aeruginosa* (10.6%), *P. mirabilis* (5.3%), *S. maltophilia* (1.1%), *E. coli* (1.1%) GP: *C. difficile* (14.9%), *S. aureus* (2.1%), *S. epidermidis* (1.1%) Fungus: *Candida* spp. (10.6%)	
2019	Acta Med Port	Costa RD, et al.[12]	Portugal	Observational Cross-sectional	60	TI%: (58.3%) HAP acquired in the ICU; (41.7%) HAP acquired outside the ICU. SI: (58.3%) VAP RR: use of ATB in the last 30 days (75%) and immunosuppression (16.7%)	GN: *P. aeruginosa* (20%), *A. baumanni* (9.2%), *K. pneumoniae* (7.7%), *S. marcescens* (3.1%) GP: *S. aureus* (26.2%). Fungi: *C. albicans* (6.1%)	-
2020	Antimicrob Resist Infect Control	Saharman YR, et al.[28]	Indonesia	Observational Cross-sectional	412	TI%: (32.1 %) HAIs	GN: *K. pneumoniae* (32.1%)	96% of the isolates produced the blaNDM MDL-resisting gene.
2020	Rev Esp Quimioter	Pintos-Pascual I, et al.[29]	Spain	Observational Cross-sectional	272	TI%: (63.2%) HAIs SI: UTI (58.7%), IRTI (14.8%), skin and soft tissues (11.7%), intra-abdominal (10.5%) FR: male gender, transplants, immunosuppressive use, ICU and SC admission, and previous antibiotic treatment	GN: *K. pneumoniae* (62.7), *E. cloacea* (10.1%), *K. oxytoca* (8.9%), *E. coli* (6.6%)	OXA-48 (53.8%) VIM (43%), KPC (2.8%), NDM (0.4%)
2021	Scientific Rep	Lakbar I, et al.[30]	France	Cohort	18,497	TI%: (8.6%) HAIs SI: VAP	*S. aureus, P. aeruginosa, A. baumanni, Enterobacteriaceae,*	-
2020	J Infect Dev Ctries	Salehi M, et al.[31]	Iran	Observational Cross-sectional	152	SI: VAP	*A. baumanni* (56.6%) *K. pneumoniae ESBL.* (55.1%)	-
2020	Eur J Clin Microbiol Infect Dis.	Massart N, et al.[32]	France	Observational Cross-sectional	3,861	RF: age >65 years (p=0.07), colonization by BGN-ESBL (p<0.001).	*Enterobactereacea* (32.4%), *P. aeruginosa* (17.8%),	-
2022	Euro Surveill.	Glasner C, et al.[33]	Netherlands Germany	Observational Cross-sectional	3,365	-	GN: *E. coli* (92.2%), *K. pneumoniae* (6.8%) GP: *E. faecium* (1.8%)	-
2019	Crit Care	Zhu S, et al.[34]	China	Observational Cross-sectional	5,046	TI%: NCRBSI - 2013 (70.2%), 2014 (68.4%), 2015 (66%), 2016 (74.4%), 2017 (78.3). RF: NCRBSI (OR: 2.30; 95%CI: 1.38-3.82, p=0.001), Trauma (OR: 3.45, 95%CI 2.24–5.30, p < 0.001), Surgery (OR 1.82, 95%CI 1.19–2.78, p = 0.006), Catheter (OR 2.93, 95%CI 1.65–5.22, p <0.001), Sepsis (OR 1.69, 95%CI 1.09– 2.63, p = 0.02), Pneumonia (OR 1.53, 95% CI 1.03–2.28, p = 0.038)	NCRBSI-associated microorganisms *A. baumanni* (53%), *K. pneumoniae* (41%), *Enterobacteriaceae* (33%), *P. aeruginosa* (7%), and *B. cepacia* (5%)	-

continue

Year	Journal	Authors	Country	Study design	Number of participants	Epidemiology/Risk factors/HAI sites of infection	Prevalence of microorganisms	Microorganism resistance mechanisms
2020	Euro Surveill.	Piezzi V, et al.[35]	Switzerland	Observational Cross-sectional	5,369	-	*E. faecium* (40.5%) *E. faecalis* (59.5%)	-
2020	Rev Prev Infec Saúde	Alencar DL de, et al.[1]	Brazil	Observational Cross-sectional	181	TI%: (28.7%) HAIs SI: pulmonary and UTI	*A. baumanni* (56.25%) *K. pneumoniae* (2.25%) *P. aeruginosa* (4.41%)	-
2019	Dissertation	Ribeiro, Edlainny Araújo[36]	Brazil	Cross-sectional observational	18	-	*A. baumanni*	60% of isolates carrying the bla-OXA 23 resistance gene
2021	Int J Microbiol	Karimi K. et al.[37]	Iran	Observational Cross-sectional	83	SI: (58.9%) Pulmonary, (21.6%) UTI, (7.25%) BSI, others (12.25%)	*K. pneumoniae*	-
2021	Med J Islam Republic Iran	Khammarnia M, et al.[38]	Iran	Systematic review with meta-analysis		Overall prevalence: 0.111; 95%CI: 0.0.105 – 0.116) SI: UTI and respiratory	*E. coli* *Klebsiella* spp. *S. aureus*	-
2024	Pak Armed Forces Med J	Tariq A, et al.[39]	Pakistan	Cross-sectional observational	196	SI: PAV, UTI, SSI, PBSI	*K. pneumoniae* (33%); *E. Coli* (26%); *A. baumanni* (22%); *Pseudomonas* spp (11%), *Enterococcus* (2%) *S. aureus* (6%)	-
2021	J Infect Prev	Behera B, et al.[40]	India	Observational Cross-sectional	116	TI%: CAUTI - 9.08 per 1,000 catheter-days in 24 months	*Candida* spp.; *E. coli; Enterococcus* spp.	-
2023	Microb Infect Dis	Abdel-Salam SA, et al.[42]	Egypt	Observational Cross-sectional	60	SI: UTI (43.3%), Sputum (23.3%), CNSI (6.7%), PBSI (3.3%), others (3.3%)	*P. aeruginosa*	MexA genes (56.7%) MexB (46.7%)
2021	Infect Prev Pract	Morioka H, et al.[43]	Japan	Observational Cross-sectional	4,339	P: (9%) HAIs SI: SSI, PNM, PBSI, CRBSI, and UTI	Enterobacteria, *S. aureus, Enterococcus, Sireptococcus* spp., *P. aeruginosa, A. baumanni.*	metallo-β-lactamase-producing *E. cloacea* and KPC-producing *K. pneumoniae*
2022	J Antibiotics	Papanikolopoulou A, et al.[44]	Greece	Observational Cross-sectional	4,754	I: VAP ranged from 10.1-10.9/1,000 ventilated patients	*A. baumanni* *K. pneumoniae*	-
2019	Egypt J Med Micro	Sultan AM, et al.[45]	Egypt	Observational Cross-sectional	240	SI: UTI (35.4%), VAP (32.5%), PBSI (23.3%), and SSI (8.8%).	*P. aeruginosa* (31.3%), *E. coli* (25.8%), *K. pneumoniae* (19.2%), *A. baumanni* (18.8%), *P. mirabilis* (5%)	Production in cAMP (40.9%)
2022	Microb Infect Dis	Thabet A, et al.[46]	Egypt	Observational Cross-sectional	225	SI: SSI (24%), UTI (16%), VAP (8%), fabrics (12%) RF: DM, debilitating chronic disease, anemia, broad-spectrum ATB use, MV, surgery, prolonged hospitalization, tracheostomy wound and devices.	*P. aeruginosa* (33.3%)	-
2022	J Infect Prev	Shrestha SK, Shrestha S, Ingnam S[47]	Nepal	Observational Cross-sectional	160	P: 11.25% HAIs SI: UTI 72.2%, PAV (16.6%), SSI (11.2%)	-	-
2024	J Health Popul Nutr	Bai HJ, et al.[48]	China	Cross-sectional observational	-	SI: PBSI, PNM, and UTI	GP: *S. aureus, E. faecalis, S. epidermidis,* and *S. haemolyticus.* GN: *E. coli, K. pneumoniae, A. baumanni,* and *P. aeruginosas.*	-
2022	J Renal Inj Prev	Khaleel RA, et al.[49]	Iraq	Observational Cross-sectional	710	SI: UTI	*S. aureus* (7.7%)	tetK (85.4%), gyrA (63.3%), msrA (45.4%), blaZ (100%)

Chart 1. Selected articles for this scoping review and main results, Bahia, Brazil, 2019–2024.

Abbreviations: No.: number; I: incidence; TI%: HAI rate; P: prevalence; HAIs: healthcare-related infections; RF: risk factor; SI: site of infection; GN: Gram-negative; GP: Gram-positive; SSI: surgical site infection; BSI: bloodstream infection; PBSI: primary bloodstream infection; lRTI: lower respiratory tract infection; VAP: ventilator-associated pneumonia; PMN: pneumonia; HAP: hospital-acquired pneumonia; NCRBSI: non-catheter-related bloodstream infection; CNSI: central nervous system infection; CAUTI: catheter-associated urinary tract infection; UTI: urinary tract infection; CRBSI: central venous catheter-related bloodstream infection; ATB: antimicrobials; LHS: length of hospital stay; HD: hemodialysis; ICU: intensive care unit; DM: diabetes mellitus; SC: surgical center; MV: mechanical ventilation; CVC: central venous catheter; IUC: indwelling urinary catheter; TCT: tracheostomy; OXA: oxacillinases; GNB: Gram-negative bacillus; β-lactamases: beta-lactamases; EBSL: extended-spectrum beta-lactamase; VIM: Verona integron-encoded metallo-β-lactamase; KPC: carbapenemase-producing *K. pneumoniae*; NDM: New Delhi metallo-β-lactamases; MβL: metallo-β-lactamases; cAMP: cyclic adenosine monophosphate; tetK: tetracycline-encoding gene, gyrA: quinolone-encoding gene, msrA: macrolide-specific resistance gene, blaZ: penicillin-resistance encoding gene.

This scoping review shows that HAI incidence has progressively increased in Brazil and worldwide, representing a serious public health problem as its development prolongs hospitalization and increases

morbidity and mortality rates and hospitalization costs.[4] However, some research in France, Serbia, and Switzerland from 2013 to 2020 pointed to a decrease in the overall prevalence rate of HAIs: 6.1, 11.5, and 2%, respectively.[13,32,35]

Brazil showed study variability. Research from 2012 to 2018 in the state of Paraná found a 22.6% HAI incidence.[8] On the other hand, a study in an ICU the state of Minas Gerais showed a lower incidence of HAI over the years: 3.4% in 2014, 2.4% in 2015, and 1.8% in 2016.[4] The care profile of the institution and the incorporation of HAI prevention and control actions may explain these findings. Health education practices configure an effective tool to control HAIs, in which the adherence of health professionals to hand hygiene constitutes one of the essential measures.[1]

UTI stands out as the first cause of nosocomial infection in the selected studies.[25,27,29] It can be defined as the presence of one or more pathogens in a urine sample in patients with clinical manifestations. Its main predictor refers to IUC use.[50] A study in the United Kingdom indicated an incidence rate for UTI of 52.2/100,000 days of occupied beds and associated IUC use with infections in 37.8% of cases, the onset of symptoms of which began seven days after admission.[25]

Observational studies in Italy, Scotland, and Brazil have pointed to PBSI as the second leading cause of hospital infections.[22,25,27] The research'' in Scotland showed that 95.1% of the cases were related to vascular catheters, reinforcing that device use has increased the development of HAIs, necessitating prevention and control measures and the reassessment of institutional protocols in units.[22,25]

The development of pneumonia in patients undergoing MV worsens prognoses and increases length of hospital stays. A study in Rio de Janeiro showed that 92.31% of individuals suffered from VAP, which may have stemmed to the lack of adherence to protocols such as bundles (sets of standardized and evidence-based interventions to be applied simultaneously by care teams) to prevent pneumonia (contributing to reducing cases and increasing therapy success).[1,8] As in a Chinese study on ICU patients, about 93% of hospitalized individuals received MV, only 2.9% of whom developed MV-associated pneumonia, a result attributed to adherence to institutional prevention protocols.[26]

Regarding predictive factors, older adults show a high risk for infections, the main cause of death in individuals aged > 65 years.[52] Its associated factors include a decline in immune function due to multiple comorbidities and metabolic and hormonal changes related to the physiological process of senility, which hinders recovery and can increase the length of hospital stay.[8,52]

Males constitute the gender most affected by HAIs, corroborating the findings of studies across Brazil. In total, three cross-sectional studies with ICU patients showed a predominance of nosocomial infections in men (from 47.5 to 71.9%).[4,53,54] However, no analyzed study discussed the possible biological, behavioral, or care mechanisms that could justify this greater susceptibility of men to HAIs.

Invasive devices have also been linked to HAIs. Thus, care professionals must daily assess the need for these devices, adhere to standard institutional operating procedures to properly handle catheters and probes, and replace them after any sign of infection.[27] Measures such as hand hygiene and aseptic techniques are essential in care plans.[1]

The prolonged and indiscriminate use of antimicrobials increases microbial resistance and causes the emergence of HAIs, such as those by *Clostridioides difficile*.[55] Irrational use unbalances the gut microbiota due to competition between commensal bacteria.[55] Thus, antimicrobial stewardship programs are essential to evaluate, control, and monitor the rational use of antimicrobials. Awareness and sensitization practices also belong to this proposal.[52]

The chosen articles evince the prevalence of Gram-negative microorganisms, especially: *A. baumanni*, *K. pneumoniae*, *P. aeruginosa*, and *E. coli*. Other microorganisms stand out, but in a smaller proportion, such as: *S. maltophilia*, *P. mirabilis*, and *S. marcescens*. The most frequent Gram-positive bacteria were *S. aureus*, *E. faecalis*, *E. faceium*, and *C. difficile*. *Candida albicans* constituted the main pathogen in fungal infections.

Gram-negative microorganisms are widely disseminated in the environment and are directly associated with HAIs, especially in immunocompromised patients.[56] They can resist many available antibiotics due to their ability to acquire resistance genes and to adhere to surfaces and remain for long periods in health environments.[51]

A. baumanni, a microorganism that belongs to the *Moraxellaceae* family, commonly occurs in HAIs, most often in VAP, UTI, PBSI, intra-abdominal infections, among others.[21,36] In 2022, the World Health Organization reported the surveillance of antibiotic resistance and consumption, monitoring eight microorganisms that represent public health problems, the genus *Acinetobacter* spp. occupied the top of the list, highlighting *A. baumanni* as the most prevalent in PBSI and as having a higher multidrug resistance profile.[57]

The enterobacteria *K. pneumoniae* and *E. coli* stand among the most prevalent species in hospital units, affecting critically ill patients. Alvim et al., evaluating the epidemiological profile of enterobacteria, found *K. pneumoniae* to be the most prevalent topography in enterobacterial infections: BSI (30%), UTI (25%), and lRTI (20%).[2] Observational research in Brazil, Serbia,

and Indonesia has pointed to *K. pneumoniae* as the first cause of HAIs, totaling 53, 69.3, and 32.1% of the cases, respectively.[13,19,28]

P. aeruginosa has been described as the main pathogen of infections in ICUs.[18,24] A survey in a Palestinian hospital showed a 26.3% prevalence of infections caused by *P. aeruginosa*, with the following main sites of infection: soft tissues, urinary tract, and ventilator entry.[24]

Studies in China and Italy found an association of infections with *S. aureus* and prolonged hospitalization.[26,27] The former also found an association with hospital deaths, highlighting the importance of measures to prevent Gram-positive bacterial infections, the pathogenicity of which occurs from local or systemic multiplication and the subsequent production of exotoxins and enzymes, which can induce microbial resistance.[58]

The most common species of *Enterococcus* spp. Gram-positive bacilli in the human gastrointestinal flora refer to *E. faecalis* and *E. faecium*. Europe considers this genus the fourth most prevalent in PBSI causes.[35] A study on prevalence in Colombia showed that about 57.0% of HAIs were due to *Enterococcus* spp. since the most prevalent species is the *E. faecalis* (72.0%), followed by *E. faecium* (28%), which mainly caused UTI (31.0%) and BSI (29.0%).[17] The factors in infections by this genus include previous use of vancomycin, third-generation cephalosporin, prolonged hospitalization, neutropenia, diabetes, use of MV, and gastrointestinal colonization.[17,25]

Regarding resistance mechanisms, 11 studies (in which the main carbapenemase-producing bacteria referred to enterobacteria, followed by *A. baumanni* and *P. aeruginosa*) treated this problem.[2,16,21,23,28,29,42,43,45,49,59] Phenotypic tests mentioned the following carbapenemases the most: VIM, NDM, KPC, and the OXA-48, OXA-23, OXA-58 oxacillinases.

Bacteria can develop resistance to antibiotics by several mechanisms that decrease their susceptibility, including changes in outer membrane permeability, the production of enzymes that can inactivate antimicrobials or altering their binding site, and the activation of the efflux pump system.[11,21]

The association of several resistance mechanisms by bacteria generates multidrug resistance. On the other hand, the alteration of the site of action of penicillin-binding proteins prevents the binding of the antibiotic to the protein, limiting its function, whereas the modifications that alter membrane permeability comprise the loss or reduction of the expression of the genes responsible for the expression of porins since this reduces the entry of the antibiotic into the cell, reducing its plasma concentration.[4] Moreover, the efflux pump mechanism prevents toxic compounds from accumulating at the intracellular level, causing bacterial resistance.[36]

The most discussed resistance mechanism in the eligible studies refer to the production of β-lactamases, i.e., enzymes that can hydrolyze antibiotics. This may stem from the prevalence of Gram-negative bacteria in the articles as these microorganisms use this mechanism most often.[36]

A. baumanni produces metallo-β-lactamases and oxacillinases.[36] However, the latter show the greatest prevalence and variety, as studies have found more than 490 types of genes for them. This enzyme can hydrolyze most forms of penicillin (and carbapenems at a lower proportion).[21,36] A cross-sectional study in Türkiye isolated *A. baumanni* in 50.0% of the HAIs and found oxacillinase production in 76.0% of its culture samples, the most common of which referring to the OXA-23 gene.[23]

Research in Spain investigated the prevalence of carbapenemase production in Enterobacteria, pointing out the main species involved: *K. pneumoniae*, Enterobacter spp., and E. coli, the most common carbapenemase referring to OXA-48 (53.8%), followed by VIM (43%), KPC (2.8%), and NDM (0.4%).[29] On the other hand, a study in Indonesia found *K. pneumoniae* as the main producer of the bla-NDM gene, occurring in 96% of microbiological isolates.[28] The NDM and VIM genes participate in the MβLs group, which confer resistance to all beta-lactams and carbapenems.[4]

Enterobacteria that produce the bla-KPC gene emerged in a study of the prevalence of HAI in Brazil. It belongs to penicillinases, enzymes that can hydrolyze carbapenems at the site of serine action. *K. pneumoniae* produce these enzymes the most.[2]

This scoping review showed that carbapenem-resistant *A. baumannii*, third-generation cephalosporin-resistant *Enterobacteriaceae*, and carbapenem-resistant *Enterobacteriaceae* constitute a reality in health institutions across geographic regions. Hospitals should improve their surveillance of infections by these bacteria the World Health Organization classified as critical by implementing sanitary measures to prevent and control them to minimize their spread (multidisciplinary actions that permeate management and care in which all play a role for the benefit and care of patients).[59]

The limitations of this review include its exclusive assessment of articles published in English, Portuguese, and Spanish and its publication period (2019-2024). Also, each territory has different rules, practices, and realities regarding the identification, prevention measures, and control of HAIs, which can influence finding comparability. Added to this are the variation in the number of participants in the included studies (some with expressive samples and others with reduced

numbers) and the heterogeneity of methodological designs, which can hinder result synthesis and interpretation. Its strengths refer to the produced knowledge about the main microorganisms and the profile of resistance that cause nosocomial infections in hospital units, a measure to guide health institutions and encourage the implementation of control and prevention programs against the dissemination of multidrug-resistant microorganisms and toward the rational use of antimicrobials.

CONCLUSION

The results showed the relevance of continuous monitoring and the implementation of preventive measures to cope with HAIs. The increase in incidence, associated with the use of invasive devices, senility, previous use of antimicrobials, and prolonged hospitalization reinforce the need for safe care practices and the strengthening of prevention protocols.

The predominant microorganisms, mostly multidrug-resistant Gram-negatives, highlight the seriousness of the situation since their resistance mechanisms limit therapeutic options and increase hospital mortality and health costs. This scenario must effectively implement hospital infection control programs focusing on the proper management of antimicrobial use, continuous training of healthcare providers, and systematic epidemiological surveillance.

Thus, these results reinforce that the fight against HAIs should go beyond treatment, aiming, above all, at prevention by robust and integrated institutional policies that can reduce the spread of multidrug resistance, ensuring the rational use of antimicrobials and greater patient safety.

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AUTHORS' CONTRIBUTIONS

Karla Neco Rodrigues contributed to the bibliographic research, drafting of the abstract, introduction, methodology, discussion, and interpretation, description of the results, and the elaboration of tables, conclusions, and references. **Adriano Max Moreira Reis** contributed to the review and correction of the bibliographic research, analysis of the results, and discussion. **Tuany Santos Souza** contributed to the review of the abstract, methodology, interpretation of results, conclusions, review, and statistics. **Gisele da Silveira Lemos** contributed to the review and correction of the bibliographic research, analysis of the results, and discussion.

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