Summary

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Original Article

Epidemiological profile of tuberculosis in Uberaba, a priority municipality in Minas Gerais, 2013 to 2023

Perfil epidemiológico da tuberculose em Uberaba, município prioritário de Minas Gerais, 2013 a 2023
Perfil epidemiológico de la tuberculosis en Uberaba, municipio prioritario de Minas Gerais, 2013 a 2023

Corresponding author:
E-mail: aline.paiva@uftm.edu.br
Address: Manoel Terra Square, 330, Abadia, Uberaba, Minas Gerais, Brazil.

Apollo Nobre Torres[1] iD
Mírian Akiko Kawamura[1] iD
Yasmin Neves Vieira Sabino[2] iD
Aline Dias Paiva[1] iD

[1]Federal University of Triângulo Mineiro, Uberaba, Minas Gerais, Brazil.
[2]Federal University of Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil.

ABSTRACT

Background and Objectives: Tuberculosis is an infectious disease and presents risk factors linked to social and behavioral issues, as well as comorbidities. This study aimed to evaluate tuberculosis cases reported in Uberaba/MG between 2013 and 2023. **Methods:** A cross-sectional study was conducted using data from the Notifiable Diseases Information System regarding the notified cases of tuberculosis in the city of Uberaba, over a 10-year period (2013-2023). **Results:** During the evaluation period, 931 cases of tuberculosis were notified in Uberaba, with an average incidence of 25.6 cases/100,00 inhabitants. The majority of the cases were recorded in men (74.2%), aged between 25 and 44 years (48.3%), with elementary or high school education (complete or incomplete) (61.6%). In terms of social factors, 9.8% of tuberculosis cases were associated with individuals deprived of liberty and 5.4% of the patients were homeless. Regarding comorbidities, 20.1% of the patients with tuberculosis were co-infected with HIV, 32.1% were alcoholics, 7.5% were diabetic and 27.5% used illicit drugs. Laboratory confirmation of the disease occurred in 60.9% of the cases. The most common form of tuberculosis diagnosed was pulmonary (77.1%); pleural tuberculosis was the most common extrapulmonary form of the disease (36.6%). The majority of cases were classified as new cases (81.8%) with the most common outcomes being cure (55.4%), loss to follow-up (14.9%), and death from tuberculosis (10.6%). **Conclusion:** The results highlight well-defined sociodemographic characteristics among tuberculosis patients, such as adult males with low education level, comorbidities, and engaging in risky behaviors.
Keywords: *Tuberculosis. Epidemiology. Health Vulnerability.*

RESUMO

Justificativa e Objetivos: A tuberculose é uma doença infecciosa e apresenta fatores de risco associados a questões sociais e comportamentais, bem como comorbidades. Este estudo teve como objetivo avaliar os casos de tuberculose notificados em Uberaba/MG, entre 2013 e 2023. **Métodos:** Foi realizado um estudo transversal utilizando dados do Sistema de Informação de Agravos de Notificação, sobre os casos de tuberculose notificados em Uberaba, ao longo de 10 anos (2013-2023). **Resultados:** Durante o período de avaliação, foram notificados 931 casos de tuberculose em Uberaba, com uma incidência média de 25,6 casos/100 mil habitantes. A maioria dos casos foi registrada em homens (74,2%), com idade entre 25 e 44 anos (48,3%), e com escolaridade de nível fundamental ou médio (completo ou incompleto) (61,6%). No aspecto social, 9,8% dos casos de tuberculose estavam associados a indivíduos privados de liberdade e 5,4% dos pacientes eram moradores de rua. Em relação às comorbidades, 20,1% dos pacientes com tuberculose eram co-infectados com HIV, 32,1% eram alcoólatras, 7,5% eram diabéticos e 27,5% faziam uso de drogas ilícitas. A confirmação laboratorial da doença ocorreu em 60,9% dos casos. A forma de tuberculose mais comum diagnosticada foi a pulmonar (77,1%), sendo a forma extrapulmonar mais frequente a pleural (36,6%). A maioria dos casos foi classificada como novos casos (81,8%), com os desfechos mais comuns sendo cura (55,4%), perda de seguimento (14,9%) e morte por tuberculose (10,6%). **Conclusão:** Os resultados ressaltam características sociodemográficas bem definidas entre os pacientes com tuberculose, como homens adultos com baixa escolaridade, comorbidades e comportamentos de risco.
Descritores: *Tuberculose. Epidemiologia. Vulnerabilidade em saúde.*

RESUMEN

Justificación y Objetivos: La tuberculosis es una enfermedad infecciosa que presenta factores de riesgo vinculados a cuestiones sociales y comportamentales, así como comorbilidades. Este estudio tuvo como objetivo evaluar los casos de tuberculosis notificados en Uberaba/MG, entre 2013 y 2023. **Métodos:** Se realizó un estudio transversal utilizando datos del Sistema Nacional de Información de Enfermedades de Notificación Obligatoria, sobre los casos de tuberculosis notificados en Uberaba, a lo largo de 10 años (2013-2023). **Resultados:** Durante el período de evaluación, se notificaron 931 casos de tuberculosis en Uberaba, con una incidencia promedio de 25,6 casos/100 mil habitantes. La mayoría de los casos fueron registrados en hombres (74,2%), con edad entre 25 y 44 años (48,3%), y con educación de nivel básico o medio (completa o incompleta) (61,6%). En el aspecto social, el 9,8% de los casos de tuberculosis estaban co-infectados con individuos privados de libertad y el 5,4% de los pacientes eran personas sin hogar. En cuanto a las comorbilidades, el 20,1% de los pacientes con tuberculosis estaban co-infectados con VIH, el 32,1% eran alcohólicos, el 7,5% eran diabéticos y el 27,5% usaban drogas ilícitas. La confirmación laboratorial de la enfermedad ocurrió en el 60,9% de los casos. La forma más común de tuberculosis diagnosticada fue la pulmonar (77,1%), siendo la forma extrapulmonar más frecuente la pleural (36,6%). La mayoría de los casos se clasificaron como nuevos casos (81,8%), siendo los resultados más comunes la cura (55,4%), pérdida de seguimiento (14,9%) y la muerte por tuberculosis (10,6%). **Conclusión:** Los resultados subrayan características sociodemográficas bien definidas entre los pacientes con tuberculosis, como hombres adultos con baja educación, comorbilidades y comportamientos de riesgo.
Palabras Clave: *Tuberculosis. Epidemiología. Vulnerabilidad en Salud.*

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INTRODUCTION

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. This infection presents risk factors linked to social and behavioral issues, as well as comorbidities, such as incarceration, smoking, alcoholism, illicit drug use, diabetes mellitus, hepatitis C, and Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/Aids).[1] Pulmonary tuberculosis is the most common form of the disease, although the microorganism can spread hematogenously, affecting the bones and/or meninges, spreading through the lymphatic pathways, or extending by contiguity, leading to the pleuropulmonary form.[2]

Although preventable and curable, tuberculosis is considered a global public health threat according to the World Health Organization. In 2023, tuberculosis returned to being the world's leading cause of death from a single infectious agent, accounting for almost twice as many deaths as HIV/Aids.[3] According to the Epidemiological Bulletin of Tuberculosis in Brazil, 84,994 new cases of tuberculosis were reported in 2023, corresponding to an incidence of 40.1 cases per 100,000 inhabitants. In 2023, 6,025 deaths due to tuberculosis were notified in Brazil (2.8 deaths per 100,000 inhabitants).[4]

The city of Uberaba, located in the Triângulo Mineiro, state of Minas Gerais, has 337,836 people, ranking as the 7th largest population in the state and the 81st in the country.[5] In 2023, the city notified 114 cases of tuberculosis, representing an incidence of 33.7 cases per 100,000 inhabitants.[4] In 2024, Uberaba was designated a priority municipality in the Healthy Brazil Program, a government initiative aimed at combating 14 diseases and infections that disproportionately affect socially vulnerable populations, such as tuberculosis. The municipality is one of the 175 out of 5,571 Brazilian cities facing the highest burdens of diseases/infections, requiring special attention in the planning and implementation of public health policies aimed at addressing the needs of the groups most affected by social inequalities.[6]

This study aimed to evaluate the epidemiological profile of tuberculosis cases reported between 2013 and 2023, in Uberaba (MG).

METHODS

This is a cross-sectional, quantitative, descriptive, and retrospective study. Data on notified cases of tuberculosis in the city of Uberaba-MG, over 10 years (2013-2023), was collected from the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação*-SINAN), from the online platform DATASUS (Brazilian Health System Database) of the Ministry of Health.[7] Data was collected from January to June 2024. The search was made using "Tuberculosis Cases - Since 2001 (SINAN)"; the years 2013 to 2023 were selected in the "Available Periods" field, and the code "317010 Uberaba" was entered in the "Notification Municipality" field. Based on the recorded number of cases of the disease, the annual incidence was calculated using the population of each respective year.

The variables analyzed were number of cases, sex, race, age, education level, if homeless/deprived of liberty or beneficiary of government cash transfer program, presence of comorbidities, alcoholism, use of illicit drugs, smoking, laboratory diagnoses and form of tuberculosis, type of entry, outcome of the disease, susceptibility test and directly observed treatment.

Population estimates for the city of Uberaba from 2013 to 2023 were obtained from data available on the Brazilian Institute of Geography and Statistics (IBGE) website. Incidence rates were calculated using the formula: number of new tuberculosis cases in Uberaba in a given year/total population residing in the city in the same year x 100,000.

Regarding the inclusion criteria, all reported cases with confirmed diagnosis of tuberculosis in Uberaba, from 2013 to 2023, and notified in DATASUS were included, regardless of the degree of data completeness. Exclusion criteria were not applied.

This research was conducted in accordance with the principles outlined in Resolutions 466/2012 and 510/2016, which govern ethics in scientific studies involving humans directly or indirectly. As the present research has used secondary data obtained from publicly available platforms, approval by the Ethics and Research Committee was not required. The data was tabulated and subjected to statistical analysis using GraphPad Prism 5.0 software. When the variable consisted of two groups, pairwise inferences were made using the nonparametric Mann-Whitney test. Nonparametric Kruskal-Wallis test, followed by Dunn's post-test, was used for three or more independent group comparisons. A statistical significance level of $p<0.05$ was established.

RESULTS

A total of 931 cases of tuberculosis were reported in the city of Uberaba, between 2013 and 2023, with the lowest number of notifications occurring in 2016 (n = 67) and the highest in 2023 (n = 114). The annual mean number of cases for the period was 85 cases (standard deviation of 14.9), resulting in an average tuberculosis incidence of 25.6 cases per 100,000 inhabitants, with rates ranging from 20 to 33.7 cases per 100,000 inhabitants (Figure 1).

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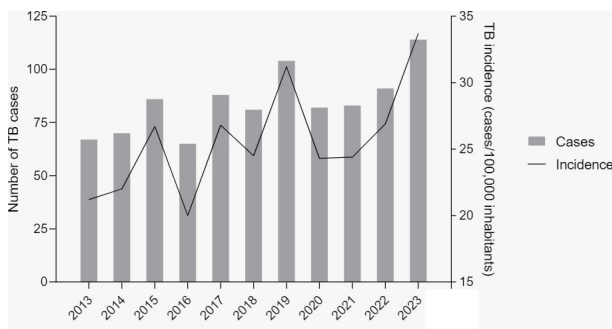
Figure 1. Number of cases and incidence rates of tuberculosis in the city of Uberaba-MG between 2013 and 2023.

There was a higher occurrence of tuberculosis cases among men (p < 0.01), with a male-to-female ratio of approximately 3:1. The majority of patients fell within the 25 - 44 age range (48.3%) and had complete or incomplete elementary or high school education (61.6%). Individuals of white (39.3%), black (16.9%), or mixed race (30.7%) were the most affected by the disease, although the proportion of tuberculosis cases showed a significant increase (approximately 10 times) among individuals who self-identified as black and mixed race in the city of Uberaba during the evaluated period. This proportion rose from 5.97% (n = 4) in 2013 to 55.3% (n = 63) in 2023. Only 9.8% of tuberculosis cases occurred in incarcerated individuals, 5.4% of patients were homeless, and 3.5% were beneficiaries of government cash transfer programs (Table 1).

Table 1. Profile of patients diagnosed with tuberculosis in the city of Uberaba-MG between 2013 and 2023.

Variable	N (%)	p
Sex		<0.01
Male	691 (74.2)	
Female	240 (25.8)	
Race		<0.01
White	366[a] (39.3)	
Black	157[a] (16.9)	
Mixed	286[a] (30.7)	
Yellow (Asian)	9[b] (1.0)	
Indigenous	2[b] (0.2)	
Ignored/blank	111[a] (11.9)	
Age range (years old)		<0.01
0 to 14	29[a] (3.1)	
15 to 24	110[a,c] (11.8)	
25 to 34	239[b] (25.7)	
35 to 44	210[b] (22.6)	
45 to 54	148[b,c] (15.9)	
55 to 64	100[a,c] (10.7)	
65 or more	95[a,c] (10.2)	
Education		<0.01
Illiterate	11[a] (1.2)	
Incomplete elementary education	289[b] (31.0)	
Complete elementary education	101[b] (10.8)	
Incomplete high school	64[a,b] (6.9)	
Complete high school	120[b] (12.9)	
Incomplete higher education	19[a] (2.0)	
Complete higher education	28[a] (3.0)	
Not applicable	25[a] (2.7)	
Ignored/blank	274[b] (29.4)	
Homeless population*		<0.01
Yes	50[a] (5.4)	
No	809[b] (86.9)	
Ignored/blank	72[a] (7.7)	
Population deprived of liberty*		<0.01
Yes	91[a] (9.8)	
No	766[b] (82.3)	
Ignored/blank	74[a] (7.9)	
Beneficiary of a government cash transfer program*		<0.01
Yes	33[b] (3.5)	
No	610[a] (65.5)	
Ignored/blank	288[a] (30.9)	

Abbreviation: Different letters indicate different data, considering a statistical significance level of p < 0.05. *These variables were included in the notification forms in 2014.

Regarding the presence of comorbidities, 20.1% of patients diagnosed with tuberculosis during the evaluated period were HIV positive, 32.1% suffered from alcoholism, 7.5% were diabetic, and 27.5% were

using some illicit drug. The frequency of tuberculosis was similar between tobacco smokers and non-smokers (Table 2).

Table 2. Comorbidities in tuberculosis cases reported in the city of Uberaba-MG between 2013 and 2023.

Comorbidity	N (%)	p
HIV		<0.01
Positive	187[a] (20.1)	
Negative	568[b] (61.0)	
Test in progress	1[c] (0.1)	
Not performed	175[a] (18.8)	
Alcoholism		<0.01
Yes	299[a] (32.1)	
No	580[b] (62.3)	
Ignored/Blank	52[c] (5.6)	
Diabetes		<0.01
Yes	70[a] (7.5)	
No	825[b] (88.6)	
Ignored/Blank	36[a] (3.9)	
Illicit drugs		<0.01
Yes	256[a] (27.5)	
No	541[b] (58.1)	
Ignored/Blank	134[a] (14.4)	
Tobacco smoking		<0.01
Yes	368[a,b] (39.5)	
No	434[a] (46.6)	
Ignored/Blank	129[b] (13.9)	

Abbreviation: Different letters indicate different data, considering a statistical significance level of $p < 0.05$.

The diagnosis of tuberculosis was confirmed by laboratory tests in 60.9% of the cases, with positive results provided by the sputum smear microscopy of the 1st sample (31.7%) and by sputum culture (40.4%). In most cases (87.1%; $p < 0.01$), the sputum smear microscopy of the 2nd sample was left blank/ignored, and it is no longer being recorded in Uberaba since 2015 (table 3). In the rapid molecular test, susceptibility to rifampicin was detected in 44.4% of the tests performed, while resistance to that antimicrobial agent has been detected in 12.9% of the tests performed. The form of tuberculosis predominantly diagnosed was pulmonary (77.1%, $p < 0.01$), while the extrapulmonary form included mainly pleural tuberculosis (36.6%), followed by peripheral lymph node (14.6%) and miliary (15.0%) tuberculosis ($p < 0.01$) (Table 3).

Table 3. Laboratory diagnosis and form of tuberculosis in cases reported in the city of Uberaba-MG between 2013 and 2023.

Variable	N (%)	p
Laboratory confirmation		0.03
Yes	567 (60.9)	
No	364 (39.1)	
1st sputum smear microscopy		<0.01
Positive	295[a] (31.7)	
Negative	196[b] (21.1)	
Not performed	387[a] (41.6)	
Not applicable	53[b] (5.7)	
2nd sputum smear microscopy		<0.01
Positive	40[a] (4.3)	
Negative	20[a] (2.1)	
Not performed	60[a] (6.4)	
Ignored/Blank	811[b] (87.1)	
Sputum culture		<0.01
Positive	376[a] (40.4)	
Negative	162[b] (17.4)	
Not performed	385[a] (41.4)	
In progress	8[b] (0.9)	
Form of tuberculosis		<0.01
Pulmonary	718[a] (77.1)	
Extrapulmonary	181[b] (19.4)	
Pulmonary + Extrapulmonary	32[c] (3.4)	

Variable	N (%)	p
Type of Extrapulmonary		<0.01
Pleural	78[a] (36.6)	
Peripheral ganglionic	31[a,d] (14.6)	
Miliary	32[a] (15.0)	
Meningoencephalitis	15[b,d] (7.0)	
Genitourinary	7[c] (3.3)	
Bone	7[c] (3.3)	
Ocular	2[c] (0.9)	
Cutaneous	5[c] (2.3)	
Others	36[a] (16.9)	
Rapid molecular test		0.04
Susceptible to Rifampicin	413[a] (44.4)	
Resistant to Rifampicin	12[b] (12.9)	
Undetectable	97[a] (22.5)	
Inconclusive	17[b] (18.3)	
Not performed	315[a] (33.8)	
Ignored/Blank	77[b] (8.3)	

Abbreviation: Different letters indicate different data, considering a statistical significance level of p < 0.05.

The majority of notified cases were new cases (81.8%, p < 0.01), followed by re-entry after loss to follow-up (9.7%) and recurrence (5.3%). Most notified cases progressed to cure (55.4%, p < 0.01), although 14.9% of patients were lost to follow-up. The number of tuberculosis deaths recorded during the evaluated period was 99 (10.6% of the patients) (Table 4).

Approximately 29% of the *M. tuberculosis* strains were susceptible to the drugs used in tuberculosis treatment. However antimicrobial susceptibility analysis was not performed in a high number of cases (28.8%) or it was ignored (37.5%). Directly observed treatment (DOT) was conducted in 52.6% of patients (Table 4).[8] DOT refers to the ingestion of medications by the patient in the presence of a healthcare professional.[8]

Table 4. Type of entry, outcome, susceptibility test and directly observed treatment in tuberculosis cases reported in the city of Uberaba-MG between 2013 and 2023.

Variable	N (%)	p
Entry type		<0.01
New case	762[a] (81.8)	
Recurrence	49[b] (5.3)	
Reentry after abandonment	90[b] (9.7)	
Transfer	21[b,c] (2.3)	
Post-death	9[c] (1.0)	
Outcome		<0.01
Cure	516[a] (55.4)	
Abandonment	139[a,b] (14.9)	
Death from tuberculosis	99[a,b] (10.6)	
Death from other causes	40[b] (4.3)	
Transfer	55[b] (5.9)	
Drug resistant tuberculosis	14[c] (1.5)	
Regimen change	7[c] (0.8)	
Primary abandonment	11[c] (1.2)	
Ignored/Blank	50[c] (5.4)	
Directly observed treatment		<0.01
Yes	490[a] (52.6)	
No	345[a] (37.1)	
Ignored/Blank	96[b] (10.3)	
Susceptibility Test		<0.01
Susceptible	268[a] (28.8)	
1st line drug resistant	5[b] (0.5)	
Isoniazid resistant	5[b] (0.5)	
Rifampicin resistant	1[b] (0.1)	
Resistant to Isoniazid and Rifampicin	4[b] (0.4)	
Test in progress	31[b] (3.3)	
Not performed	268[a] (28.8)	
Ignored/Blank	349[a] (37.5)	

Abbreviation: Different letters indicate different data, considering a statistical significance level of p < 0.05.

DISCUSSION

During the decade 2013-2023, Uberaba had an average annual tuberculosis incidence of 25.6 cases per 100,000 inhabitants, a value that was below the national average (36.4) and above the state average (20.6) for the same period.[7] This discrepancy can be explained by the different sociodemographic and health characteristics of the Brazilian regions.[9]

A discontinuous growth in the incidence of tuberculosis was observed during the period evaluated in this study. From 2013 to 2019 the incidence increased from 21.2 to 31.2 cases per 100,000 inhabitants. A decline was observed in 2020 (24.3), followed by a resurgence of cases in the years 2021 to 2023. The reduction in 2020 can be attributed to the Covid-19 pandemic, a phenomenon also highlighted in another study, while the larger number of new diagnoses in 2021-2023 likely included a backlog of people who developed TB in previous years, but whose diagnosis and treatment was delayed by Covid-related disruptions.[10]

Geographical differences in tuberculosis also extend to individual variables. The higher incidence of the disease among male patients (74.2%) was also reported in the studies which evaluated the profile of tuberculosis patients in Brazilian municipalities and identified the predominance of men in 69.0%.[11] The reasons explaining why men are more affected by the disease include lack of self-care, low priority of health campaigns targeting this audience, and greater involvement of men in the job market, exposing them more to the disease.

During the evaluated period, there was no predominance of tuberculosis in any specific race in the city of Uberaba, which was also noted when analyzing tuberculosis notification data in the state of Mato Grosso do Sul from 2001 to 2009.[12] However, it is noteworthy that the number of disease records with race left blank or ignored in Uberaba decreased from 74.6% in 2013 to 0.9% of records in 2023, indicating improved completion of notification forms. In this sense, an increasing proportion of tuberculosis cases among individuals who self-identified as black or mixed race was observed (5.97% of tuberculosis cases in 2013 and 55.3% in 2023). A higher incidence of tuberculosis among black and mixed-race individuals was reported in the city of Belém-PA.[13] The racial discrepancies observed in these studies may be linked to regional differences in the population composition of the country.

The low level of education identified among tuberculosis patients in Uberaba (elementary or high school education in 61.6% of cases) resembles the education profile of tuberculosis patients in Belo Horizonte, the capital of Minas Gerais, from 2001 to 2017, which was 12 years of schooling.[14] In general, black or mixed-race populations and those with lower levels of education are more susceptible to poorer housing conditions, lack of basic sanitation, and limited access to health services. These factors can facilitate disease transmission and hinder diagnosis and treatment.[15]

The vulnerability of patients to acquiring tuberculosis is also correlated with socioeconomic status. In this study, 5.4% of the patients diagnosed with tuberculosis were homeless and 9.8% were incarcerated. Research using SINAN data on tuberculosis in the city of Belo Horizonte described the profile of homelessness in 0.8% of cases and incarceration in 1.6% of notifications.[14] Furthermore, each group has peculiar factors that favor *M. tuberculosis* infection: in the incarcerated population, the existence of a plurality of incarcerated individuals, as well as their respective health problems, the situation of confinement, and overcrowded cells; in the homeless population, the lack of access to food, rest, and health services.[16]

Government cash transfer programs can benefit tuberculosis patients by providing financial resources that could enable treatment continuity. However, nearly two-thirds of the cases analyzed in our study lacked the information regarding receiving the benefit. The incompleteness of this data in health systems compromises the analysis of the impact of cash transfer programs on the number of confirmed cases, and on tuberculosis treatment success. However, other studies have identified that most tuberculosis notifications involve patients who are not beneficiaries of government programs.[17,18]

The coinfection *M. tuberculosis* and HIV was present in one-fifth of the patients, however, it should be noted that this number may be underreported, as 18.8% of patients were not tested for HIV. Similarly, 21.5% of the patients diagnosed with tuberculosis in Ribeirão Preto-SP were co-infected with HIV.[19] These findings reinforce that immunosuppression caused by the virus may facilitate the multiplication of *M. tuberculosis* and the onset of the disease.[20] A HIV-positive patient is 18 times more susceptible to tuberculosis than non-infected individuals, also demonstrating that these diseases have similar epidemiological profiles, such as male patients, young age, alcohol use, smoking, and illicit drug use.[21]

Alcohol use and tobacco smoking were reported by 32.1% and 39.5%, respectively, of tuberculosis patients in Uberaba, while the prevalence for the general population is 18.4% for alcoholism, and 17.3% for smoking.[22] These percentages demonstrate that the occurrence of alcoholism and smoking is 1.7 and 2.3 times higher, respectively, among tuberculosis patients in the city of Uberaba when compared to the Brazilian population.

The diagnosis is identified as one of the bottlenecks in the fight against tuberculosis in Uberaba, where laboratory tests were not performed in 39.1% of the cases. The most neglected test in the city of Uberaba was sputum microscopy of the second sample, accounting for 93.5% of patients, when considering both non-performed (6.4%) and blank/ignored completion (87.1%). The municipality of Uberaba ceased to register this examination since 2015, a conduct incompatible with the recommendations of the Brazilian Ministry of Health, which determines that sputum microscopy should be performed in two samples: the first sample at the initial consultation and the second sample on the morning of the following day.[23] Failure to perform this laboratory test may have important implications for the treatment and outcome of the disease.

Another test with low performance was the antimicrobial susceptibility test of the bacterium, which was not performed (28.8%) or had blank/ignored completion (37.5%) in most reported cases. The low testing aligns with other results indicating that only 15 to 20% of the tuberculosis cases undergo evaluation of *M. tuberculosis* susceptibility profile to treatment drugs.[24] The deficiency in performing this test hampers the detection of strains resistant to rifampicin and isoniazid, which complicates the treatment of patients. This highlights the need for training the healthcare team on the importance of requesting and offering the test.[25]

Implemented nationally in 2014, the rapid molecular test for tuberculosis was introduced in the same year in the city of Uberaba. During the study period, the detection of rifampicin susceptibility profile among *M. tuberculosis* strains was useful for guiding treatment. However, the high rate of undetectable or inconclusive results (40.8%) can be considered a limitation for tuberculosis diagnosis in Uberaba. The main challenge in the widespread use of the rapid molecular test is the requirement for training healthcare professionals to ensure the quality of samples collected and the proper processing of sputum, aiming to assure an accurate and reliable diagnosis from the test.[26]

The pulmonary form of tuberculosis was the most prevalent (77.1%) in this study, while the extrapulmonary form (19.4%) predominantly affected sites such as the pleura, peripheral lymph nodes, and others, causing the disseminated form (miliary). These findings could be explained by the preference of *M. tuberculosis* for these areas of the body due to increased oxygen concentrations.[27]

The entry of patients into the health system predominated as a new case (81.8%). However, it is noteworthy the number of patients who re-entered the system after treatment abandonment (9.7%) and recurrence (5.3%), demonstrating that patients returned to the health system after dropping out of treatment or experiencing a recurrence of the disease, which also reinforces the importance of requesting a drug susceptibility test in order to offer a more appropriate treatment for the patient.

Regarding the outcome, although most cases resulted in cure (55.4%), the proportions of abandonment (14.9%) and death from tuberculosis (10.6%) reveal that there is still much work to be done to maintain treatment adherence and effectiveness. The numbers presented here are in line with the study which analyzed tuberculosis notifications in the state of São Paulo and identified 53% of cure, 11% of death, and 8% of abandonment.[11] However, these numbers are below the targets indicated by the WHO, which recommends a minimum cure rate of 85% for tuberculosis patients, and a maximum of 5% of patients with loss to treatment follow-up.[3]

As an approach to ensure that medication is taken correctly, increasing the cure rate and reducing abandonment in tuberculosis treatment, the ingestion of medications by the patient in the presence of a healthcare professional, referred to as DOT, is a good strategy. It is done daily in the intensive phase and at least three times weekly in the maintenance phase of treatment.[8] In Uberaba, DOT reached 52.6%, significantly lower than the 63.5% reported in municipalities with 301 to 400 thousand inhabitants in the state of São Paulo.[28]

Some limitations must be considered when interpreting the results of this study, which utilized tuberculosis data from DATASUS. First, the data is subject to potential inaccuracies due to underreporting, misclassification, or delayed reporting, as well as the use of preliminary data for the year 2023 and the alterations in the notification forms in 2014, which may lead to biases in the estimation of tuberculosis incidence and outcomes. Another limitation is the observational nature of the study design precludes causal inferences, as the use of secondary data from DATASUS does not allow control over confounding factors or biases related to the data collection process. Thus, while the study provides valuable insights into tuberculosis trends, the findings should be interpreted with caution.

This study outlines the epidemiological, clinical, diagnostic, and evolutionary profile of tuberculosis in the city of Uberaba over a period of 10 years. Although nationwide data is available in SINAN, regional differences require a closer examination of the unique reality of a municipality to identify the variables that contribute to the success or insufficiency of health policies in managing the disease. The identification of the tuberculosis epidemiological profile, which affects more males, adults with a low education profile, and the presence of comorbidities such as AIDS, as well as risk behaviors including alcohol use, tobacco smoking, and illicit drug use serve to direct and prioritize health

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actions for these groups in the city of Uberaba. The low quantity of tuberculosis laboratory confirmations and directly observed treatment are points that need to be discussed and reorganized by the healthcare system in order to improve treatment adherence and increase the chances of tuberculosis cure. The multifactorial nature of tuberculosis requires a multidisciplinary health approach, aiming to integrate the patient into the healthcare system and establish bonds to ensure that the therapeutic journey, from entry to outcome, is as short and successful as possible.

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AUTHORS' CONTRIBUTIONS

Apollo Nobre Reis contributed to the database search, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions and review. **Mírian Akiko Kawamura** contributed to writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions and review. **Yasmin Neves Vieira Sabino** contributed to writing the abstract, interpretation of results, conclusions and review. **Aline Dias Paiva** contributed to writing the abstract, interpretation and description of results, preparation of tables, 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

Temporal trend and spatial distribution of mortality from Chagas heart disease in Pernambuco, 2007-2022

Tendência temporal e distribuição espacial da mortalidade por doença cardíaca chagásica em Pernambuco, 2007-2022

Tendencia temporal y distribución espacial de la mortalidad por cardiopatía chagásica en Pernambuco, 2007-2022

Corresponding author:
E-mail: enfmatheusvinicius@outlook.com
Address: Princess Isabel Street, São Vicente de
Paulo, Vitória de Santo Antão, Pernambuco,
Brazil.

Matheus Vinicius Barbosa da Silva[1] [iD]
Fabiana Vieira de Melo[2] [iD]
Valdir Vieira da Silva[3] [iD]
Augusto César Barreto Neto[1] [iD]
Simone Maria Muniz Bezerra da Silva[1] [iD]

[1]Federal University of Pernambuco, Recife, Pernambuco, Brazil.
[2]Brazilian University Center, Recife, Pernambuco, Brazil.
[3]Federal Rural University of Pernambuco, Recife, Pernambuco, Brazil.

ABSTRACT

Background and Objectives: Chagas heart disease is one of the most frequent forms of Chagas disease progression. Despite published studies on the impact of the disease in Pernambuco, there is a lack of data regarding this profile for the form with cardiac involvement. Therefore, the objective of this study was to analyze the temporal trend and spatial distribution of mortality from Chagas heart disease in the state of Pernambuco from 2007 to 2022. **Methods:** This is an ecological, time series, and spatial study. The variables (number of deaths, year of death, age group, sex, and Regional Health Management) of the occurrence of deaths were extracted from the Mortality Information System. The mortality rate, temporal trend, and spatial distribution were estimated. **Results:** A stationary pattern was observed in the deaths reported in the state of Pernambuco. Males were the most impacted. The municipalities of Ingazeira (152.53/100,000), Itapetim (143.47/100,000), and São Benedito do Sul (141.38/100,000) had the highest mortality rates per 100,000 inhabitants. Regarding the age group, decreasing trends were found in the age groups of 15 to 24 (VPA: -11; p=0.015), 25 to 34 (VPA: -10.3; p=0.013), 35 to 44 (VPA: -8.43; p=0.003), and 55 to 64 years (VPA: -3.11; p=0.189). **Conclusion:** The findings contribute to a better understanding of the dynamics of the disease in Pernambuco and can serve as a basis for the formulation and implementation of strategies that intensify preventive and assistance measures focused on reducing deaths.
Keywords: *Chagas disease. Chagas Cardiomyopathy. Mortality. Temporal distribution.*

RESUMO

Justificativa e Objetivos: A doença cardíaca chagásica é uma das mais frequentes formas de evolução da doença de chagas. Embora existam dados publicados sobre o impacto da doença em Pernambuco, há uma escassez de informações a respeito desse perfil para a forma com acometimento cardíaco. Logo, o objetivo deste estudo foi analisar a tendência temporal e a distribuição espacial da mortalidade por doença cardíaca chagásica no estado de Pernambuco no período de 2007 a 2022. **Métodos:** Estudo ecológico, de série temporal e espacial. As variáveis (número de óbitos, o ano do óbito, a faixa etária, o sexo e a Gerência Regional de Saúde) da ocorrência dos óbitos foram extraídas do Sistema de Informação de Mortalidade. A taxa de mortalidade, tendência temporal e distribuição espacial foram estimadas. **Resultados:** Observou-se um padrão estacionário nos óbitos notificados no estado de Pernambuco. O sexo masculino foi o mais acometido. Os municípios Ingazeira (152,53/100 mil), Itapetim (143,47/100 mil) e São Benedito do Sul (141,38/100 mil) apresentaram as maiores taxas de mortalidade por 100 mil habitantes. Em relação à faixa etária, evidenciaram-se tendências decrescentes nas faixas de 15 a 24 (VPA: -11; p=0,015), 25 a 34 (VPA: -10,3; p=0,013), 35 a 44 (VPA: -8,43; p=0,003), e 55 a 64 anos (VPA: -3,11; p= 0189). **Conclusão:** Os achados contribuem para uma melhor compreensão da dinâmica da doença em Pernambuco, podendo servir como base para a formulação e implementação de estratégias que intensifiquem medidas preventivas e assistenciais com foco na redução das mortes.

Descritores: *Doença de Chagas. Cardiomiopatia Chagásica. Mortalidade. Distribuição temporal.*

RESUMEN

Justificación y Objetivos: La cardiopatía de Chagas es una de las formas más comunes de progresión de la enfermedad de Chagas. Aunque existen datos publicados sobre el impacto de la enfermedad en Pernambuco, faltan datos sobre ese perfil para la forma con afectación cardíaca. Por lo tanto, el objetivo de este estudio fue analizar la tendencia temporal y la distribución espacial de la mortalidad por cardiopatía chagásica en el estado de Pernambuco (Brasil) en el período de 2007 a 2022. **Métodos:** Estudio de series ecológicas, temporales y espaciales. Las variables (número de defunciones, año de defunción, grupo de edad, sexo y Gestión regional de salud) para la ocurrencia de defunciones se extrajeron del Sistema de Información de Mortalidad. Se estimó la tasa de mortalidad, la tendencia temporal y la distribución espacial. **Resultados:** Se observó un patrón estacionario en las muertes reportadas en el estado de Pernambuco. Los hombres fueron los más afectados. Los municipios de Ingazeira (152,53/100.000), Itapetim (143,47/100.000) y São Benedito do Sul (141,38/100.000) tuvieron las mayores tasas de mortalidad por 100.000 habitantes. En relación con grupo de edad, se evidenciaron tendencias decrecientes en los rangos de 15 a 24 (VPA: -11; p=0,015), de 25 a 34 (VPA: -10,3; p=0,013), de 35 a 44 (VPA: - 8,43; p=0,003), y de 55 a 64 años (VPA: -3,11; p= 0189). **Conclusión:** Los hallazgos contribuyen a una mejor comprensión de la dinámica de la enfermedad en Pernambuco y pueden servir como base para la formulación e implementación de estrategias que intensifiquen las medidas preventivas y asistenciales con foco en la reducción de muertes.

Palabras Clave: *Enfermedad de Chagas. Cardiomiopatía Chagásica. Mortalidad. Distribución temporal.*

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Matheus Vinicius Barbosa da Silva, Fabiana Vieira de Melo, Valdir Vieira da Silva, Augusto Cesar Barreto Neto, Simone Maria Muniz Bezerra da Silva

INTRODUCTION

American trypanosomiasis, also known as Chagas disease, is a chronically evolving anthropozoonosis caused by protozoan *Trypanosoma cruzi* infection. It is a neglected tropical disease predominant in Latin American countries, where socioeconomic and environmental factors favor its spread. However, globalization and migration processes have increased its presence in non-endemic regions like the United States, Canada, and several European countries.[1,2]

In its natural evolution, when not properly diagnosed and treated in a timely manner, Chagas disease usually resolves spontaneously in the initial phase of infection. Over time, however, a state of subclinical parasitemia may occur which, throughout life, characterizes the chronic phase. This phase can manifest itself in four different ways: indeterminate, cardiac, digestive or mixed, involving cardiac and digestive manifestations.[3,4]

Chagas heart disease (CHD) is one major form of chronic evolution, accounting for about 30% of cases and is characterized as one of the most severe non-ischemic heart diseases.[4] In CHD, the various clinical manifestations result from chronic inflammatory process generated in the heart tissue, which culminates in destructive and fibrosing processes. Electrical disturbances, which are manifested by arrhythmias and blockages in the conduction of electrical impulses, stand out among these. Additionally, structural alterations such as left ventricular aneurysms, thromboembolic complications secondary to thrombus formation and heart failure occur.[5]

Chagas disease and its cardiac form not only compromise the health of individuals, but also generate significant economic impacts on health systems.[6] Patients often face high costs related to hospitalizations, long-term treatments, and the need for devices like pacemakers, resulting in a substantial financial burden for both individuals and public health systems.[7] This condition, therefore, requires attention from both clinical and economic points of view given its lasting impact on the quality of life of those affected.

In Brazil, recent estimates have shown a decreasing incidence of Chagas disease cases due to public health actions implemented since the mid-1970s, responsible for interrupting vector transmission by the species *Triatoma infestans* in 2006.[8] Transmission is still endemic,however, to other species of triatomines such as *Triatoma brasiliensis*, *Triatoma pseudomaculata*, *Panstrongylus megistus* and *Rhodnius robustus*.[9]

In Northeastern Brazil, recent data on hospital morbidity and mortality registered approximately 1884 hospitalizations due to Chagas disease between 2008 and 2018, of which 9.5% died.[10] Regarding incidence, the state of Pernambuco stands out as the second place with the most cases, behind only Maranhão.[11]

Despite published data on the impact of Chagas disease in Pernambuco, data related to the form with cardiac involvement is scarce. Thus, this study analyzes the time trend and spatial distribution of mortality from Chagas heart disease in the state of Pernambuco from 2007 to 2022.

METHODS

Design

This ecological, time and spatial series, descriptive and quantitative study analyzed deaths from Chagas heart disease in residents of the state of Pernambuco, notified from 2007 to 2022. The STROBE guide recommendations for observational studies was followed.[12]

Context

Data from the state of Pernambuco recorded from January 2007 to December 2022 were obtained. Located in Northeastern Brazil, Pernambuco has an estimated population of 9,058,931 inhabitants divided into 184 municipalities plus the Fernando de Noronha archipelago, which are structured according to political and geographical characteristics in 12 Regional Health Managements (GERES) to ensure the best execution of the Unified Health System (SUS) activities.[13]

Data source and selection criteria

Data on deaths from Chagas heart disease were extracted from the Mortality Information System (SIM) between August and September 2024, using TabWin, a public domain tool available on the SUS Department of Informatics (DATASUS) website. After tabulation, data were exported into a Microsoft Excel spreadsheet. Information on deaths was included in the following International Classification of Diseases tenth version (ICD-10) category: B57.0 (acute form of Chagas disease with cardiac involvement), notified and tabulated by date of notification in the state of Pernambuco (2007 to 2022). Incomplete notifications were excluded.

Variables

Selected variables included: year of death (2007 to 2022); municipalities of Pernambuco; age group (15 to 24 years; 25 to 34 years; 35 to 44 years; 45 to 54 years; 55 to 64 years; and >65 years); gender (male; female); and GERES of occurrence (I – Recife, II – Limoeiro, III – Palmares, IV – Caruaru, V – Garanhuns, VI – Arcoverde, VII – Salgueiro, VIII – Petrolina, IX – Ouricuri, X – Afogados da Ingazeira, XI – Serra Talhada and XII – Goiana) (Figure 1).

Mortality rate (MR) due to Chagas heart disease was one of the indicators analyzed, estimated for the general population and by gender using the formula below: MR = (Cases of death from Chagas heart disease in one

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municipality and year X 100 thousand) / Population residing in that municipality and year.
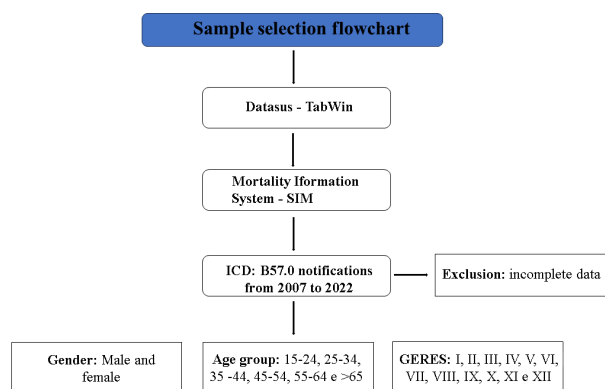
Figure 1. Sample selection flowchart.

Data analysis

Time trend was calculated for CHD mortality using Joinpoint Regression Program version 5.2.0.0. This analysis considered the year as an independent variable and the mortality rate as the dependent variable. It enables identifying changes in the trend of an indicator over time, adjusting the data with as few joinpoints as possible. The time series may thus reveal an increasing trend (p-value <0.05 and positive regression coefficient), a decreasing trend (p-value <0.05 and negative regression coefficient), or stationary (p-value >0.05). Additionally, the annual percentage change (APC) with respective 95% confidence intervals (CI) was presented.

Spatial distribution of CHD deaths was performed for the entire study period (2007-2022) via QGIS software version 3.38 (Open Source Geospatial Foundation,

Beaverton, USA). A shapefile of the 185 municipalities in Pernambuco was extracted from the Brazilian Institute of Geography and Statistics (IBGE) database, using SIRGAS 2000 as a coordinate reference system for the maps made. To better understand the spatial and time evolution of deaths in Pernambuco, the distribution of CHD deaths was stratified by quadrennium into four intervals: 2007-2010, 2011-2014, 2015-2018 and 2019-2022. Results were presented using choropleth maps for better visualization of the spatial panorama.

Descriptive data were analyzed using Bioestat version 5.3. Results were considered significant with p < 0.05.

Ethical aspects

As this study uses secondary data in the public domain, the project did not require submission to a research ethics committee, as recommended by Resolution No. 510, of 2016, from the National Health Council (CNS). However, all ethical recommendations for elaborating this type of study were followed.[14]

RESULTS

From 2007 to 2022, Pernambuco registered 1,556 deaths from CHD. Of these, 898 (57.71%) were males and 658 (42.29%) were females. The highest mortality rate occurred in 2021, with 1.17 deaths per 100 thousand inhabitants, followed by 2016 with 1.16 deaths/100 thousand inhabitants. Mortality rates predominated in males except for 2019, when the rates were 0.45 deaths/100 thousand inhabitants for both groups (Figure 2).
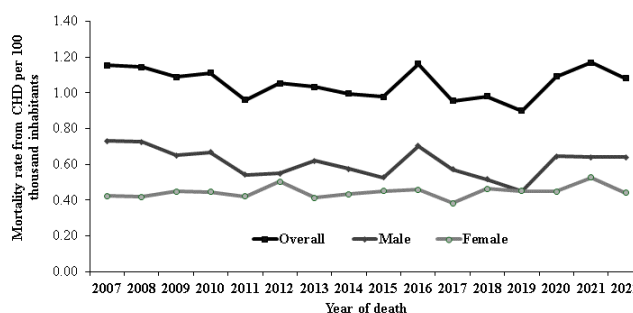
Figure 2. Distribution of overall mortality rate and according to gender from Chagas heart disease in Pernambuco, Brazil, from 2007 to 2022.

Considering the entire studied period, Ingazeira, Itapetim and São Benedito do Sul stand out as the Pernambuco municipalities with the highest death rates, reaching 152.53, 143.47 and 141.38 deaths per 100 thousand inhabitants, respectively (Figure 2).

Time trend analysis of CHD mortality revealed a stationary pattern between genders. Despite the decrease observed in males (APC: -0.5; 95%CI -3.0; 1.2) and increase in females (APC: 0,5; 95%CI -0.4; 1.4), the trends were not statistically significant (p=0.334 and p=0.262, respectively) (Table 1).

Regarding age group, the 15 to 24 (APC: -11; 95%CI -24.6; -3; p=0.015), 25 to 34 (APC: -10.3; 95%CI -20.3; - 3,2; p=0.013), 35 to 44 (APC: -8.4; 95%CI -15.1; -3,3; p=0.003) and 55 to 64 (APC: -3.11; 95% CI -4.84; 1,37; p= 0189) age groups showed decreasing trends. Age groups of 45 to 54 and ≥65 years showed a stationary time pattern (Table 1). Analysis by health regions found a decreasing trend in CHD mortality only in II GERES (APC: -4.0; 95%CI -6.5; -1,7; p=0.001). Other regions exhibited a stationary behavior.

Table 1. Annual percentage change (APC) and confidence intervals (95%CI) for Chagas heart disease according to sociodemographic variables in Pernambuco, Brazil, from 2007 to 2022.

Characteristics	Mortality rate per 100 thousand inhabitants		APC (95% CI)	*p* - value	Trend
	2007	2022			
Gender					
Male	1.52	1.34	-0.91 (-3.05; 1.24)	0.343	Stationary
Female	0.82	0.84	0.51 (-0.41; 1.48)	0.262	Stationary
Age group (years)					
15 to 24	0.01	0.01	-11.04 (-24.60; -3.07)	0.015	Decreasing
25 to 34	0.35	0.01	-10.33 (-20.3; -3.24)	0.013	Decreasing
35 to 44	0.86	0.28	-8.43 (-15.10; -3.39)	0.003	Decreasing
45 to 54	1.31	0.77	-3.02 (-6.34; 0.25)	0.067	Stationary
55 to 64	3.78	2.66	-3.11 (-4.84; 1.37)	0.004	Decreasing
>65	8.84	6.61	-1.01 (-2.46; 0.55)	0.189	Stationary
GERES					
I GERES (Recife)	0.69	0.79	-0.00 (-2.54; 2.56)	0.971	Stationary
II GERES (Limoeiro)	3.16	1.49	-4.02 (-6.51; -1.76)	0.001	Decreasing
III GERES (Palmares)	1.57	0.64	-3.82 (-11.64; 4.08)	0.237	Stationary
IV GERES (Caruaru)	0.57	0.43	-0.12 (-4.89; 5.12)	0.986	Stationary
V GERES (Garanhuns)	0.97	0.55	-2.09 (-7.52; 3.02)	0.339	Stationary
VI GERES (Arcoverde)	1.06	2.08	2.85 (-1.14; 7.59)	0.134	Stationary
VII GERES (Salgueiro)	0.07	2.69	1.75 (-7.52; 12.74)	0.557	Stationary
VIII GERES (Petrolina)	1.91	1.35	-0.24 (-6.14; 6.65)	0.994	Stationary
IX GERES (Ouricuri)	0.03	1.39	-0.24 (-7.51; 7.89)	0.987	Stationary
X GERES (Afogados da Ingazeira)	6.02	5.76	0.54 (-2.93; 4.30)	0.747	Stationary
XI GERES (Serra Talhada)	3.57	0.83	-2.70 (-9.18; 3.39)	0.293	Stationary
XII GERES (Goiana)	1.30	1.27	2.14 (-2.87; 7.99)	0.362	Stationary
Pernambuco	1.15	1.08	-0.3 (-1.4; 0.8)	0.334	Stationary

Abbreviations: Geres: Regional health management; APC: annual percentage change; CI: confidence interval.

Time distribution analysis of mortality rates per 100,000 inhabitants (Figure 3) showed that the municipalities of Machados (44.66/100,000), São Benedito do Sul (43.14/100,000) and Carnaube (42.14/100,000)had the highest rates in the first four-year period (2007-2010). In the following period (2011-2014), São Benedito do Sul (74.71/100 thousand), Calumbi (34.66/100 thousand) and Itapetim (28.49/100 thousand) stood out. In the third four-year period (2015-2018), Brejinho (53.44/100,000), Itapetim (50.81/100,000) and Ingazeira (43.84/100,000) presented the highest rates. Finally, in the last four-year period (2019-2022), Quixaba (88.99/100 thousand), Ingazeira (86.99/100 thousand) and Brejinho (39.76/100 thousand) recorded the highest rates (Figure 3).
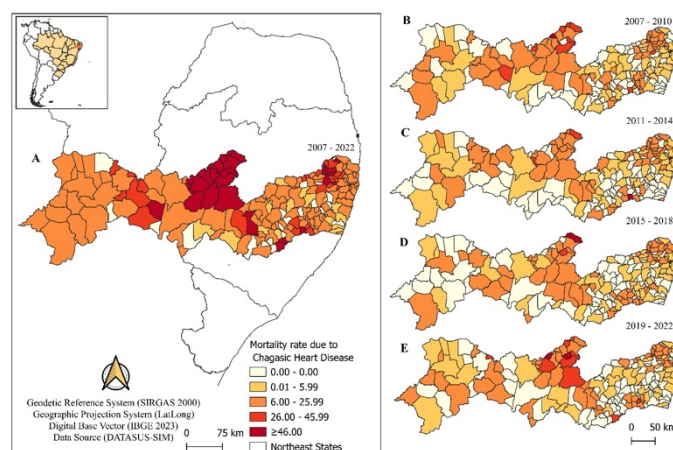
Figure 3. Spatial distribution of deaths from Chagas heart disease in the municipalities of Pernambuco, Brazil, from 2007 to 2022.

DISCUSSION

Our study analyzed the time behavior and distribution of deaths from CHD cases in the state of Pernambuco. Number of deaths was higher in males, aged over 65 years and living in X GERES. Pernambuco showed a stationary trend in the death rate, with a decreasing panorama only in the health region of Limoeiro. Additionally, a decreasing trend occurred in three age groups (15 to 24, 25 to 34, 45 to 44 and 55 to 64 years).

Regarding the stationary pattern in reported deaths, with a decreasing trend in some age groups, our results contrast with those of a previous time study conducted in Brazil which showed that mortality from neglected tropical diseases, including Chagas disease, showed a reduction of 1.24% per year from 2000 to 2019. Among the regions investigated, the Northeast showed a decreasing pattern of deaths in certain time stratifications,[15] although another study has shown that the prevalence of acute Chagas cases has increased in the North, Northeast and Southeast.[16]

The higher mortality observed among males compared with females aligns with findings from a previous study, which reported higher mortality in this group.[17] Another study, also conducted in a Northeastern state, found a predominance of mortality in males.[18] Similar proportions were also found for other neglected diseases like leishmaniasis and leprosy.[19,20]

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Such a scenario may be related to biological, behavioral, and social factors. Studies indicate that men generally have greater exposure to risk factors such as living in rural areas and professional activities that favor contact with the triatomine.[21,22] Additionally, delayed seeking medical attention behavior may be more common among men, contributing to the severity of the disease in more advanced stages.[23] Hormonal factors and the difference in immune responses between genders can influence CHD evolution.[24]

Regarding the CHD mortality rate among the Pernambuco municipalities, Ingazeira, Itapetim and São Benedito do Sul presented the highest rates. This finding can be explained by the population density in these locations. As for the GERES, deaths due to CHD decreased only in the II GERES which may be related to local public actions and the intensification of epidemiological surveillance activities.[25]

Pernambuco showed a stationary trend in CHD mortality over the studied years. This finding corroborates a previous study, which analyzed the time trend of deaths from Chagas disease in Pernambuco from 1980 to 2007, showing a stationary state for this rate.[26]

Certain age groups exhibited a downward trend, as observed in another study in which the highest rate of deaths occurred in the public aged 15 to 59 years.[27] Frequency of exposure in this population is related to occupational activities that increase risk of transmission, such as in rural areas.

Our findings indicate a stability trend in CHD deaths in Pernambuco, but studies in the literature with similar methodologies at the regional and national levels are scarce. Hence, greater vector control actions and preventive and care measures are still necessary in Brazil, especially in regions that face a high burden of social and economic inequities.

As for study limitations, we can cite the use of secondary data, subject to underreporting, and the fact that analyses are restricted to a single federative unit which limits generalizing the results to a larger context. Additionally, we did not consider characteristics like schooling and race which can be influenced by time and seasonal factors. Despite these limitations, to our knowledge this is the first study to investigate the time pattern and spatial distribution of CHD deaths in Pernambuco. Moreover, despite using secondary data, they come from a health information system with high coverage and mandatory registration which confers greater reliability to our findings.

Our findings contribute to a better understanding of the CHD dynamics in Pernambuco and can serve as a basis for formulating and implementing strategies that intensify preventive and care measures focused on reducing deaths from CHD. During the period analyzed, the analysis revealed a stationary trend in CHD mortality in the state, predominant among genders and health regions, except for decreases in certain age groups.

Our results contribute to a better understanding of mortality associated with Chagas heart disease, highlighting the importance of early diagnosis and specialized follow-up to reduce mortality. Thus, preventive measures based on vector control should be implemented in the study area to favor the reduction of incidence and deaths from Chagas disease.

Additionally, further research focused on improving therapeutic approaches is needed, as is the inclusion of affected patients in specialized care lines focused on reducing complications and preventing disease chronicity. Emphasizing factors such as the presence of comorbidities or demographic characteristics is paramount to understand the mechanisms behind these differences and assist in developing more targeted health policies. Finally, we must consider the impact of the Covid-19 pandemic on death records, since the worsening of public health may have altered diagnosis and treatment patterns which also makes it necessary to consider how it affected the mortality dynamics from the condition like underreporting of deaths or changes in access to treatment during this critical period.

In the context of public policies, the information generated by this study should be used to improve public health strategies, especially in early identification and the implementation of long-term follow-up programs for affected individuals. Such initiatives can significantly improve patient quality of life and reduce the mortality associated with CHD.

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AUTHORS' CONTRIBUTIONS

Matheus Vinicius Barbosa da Silva contributed to the bibliographic research, drafting the abstract, introduction, methodology, discussion, interpretation and description of the results, preparation of tables, conclusions, review and statistics. **Fabiana Vieira de Melo** contributed to the bibliographic research, drafting the abstract, introduction, methodology, discussion, interpretation and description of the results, conclusions and review. **Valdir Vieira da Silva** contributed to drafting the abstract, methodology, interpretation of results, conclusions, review and statistics. **Augusto César Barreto Neto** contributed to project management, review and statistics. **Simone Maria Muniz Bezerra da Silva** contributed to project management, review and statistics.

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

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Original Article

Development and evaluation of equipment for disinfection by ultraviolet radiation in healthcare environments

Desenvolvimento e avaliação de equipamentos para desinfecção por radiação ultravioleta em ambientes de saúde
Desarrollo de equipo para la desinfección por radiación ultravioleta en entornos sanitarios

Aline Teichmann[1] ORCID 0000-0002-8019-7063
Demis Pessatto Faqui[1] ORCID 0009-0001-8551-9893
Eduardo Dullius[1] ORCID 0009-0002-5744-4406
Gilson Augusto Helfer[1] ORCID 0000-0002-3256-8069
Nayanna Dias Bierhals[1] ORCID 0000-0002-3010-8317
Maitê Souza Magdalena[1,2] ORCID 0000-0001-9561-896X
Andréia Rosane de Moura Valim[1] ORCID 0000-0001-9611-3103
Jane Dagmar Pollo Renner[1] ORCID 0000-0003-0649-7081
Janine Koepp[1] ORCID 0000-0003-4873-7696
Mari Ângela Gaedke[1] ORCID 0000-0002-3032-081X
Adilson Ben da Costa[1] ORCID 0000-0003-3009-7459

[1]University of Santa Cruz do Sul, Santa Cruz do Sul, Rio Grande do Sul, Brazil.
[2]Santa Cruz Hospital, Santa Cruz do Sul, Rio Grande do Sul, Brazil.

ABSTRACT

Background and Objectives: In hospitals, where there is a high circulation of microorganisms, complementary technologies are essential to improve disinfection. This study aimed to develop a technology adapted to our reality, produced and tested by our research group, safe, easy to operate and with low construction cost so that it can be used in health environments such as hospitals with limited resources. **Methods:** After research, 55W lamps, T8 - G13 - 909 mm with emission of ultraviolet radiation at 254 nm were chosen as the UVC source. The "Torre UVC" application was created using the Android Studio IDE. Power measurements taken with a radiometer were used to assess the efficiency of the UVC tower and determine the appropriate doses. The efficiency of the tower against some clinically important microorganisms was evaluated. **Results:** The UVC tower was constructed with an aluminum frame and 8 lamps, allowing remote operation. The app was designed for easy and intuitive use. The efficiency tests conducted with the radiometer demonstrate an exponential decrease in radiation dosage as objects or surfaces move away from the tower. The tower effectively inhibited microbial growth (bacteria and fungi) even with low doses of UVC radiation (12 mJ/cm²) and reduced the viral load of the SARS-CoV-2 positive sample. **Conclusion:** It was possible to develop a safe and easy to operate technology with low construction costs that can be used in healthcare environments with satisfactory results in the disinfection of microorganisms.
Keywords: Decontamination. Disinfection. Ultraviolet Rays. UV Light. NonIonizing Radiation.

RESUMO

Justificativa e Objetivos: Em hospitais, onde há alta circulação de microrganismos, tecnologias complementares são essenciais para melhorar a desinfecção. Este estudo teve como objetivo desenvolver uma tecnologia adaptada à nossa realidade, produzida e testada pelo nosso grupo de pesquisa, que seja segura e fácil de operar, com baixo custo de construção para que possa ser utilizada em ambientes de saúde com recursos limitados. **Métodos:** Após a investigação, lâmpadas de 55W, T8 - G13 - 909 mm com emissão de radiação ultravioleta a 254 nm foram escolhidas como fonte de UVC. O aplicativo "Torre UVC" foi criado usando o Android Studio IDE. Para verificar a eficiência do equipamento e determinar as doses a serem utilizadas, foram realizadas medições de potência através de radiômetro. Foi avaliada a eficiência da torre frente a alguns microrganismos clinicamente importantes. **Resultados:** A Torre UVC foi construída com uma estrutura de alumínio e 8 lâmpadas, permitindo a operação remota. O aplicativo foi projetado para uso fácil e intuitivo. Os testes de eficiência realizados com o radiômetro mostram que a diminuição da dose de radiação é exponencial à medida que objetos ou superfícies se afastam da torre. A torre inibiu o crescimento microbiano (bactérias e fungos) mesmo com baixas doses de radiação UVC (12 mJ/cm²) e reduziu a carga viral da amostra clínica positiva para SARS-CoV-2. **Conclusão:** Foi possível desenvolver uma tecnologia segura e de fácil operação, com baixo custo para que possa ser utilizada em ambientes de saúde, e com resultados satisfatórios na inativação de microrganismos.
Descritores: Descontaminação. Desinfecção. Raios ultravioleta. Luz UV. Radiação não ionizante.

RESUMEN

Justificación y Objetivos: En los hospitales, donde circulan muchos microorganismos, las tecnologías complementarias son clave para mejorar la desinfección. Este estudio tuvo como objetivo desarrollar una tecnología adaptada a nuestra realidad, que sea segura y fácil de operar, con bajo costo de construcción para que pueda ser utilizada en entornos de salud como los hospitales con recursos limitados. **Métodos:** Después de la investigación, se eligieron lámparas de 55W, T8 - G13 - 909 mm con emisión de radiación ultravioleta a 254 nm como fuente UVC. La aplicación "Torre UVC" se creó con el IDE de Android Studio. Para verificar la eficiencia de la torre UVC y determinar las dosis a utilizar, se tomaron medidas de potencia utilizando un radiómetro. Se evaluó la eficiencia de la torre frente a algunos microorganismos clínicamente importantes. **Resultados:** La Torre UVC fue construida con un marco de aluminio y 8 lámparas, lo que permite la operación remota. La aplicación fue diseñada para un uso fácil e intuitivo. Las pruebas de eficiencia realizadas con el radiómetro demuestran que la disminución de la dosis de radiación es exponencial a medida que los objetos o superficies se alejan de la torre. La torre inhibió eficazmente el crecimiento microbiano incluso con dosis bajas de radiación UVC (12 mJ/cm²) y redujo la carga viral de la muestra clínica positiva para SARS-CoV-2. **Conclusión:** Se desarrolló una tecnología segura, fácil de usar y de bajo costo, con resultados satisfactorios en la desinfección de microorganismos, adecuada para ser implementada en ambientes sanitarios.
Palabras Clave: Descontaminación. Desinfección. Rayos Ultravioleta. Luz UV. Radiación No Ionizante.

Aline Teichmann, Demis Pessatto Faqui, Eduardo Dullius, Gilson Augusto Helfer, Nayanna Dias Bierhals, Maitê Souza Magdalena, Andréia Rosane de Moura Valim, Jane Dagmar Pollo Renner, Janine Koepp, Mari Ângela Gaedke, Adilson Ben da Costa

INTRODUCTION

The coronavirus disease 2019 (Covid-19) pandemic brought the need for comprehensive methods of decontamination of environments, while exposing the lack of human and technological resources available on a large scale. Rigorous measures are necessary to optimize the quality of care provided to infected patients and reduce the risk of pathogen transmission to other patients or healthcare operators.[1] SARS-CoV-2 is highly contagious, many people are generally susceptible, and many healthcare workers have been infected during patient care.[2] This virus is mostly transmitted through infected respiratory droplets and contact with the infected person. Exposure to high concentrations of the virus in a confined space for a long period of time increases the risk of aerosol transmission.[3]

Hospital-acquired infections are a challenging health problem worldwide, as inanimate surfaces and equipment can be contaminated with microorganisms. This facilitates their sporadic transmission and even outbreaks, since healthcare workers not only contaminate their hands after direct contact with patients, but also after touching inanimate surfaces and equipment.[4]

Appropriate protocols have to be used in hospitals for the decontamination of their space to reduce infection and in-hospital transmission. The aerosol deposition of viruses on surfaces and their resuspension is a potential transmission pathway and effective sanitization is critical in minimizing aerosol transmission of pathogens. As some traditional protocols are insufficient to protect vulnerable patients from serious and life-threatening infections, new strategies for decontaminating hospital environments are crucial for reducing the spread of infections. The use of complementary technologies is indicated to supplement traditional methods and improve desired levels of surface decontamination. Regardless of the type of surface, the objective of a cleaning and sanitizing procedure is to reduce contamination to an acceptable level of safety by applying operating methods for removal of pathogens from surfaces.[5]

Several novel approaches have been developed for microorganisms' inactivation in recent years. Among these is the ultra-violet irradiation (UVC), which is able to destroy a broad range of microbes, including bacteria, fungi and viruses.[6] The ability of UVC rays to destroy microbes is largely attributed to their impact on DNA or RNA.[7] Given its advantages - including broader virus inactivation, manageable costs, and practical applicability – UV radiation can be used to supplement existing techniques.[6]

In this context, the development of a UVC radiation system is of great help to professionals directly involved with hospital environments. Thus, hygiene professionals will have an easy-to-install equipment that allows a quick and efficient disinfection process, being a supplementary technique especially in situations such as the high-contagion Covid-19 pandemic. The main objective of this study was to design, develop and evaluate the effectiveness of a UVC disinfection tower, with a focus on ensuring its performance and cost-effectiveness, so that it can be used in healthcare environments such as hospitals with limited resources.

METHODS

Study design and setting

The methodology adopted in this study was the Design Science Research, which focuses on developing and testing innovative solutions. As the development of the equipment does not involve practices with human beings, approval from the Research Ethics Committee was not necessary, in accordance with current regulations. We formulate the following hypotheses: (1) The developed technology will provide an effective means of disinfection in hospital environments; (2) The technology will be feasible for implementation in resource-limited healthcare settings. Key variables include the cost of construction and the effectiveness of disinfection.

The study was developed between August 2020 and July 2022, at the Universidade de Santa Cruz do Sul (UNISC). The tower was built in the university's prototyping laboratory, as was the smartphone app. The irradiation test, antimicrobial test, disinfection evaluation of PFF-2 masks and antiviral test were carried out in the university's technical laboratory (TecnoUNISC). The first year of the study was dedicated to setting up the equipment and carrying out the irradiation tests. In the second year, practical disinfection tests were carried out.

Definitions of requirements and material selection

Firstly, it was to evaluate the different types of UVC radiation sources available in the Brazilian market. The main technical characteristics for the use of UVC radiation sources were listed based on the documentation provided by the suppliers and information available in the literature. Commercial and market availability issues were also considered, as economic viability is one of the commitment conditions of the study, allowing production scalability of the final products developed through this research. The production of a technology that can be replicated will effectively contribute to the fight against Covid-19 and other infectious diseases. This step was time consuming, but essential for the elaboration of strategies for the development of this disinfection system and correct acquisition of the main components.

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Therefore, after carrying out an intense market research in search of models of UVC radiation sources with the objective of identifying the best relationship between wavelength, useful life, geometry, manufacturing material, power, current and voltage, lamps of 55W, T8 - G13 – 909 mm with emission of ultraviolet radiation at 254 nm were selected. This wavelength is considered the most effective for the maximum germicidal activity.[6] Thus, the disinfection tower project was dimensioned for the use of this source of UVC radiation, and 8 lamps in total were designated for the construction of the tower.

According to UV lamps manufacturers (Osram®), the radiation intensity decreases exponentially with increasing distance from the source. Another important factor is the positioning of the disinfection tower in a way to avoid shadows, since these regions may be exposed to lower-than-expected UVC doses, depending on the characteristics of the disinfection environment (surgery room, or exam room).[8] When the occurrence of shadows is unavoidable, the disinfection process must be carried out in more than one step, alternating the positioning of the tower to cover as much surface as possible. As a result, the tower was made with 8 lamps to minimize the occurrence of shadows, allowing irradiation at an angle of 360°.

App development to turn on the UVC tower

The "Torre UVC" app was created for Android® smartphones using the Android Studio IDE. An external module has been seamlessly integrated into the app to enable Bluetooth® connectivity and operations. An Android® device, such as a cell phone or tablet, with a minimum operating system version of 4.4 is necessary to use this app.

Study protocol

Several experimental procedures have been conducted to evaluate the effectiveness of the UVC tower irradiation in decontaminating pathogens, including bacteria, fungi, viruses, and commonly used healthcare materials such as PFF-2 masks. The following sections summarize the tests performed to validate the effectiveness of the device.

Irradiation test

Power measurements (mW/cm²) were taken using the Portable Radiometer 7.1 (Gen UV) with a detachable LA9 sensor, detection range between 220~280nm, with a calibration peak at 254 nm for assessment of the efficiency of the UVC tower and definition of the dosages to be used. The measurements were taken at 12 different distances ranging from 10 cm to 200 cm, and the dosage (mJ/cm²) was subsequently calculated using the exposure time.

Antimicrobial test

Staphylococcus aureus (ATCC 29213) and *Escherichia coli* (ATCC 25922) were used to test the decontamination efficacy of the tower by UVC radiation. Bacteria species were inoculated in 3 mL of BHI medium (Brain Heart Infusion) at 37°C for 24 hours, then seeded in Mueller Hinton agar and placed at 37°C for 24 hours. Cultures were prepared from a 0.5-scale suspension of MacFarland diluted in a 0.9% NaCl solution, and seeded 100 µL with sterile swab on plates containing 25 mL of Mueller Hinton agar.

Candida glabrata (ATCC) was used to test the effectiveness of UVC decontamination of the tower. The fungus species was inoculated in 3 mL of BHI medium at 37°C for 24 hours. The *C. glabrata* was seeded in Sabouraud agar and placed at 37°C for 48 hours. Cultures were prepared from a 0.5-scale suspension of MacFarland diluted in a 0.9% NaCl solution, and 100 µL were seeded with sterile swab on plates containing 25 mL of Sabouraud agar. The strains labelled ATCC were obtained from the American Type Culture Collection (Manassas, VA, USA).

The plates positioned at different distances from the tower (20, 50, 70, 100 and 200 cm) were exposed to UVC radiation for 5 minutes. Then, the plates were exposed to 37°C for 24 hours for bacteria species and 48 hours for fungus for subsequent colony counting. All tests were done in duplicates and the control had no exposure.

Disinfection evaluation of PFF-2 masks

The disinfection efficiency of PFF-2 masks (Life Protect®), was evaluated using a mask previously used for 12 hours. Briefly, the PFF-2 mask was initially placed in contact with Replicate Organism Direct Agar Contact plates (RODAC) (Laborclin®) on both sides (inside and outside) for 5 seconds. Subsequently, the mask was exposed to UVC radiation on both sides for 5 minutes, positioned at a distance of 20 cm (dose 2096 mJ/cm²) from the UVC tower. After exposure, the mask was again placed in contact with RODAC plates on both sides for 5 seconds. The plates were exposed to 37°C for 24 hours for subsequent colony counting.

Antiviral test

Samples with a positive result in real-time polymerase chain reaction (RT-PCR) for SARS-CoV-2 were used to evaluate the effectiveness of UVC radiation in a clinical nasopharyngeal swab sample for SARS-CoV-2. The samples placed in Petri dishes and positioned at different distances from the tower (70 cm, 100 cm and 200 cm) were exposed to UVC radiation for 5 minutes. Subsequently, automated viral RNA extraction of the samples was performed in the Extracta 32 equipment using the MagMAX™ CORE Nucleic Acid Purification Kit, and reverse transcriptase followed by RT-PCR was performed using the AgPath-ID™ One-Step RT-PCR

Reagents kit per manufacturer's instructions. The samples were amplified using the QuantStudio 3 to identify the human ribonuclease P gene (RNaseP) as an internal control and the SARS-CoV-2 virus envelope (E) gene for viral load detection. The number of Ct (Cycle Threshold) was evaluated in the analyzes, and when Ct was above 35, samples were considered positive. All tests were done in duplicates with a control without exposure.

RESULTS

UVC disinfection tower

The tower was built entirely with structural aluminum profile (40 x 40 mm), industrial standard. The bottom base plate is 8 mm thick carbon steel with epoxy powder coating, and the closing plates are 2 mm thick stainless-steel. The central tube, the handle, support, and assembly parts are also made of stainless-steel. The pieces were cut on a Computer Numerical Control (CNC) laser cutting machine and folded on a CNC bending machine. Some stainless-steel parts are welded, such as the central tube flanges and the upper disc (Figure 1B).

The UVC tower was designed for single-phase 220 Vac power supply, controlled by a knob type switch for manual activation. As a safety measure, a residual current circuit breaker has been included to protect against electric shocks. A 220 Vac LED indicates the tower is energized and ready for use (Figure 1C).

The activation of the lamps passes through the control system, which is carried out through a standard electronic board, from the ESP32 family. This board has Wi-Fi and Bluetooth® communication, in addition to digital inputs and outputs and analog inputs. The digital outputs were used to activate transistors, which activate relays, and then two sets of four reactors, responsible for activating the lamps. The 12 Vdc source is reduced to 5 Vdc to power the ESP32 board. The interface relays are 12 Vdc. The control circuit was mounted on a standard commercial board.

Finally, identification stickers and safety signs for the Tower were produced, as well as a protective cover for the lamps and a user manual for the UVC tower (Figure 1A). The manual was developed in an accessible language with operating instructions for the equipment and the respective application, in addition to safety procedures.

Figure 1. UVC tower and smartphone app.

App "*Torre UVC*"

The app Torre UVC was developed to allow the remote activation of disinfection lamps. It presents a set of guidelines to users for the correct use and guarantee of maximum disinfection efficiency without offering risks.

The app's home screen presents a message for the user to enable Bluetooth® in the mobile device that is operating system settings. Once Bluetooth® is activated, the user must click on the Bluetooth® icon (Bluetooth® symbol in white color) to start locating the tower. Thus, a new screen will open, and all Bluetooth® devices located within a range of up to 10 meters (without obstacles) will be scanned. The user must select the UVC tower from the list of available devices. If no device appears, the button at the bottom of the screen restarts the search.

Once the UVC tower is located and a valid connection is established, the color of the Bluetooth® symbol changes to light blue. The application screen will show the guidance to position the Tower in the first disinfection region, leave the room, and turn on the lamps (Figure 1D).

By pressing the button on the previous screen, the user will turn on the tower lamps for 6-minute periods, and the timer can be monitored via the application (Figure 1E). At the end of the disinfection time, the lamps will turn off and the tower will be available for a new disinfection process by simply repositioning it in another region (second region) and clicking on the icon to turn on the lamps.

Efficiency tests

The measurements taken with the radiometer confirmed that the UVC tower was operating efficiently. The dosage calculations were performed under real operating conditions of the UVC tower. The decay of radiation dosage is exponential, as objects or surfaces move away from the tower. These results allowed us to

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identify that the radiation dosage at distances greater than 2 meters is less than 1% of the radiation determined at 20 cm (Figure 2).
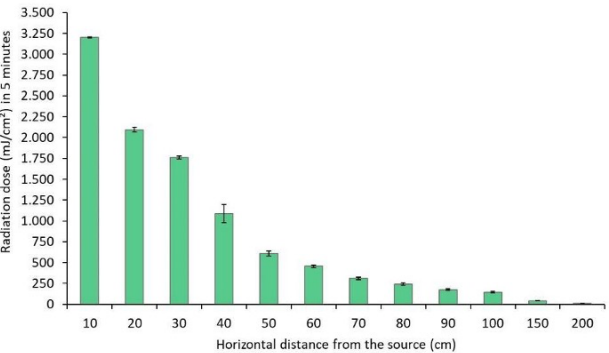
Figure 2. Exponential decay of UVC radiation with distance from the tower.

This work evaluated some of the main microorganisms of clinical importance, which are frequently associated with healthcare-associated infections and can be commonly found on contaminated surfaces and objects. In the three species tested, all control plates (not exposed to ultraviolet light) showed microbial growth > 100,000 CFU/mL (Table 1).

When comparing the two bacteria tested, we observed that E. coli (gram-negative) has a total inhibition with the dose of 146 mJ/cm² and only 2 CFU with the dose of 12 mJ/cm². S. aureus (gram-positive) has total growth inhibition with the dose of 312 mJ/cm² and only 2 CFU and 4 CFU with the dose of 146 mJ/cm² and 12 mJ/cm² respectively. Regarding C. glabrata, a species fungus responsible for invasive candidiasis, the total inhibition of growth is observed with the dose of 146 mJ/cm² and only 2 CFU with the dose of 12 mJ/cm² (Table 1).

Disinfection against microorganisms

Table 1. Results of microbial growth as a function of distance and dose of exposure to UV radiation.

Distance (cm)	0	20	50	70	100	200
Dose (mJ/cm²)	0	2096	611	312	146	12
S. aureus, CFU/mL	> 100.000	-	-	-	2	4
E. coli, CFU/mL	> 100.000	-	-	-	-	2
C. glabrata, CFU/mL	> 100.000	-	-	-	-	2

In the disinfection of PFF-2 masks, after counting the colonies, the RODAC plate placed in contact with the inside of the mask before exposure to UVC radiation showed growth of 36 CFUs (Figure 3A). The plate RODAC placed in contact with outside of the mask showed growth of 9 CFUs (Figure 3B), in addition to the growth of a biofilm on the edge of the plate. After exposure to UVC radiation, the plate placed in contact with the inside of the mask (Figure 3C) did not have CFU growth, while the plate placed in contact with the outside of the mask showed growth of 1 CFU (Figure 3D).
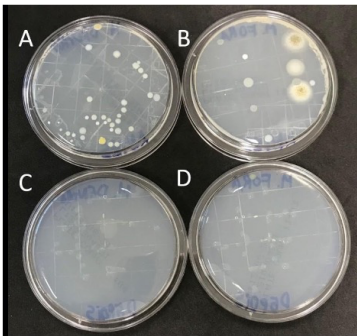
Figure 3. Effect of UVC radiation on the disinfection of PFF-2 masks.

The results show the Ct values of the E gene increase as the UV radiation dosage increases, indicating that UVC radiation is able to decrease the viral load of the tested samples (Figure 4).
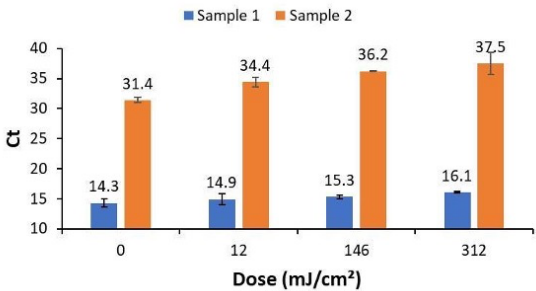
Figure 4. Effect of UVC radiation on the viral load of the samples.

Construction cost of the UVC disinfection tower

The construction costs of the UVC disinfection tower were low, considering expenses related to materials, labor, and administrative costs. All values were calculated based on prices practiced in Brazil and converted from BRL to USD (Table 2). The total equipment cost of approximately 3,300 USD is perfectly accessible to the reality of Brazilian hospitals, allowing for the widespread adoption of this indoor disinfection technology.

Furthermore, this cost is at least five times cheaper than other UVC radiation disinfection equipment available in the market.

Table 2. Construction cost values for the final version of the UVC disinfection tower.

Cost elements	Unitary value USD	Quantity	Total USD
UVC Radiation Lamp 55W, T8 - G13, 26mm	40	8	320.00
Electronic ballast 55W	30	8	240.00
Stainless steel sheets (8 mm and 2 mm), CNC laser cut	600	1	600.00
Structural aluminum profile (40 x 40mm), 150 mm	40	2	80.00
Android smartphone	160	1	160.00
Mechanical components	80	1	80.00
Electrical components	80	1	80.00
Labor			940.00
Administrative expenses			800.00
			3,300.00

DISCUSSION

Bacteria are classified into gram-positive and gram-negative according to the composition of the cell membrane structure. Gram-negative bacteria have an additional outer membrane that is not present in their gram-positive counterpart; the latter instead hold a thicker peptidoglycan layer.[9] This reinforces the findings of this study, which found greater inhibition of *E. coli*, which has a thin layer of peptidoglycan, compared to *S. aureus*, which has a thicker wall of peptidoglycan, making it difficult for UVC light to reach the genetic material.

As far as action against fungi is concerned, the results found in this study are satisfactory for a species that has various virulence factors and resistance mechanisms to antifungals that has allowed this yeast to become one of the most frequent agents of candidiasis.[10]

Other works developed with UVC radiation disinfection devices have also obtained satisfactory results. A study showed that ultraviolet radiation applied for using the UVC equipment was effective in disinfecting slides inoculated with four microorganisms involved in healthcare-associated infections such as *Pseudomonas aeruginosa*, *E. coli*, *S. aureus* and *Candida. albicans*. UVC achieved a high reduction in the microbial burden when treating discs of several materials usually present in objects of medical practice, and/or daily use (borosilicate, polycarbonate, polyurethane, silicone, Teflon and titanium) in both conditions, achieving a reduction higher than 99.95%.[11] Furthermore, another study reported 100% microbial inactivation, encompassing *E. coli*, *P. aeruginosa*, *Salmonella enterica typhimurium*, *S. aureus*, and *Staphylococcus epidermidis*, with no observed bacterial growth following UVC irradiation. Additionally, a reduction of approximately 4 logs was noted for the yeast *Candida albicans*.[12]

The number of Ct (Cycle Threshold) was used to evaluate the effectiveness of the UVC tower against SARS-CoV-2 positive clinical samples. The Ct value corresponds the number of PCR cycles needed to produce a detectable signal, it is the point of intersection between the amplification curve and the threshold line, so the Ct can serve as a relative measure of target concentration, since its value is inversely proportional to the amount of genetic material. The lower the Ct value, the fewer PCR cycles needed to produce a positive result, the greater the quantity of viral nucleic acid in the sample tested, and the greater the quantity of viral nucleic acid (the viral load) in the sample; and on the contrary, high Ct values may mean low target concentrations or even absence.[13]

In research that related Ct values and SARS-CoV-2 viral load, the mean Ct values in nasal and throat swabs obtained from patients with severe cases were lower than the values in swabs obtained from patients with mild-to-moderate cases.[14,15] Ct values also were used to determine dynamics of SARS-CoV-2 viral load with the aim to guide the isolation period for Covid-19 patients.[16] Using the RT-PCR technique, it is not possible to affirm that the virus has been eliminated, but rather that there has been a decrease in the genetic material and consequently damage to the virus RNA.

However, the use of UVC irradiation is well described for the inactivation of various viruses. A study evaluated the efficiency of UVC irradiation with a wavelength between 207-222 nm on 2 strains of human coronavirus (alpha HCoV-229E and beta HCoV-OC43) and found that this method was effective in eliminating viral particles, inactivating 99.9% of the aerosolized coronavirus.[17] Note that since all human coronaviruses have similar genomic sizes, UVC light is expected to show similar inactivation efficiency against other human coronaviruses, including SARS-CoV-2, the causative agent of Covid-19, present in the environment. Another study evaluated the effect of

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UVC irradiation on an experimental model of fomite disinfection. A lower dose of UVC (10.25-23.71 mJ/cm²) was sufficient to reduce the viral titer by >99.99%. In particular, plastic seems to be the most refractory material to UVC disinfection, followed by stainless steel and glass, with the latter showing the best adherence to treatment.[18]

UVC irradiation can be a fast and effective means of disinfecting indoor spaces. A paper describes an evidence-based approach to optimizing infection control and operating room management during the coronavirus pandemic. Improvement strategies to mitigate residual environmental contamination involve a combination of deep cleaning with surface disinfectants and UVC light in the routine cleaning of operating rooms.[19]

The high cost of equipment and the limited accessibility to available technologies are the main obstacles faced in the use of UVC light as a complementary alternative to the daily practice of health services.[20] The development of more accessible alternatives becomes a relevant contribution to the area, favoring the democratization of the use of this technology and making it viable for a wider range of users and institutions. The proposal for a low-cost UVC irradiation tower with a simplified and efficient design emerges as a solution to overcome financial barriers and facilitate the adoption of this technology.

Although the study on the UVC disinfection tower shows promising results, there are some limitations that can be better investigated in future studies. One of these limitations is the restriction of the spectrum of pathogens analyzed. For a more representative evaluation of the efficacy of UVC disinfection, we suggest further studies with an expansion of the variety of pathogens, including antibiotic-resistant strains and mycobacteria as the final step in the validation of the device to complement the disinfection routine in health services, enabling performance reports against these agents.

In addition, the study was conducted under controlled laboratory conditions, which may not accurately reflect the challenges encountered in real clinical settings. In hospital settings, variables such as temperature and humidity variations, as well as physical obstacles (such as furniture and equipment), can significantly interfere with the effectiveness of UVC disinfection. Future studies should replicate real-world clinical conditions while taking these variables into account to evaluate the technology's practical applicability in scenarios of daily use.

The results presented in this work demonstrated satisfactory performance for the UVC tower in the disinfection of pathogenic microorganisms. In addition, the developed device has a low cost, using resistant and easy to clean materials. The UVC tower was designed with wheels and handles to facilitate movement and can be manipulated by just one operator. For safety reasons, lights indicating that the tower is energized and ready for use, as well as a sound signal when it is in operation, were included. The tower is operated through the "Torre UVC" application, developed in this project, which ensures the safety of the professional who can turn on the equipment from outside the room, without being exposed to UVC radiation. It is possible to make this product scalable, as the entire development was carried out by the team, and it is possible to further improve the cost benefit ratio and access to this equipment. Considering this, we can conclude that UVC irradiation could be a quick and effective means for the disinfection of indoor spaces, and could be helpful in the setting of irradiation-based sterilization.

Finally, it is important to highlight the social impact of this study, as a total of three units of the UVC tower were built, all of which were donated to the Hospital Santa Cruz, a philanthropic hospital in the municipality of Santa Cruz do Sul, Brazil.

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DEVELOPMENT AND EVALUATION OF EQUIPMENT FOR DISINFECTION BY ULTRAVIOLET RADIATION IN HEALTHCARE ENVIRONMENTS

Aline Teichmann, Demis Pessatto Faqui, Eduardo Dullius, Gilson Augusto Helfer, Nayanna Dias Bierhals, Maitê Souza Magdalena, Andréia Rosane de Moura Valim, Jane Dagmar Pollo Renner, Janine Koepp, Mari Ângela Gaedke, Adilson Ben da Costa

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AUTHORS' CONTRIBUTIONS

Aline Teichmann contributed to the bibliographic research, execution of the project, writing of the abstract, introduction, methodology, discussion, interpretation and description of the results, preparation of tables, conclusions, review and statistics. **Demis Pesatto Faqui** contributed to the literature search, project execution, abstract writing, introduction, methodology, discussion, interpretation and description of results, conclusions, review and statistics. **Eduardo Dullius** contributed to the bibliographic research, project execution, abstract writing, methodology, interpretation of results, conclusions, review and statistics. **Gilson Augusto Helfer** contributed to the execution of the project, development and testing of the application, analysis of results, writing of the abstract, review and statistics. **Nayanna Dias Bierhals** contributed to the execution of the project, analysis of results and review. **Maitê Souza Magdalena** contributed to the bibliographic research and review. **Andréia Rosane de Moura Valim** contributed to the execution of the project, analysis of results and review. **Jane Dagmar Pollo Renner** contributed to the execution of the project, analysis of results and review. **Janine Koepp** contributed to the literature research and review. **Mari Ângela Gaedke** contributed to the execution of the project, analysis of results and review. **Adilson Ben da Costa** contributed to the project administration, procurement of inputs, project execution, abstract writing, review and conclusions.

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

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RECI

REVISTA DE EPIDEMIOLOGIA E CONTROLE DE INFECÇÃO

Original Article

Spatio-temporal analysis of congenital syphilis in Rio Grande do Norte, Brazil, from 2008 to 2022

Análise espaço-temporal da sífilis congênita no Rio Grande do Norte, Brasil, de 2008 a 2022
Análisis espacio-temporal de la sífilis congénita en Rio Grande do Norte, Brasil, de 2008 a 2022

Corresponding author:
E-mail: ketyllemcosta@gmail.com
Address: Joaquim Patrício Avenue, 1232, Pium, Parnamirim, Rio Grande do Norte, Brazil.

Dhyanine Morais de Lima Raimundo[1] (ID)
Rita de Cássia Azevedo Constantino[1] (ID)
Richardson Augusto Rosendo da Silva[1] (ID)
Angelo Maximo Soares de Araujo Filho[1] (ID)
Ketyllem Tayanne da Silva Costa[1] (ID)
Harlon França de Menezes[1] (ID)
Ana Elza Oliveira de Mendonça[1] (ID)

[1]Federal University of Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil.

ABSTRACT

Background and Objectives: Rio Grande do Norte state is experiencing an epidemic of congenital syphilis cases, with an average incidence above the national rate. In this context, this study aims to identify the Health Regions of Rio Grande do Norte most affected by congenital syphilis through spatial analysis and, from there, define the temporal trend of infection in these areas. **Methods:** This is an ecological study using secondary data, using spatial analysis techniques, and temporal trends of congenital syphilis in Rio Grande do Norte from 2008 to 2022. **Results:** The incidence of congenital syphilis in 2022 reached 525 new cases in the state, approximately 100 fewer cases compared to 2021. Of these, the 7th health region had a substantially higher average than the other regions. The 3rd health region has the highest average number of congenital syphilis cases per 1,000 live births in the territory, with 25.51 cases. Regarding the temporal trend, the most significant increase is expected in the 8th, 3rd, and 7th health regions, respectively. **Conclusion:** A greater incidence of congenital syphilis exposure was found in the 1st, 3rd, 7th, and 8th health regions. Given the data studied, an increase in these health regions is expected, which may result in service overload. Therefore, appropriate management of infected pregnant women should be reinforced in Primary Care, as well as investment in prevention and health education actions.
Keywords: *Nursing. Congenital Syphilis. Vertical Transmission of Infectious Diseases. Spatial Analysis. Time Series Studies.*

RESUMO

Justificativa e Objetivos: O Rio Grande do Norte vive uma epidemia de casos de sífilis congênita, com incidência média acima da taxa brasileira. Nesse contexto, o estudo tem como objetivo identificar quais as Regiões de Saúde do Rio Grande do Norte mais acometidas pela Sífilis Congênita por meio de análise espacial e, a partir disso, definir a tendência temporal da infecção nessas áreas. **Métodos:** Trata-se de um estudo ecológico, com uso de dados secundários, com técnicas de análise espacial e tendência temporal da sífilis congênita no Rio Grande do Norte no período entre 2008 e 2022. **Resultados:** A incidência da sífilis congênita no ano de 2022 atingiu 525 novos casos no estado, cerca de 100 casos a menos quando comparado ao ano de 2021. Desses, a 7ª região de saúde obteve uma média substancialmente maior que a das outras regiões. A 3ª região de saúde possui a maior média de sífilis congênita por 1000 nascidos vivos do território, com 25,51 casos. No que se refere a tendência temporal, o aumento mais expressivo é esperado na 8ª, 3ª e 7ª regiões de saúde, respectivamente. **Conclusão:** Constatou-se um maior acometimento pela exposição à sífilis congênita nas 1ª, 3ª, 7ª e 8ª regiões de saúde. Diante dos dados estudados, espera- se um aumento nas regiões de saúde que podem resultar em uma sobrecarga no serviço. Dessa maneira, o manejo adequado das gestantes infectadas deve ser reforçado na Atenção Básica, assim como o investimento em ações de prevenção e educação em saúde.
Descritores: *Enfermagem. Sífilis Congênita. Transmissão Vertical de Doenças Infecciosas. Análise Espacial. Estudos de Séries Temporais.*

RESUMEN

Justificación y Objetivos: Rio Grande do Norte atraviesa una epidemia de sífilis congénita, con una incidencia media superior a la tasa nacional. En este contexto, el objetivo del estudio fue identificar cuáles Regiones de Salud de Rio Grande do Norte han sido más afectadas por Sífilis Congénita a través del análisis espacial y, con base en esto, definir la tendencia temporal de la infección en esas áreas. **Métodos:** Se realizó un estudio ecológico con uso datos secundarios, empleando técnicas de análisis espacial y análisis de tendencia temporal de la sífilis congénita en Rio Grande do Norte desde 2008 hasta 2022. **Resultados:** En 2022 la sífilis congénita registró525 nuevos casos en el estado, aproximadamente 100 casos menos en comparación con 2021. De estos, la 7ª región de salud tuvo un promedio sustancialmente mayor que las otras regiones. La 3ª Región de Salud mostró la mayor media de sífilis congénita por 1,000 nacidos vivos, con 25.51 casos. En cuanto a la tendencia temporal, se espera que el aumento más significativo ocurra en las 8ª, 3ª y 7ª regiones de salud, respectivamente. **Conclusión:** Se constató un mayor impacto de la sífilis congénita en las 1ª, 3ª, 7ª y 8ª regiones de salud. Dada la información estudiada, se anticipa un aumento en estas regiones de salud, lo que podría resultar en sobrecarga de los servicios. Por lo tanto, se refuerza la necesidad de un manejo adecuado de las gestantes infectadas en la Atención Primaria, así como invertir en acciones de prevención y educación en salud.
Palabras Clave: *Enfermería. Sífilis Congénita. Transmisión Vertical de Enfermedades Infecciosas. Análisis Espacial. Estudios de Series Temporales.*

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Dhyanine Morais de Lima Raimundo, Rita de Cássia Azevedo Constantino, Richardson Augusto Rosendo da Silva, Angelo Maximo Soares de Araujo Filho, Ketyllem Tayanne da Silva Costa, Harlon França de Menezes, Ana Elza Oliveira de Mendonça

INTRODUCTION

Syphilis Syphilis is a systemic infection caused by *Treponema pallidum* (*T. pallidum*), transmitted primarily through vertical and sexual routes.[1] The ease of transmission and the complications associated with its chronic progression pose a persistent public health challenge, as a high incidence of the infection is still observed in the Brazilian population despite the availability of preventive measures.[2] Diagnosis during pregnancy increases the risk of spontaneous abortion, prematurity, congenital malformations, and neonatal death.[1]

Congenital syphilis (CS) results from vertical or transplacental transmission of *T. pallidum* from an infected pregnant woman who has not received adequate treatment to the fetus. Among the possible outcomes of CS, it is estimated that at least 11% of pregnancies result in term stillbirths, while approximately 20% of exposed newborns present signs suggestive of infection.[1]

The elimination of vertical transmission of syphilis is a global priority defined by the World Health Organization (WHO) and the Pan American Health Organization (PAHO). However, the increasing number of cases remains constant and highly challenging.[3] In 2016, the WHO reported that CS surpassed half a million notifications worldwide, resulting in 200,000 deaths, including stillbirths and neonatal deaths.[4]

In Brazil, syphilis is a notifiable disease under the Information System for Notifiable Diseases (SINAN), as established by Ordinance No. 542 of December 22, 1986, which mandated the reporting of CS in the country, and is currently regulated by Ordinance No. 264 of February 17, 2020.[5] Despite the reduction in birth rates, vertical transmission of CS remains high.[6]

According to the Epidemiological Bulletin published by the Ministry of Health (MS) in October 2023, 26,468 CS cases and 200 related deaths were recorded in 2022, representing a 16% increase compared with 2019. Of this total, 27.6% of diagnoses occurred in the Northeast, the second most affected region after the Southeast. In the state of Rio Grande do Norte (RN), the CS detection rate in the capital, Natal, exceeds the national average, approaching 50 cases per 1,000 live births.[7]

Given the current syphilis epidemic in Brazil, particularly in RN, it is necessary to identify the areas most affected by the infection and to understand its future incidence trends in order to support public health policies for prevention and control. Furthermore, spatial analysis is an efficient and relevant method for epidemiological surveillance, as it enables the development of targeted strategies for the most vulnerable territories.

Accordingly, the objective of this study is to identify the Health Regions of Rio Grande do Norte most affected by congenital syphilis through spatial analysis and, subsequently, to examine the temporal trends of infection in these areas.

METHODS

Study design

This is an ecological study based on secondary data, employing spatial analysis and temporal trend techniques to evaluate outcomes related to congenital syphilis (CS) in Rio Grande do Norte (RN) between 2008 and 2022. During this period, 70,213 births of children diagnosed with CS were reported in the state. According to the most recent census conducted by the Brazilian Institute of Geography and Statistics (IBGE) in 2022, the population of RN was estimated at 3,302,729 inhabitants.[8]

The territorial division of the state follows the Master Regionalization Plan (PDR/RN), which aims to expand access to referral and high-complexity health services within regional boundaries. RN is composed of 167 municipalities, organized into two health macro-regions and eight Health Regions (HR). Macro-region I, headquartered in the capital city, includes the 1st, 3rd, 4th, 5th, and 7th HRs, while Macro-region II comprises the 2nd, 6th, and 8th HRs.

In October 2023, the reported cases were obtained from the Information System for Notifiable Diseases (SINAN), through the Department of Informatics of the Unified Health System (DATASUS). SINAN is continuously updated by states and municipalities with information on conditions listed as nationally notifiable diseases, allowing for ongoing monitoring of the epidemiological situation in the country.

Study variables

The dependent variables were: absolute number of live births, absolute number of CS cases by place of residence, and average incidence rate of the disease from 2008 to 2022. The independent variables were Health Region and year of diagnosis.

Data analysis

Data were organized and tabulated in Microsoft Excel spreadsheets. For spatial analysis, a thematic map of CS incidence by Health Region in RN was developed. Crude rates and smoothed rates using simple moving averages were calculated with the open-source software TerraView 4.2.2, considering 1,000 live births as the constant. Purely spatial analysis was performed using SaTScan 9.6, and all maps were generated with QGIS 2.4.17.

Trend analysis of detection rates was performed using a Poisson regression model with the Joinpoint Regression Program, version 4.7.0.0, applying the following parameters: no geographical overlap of

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clusters, maximum cluster size of 50% of the exposed population, circular clusters, and 999 replications.[9] Joinpoint is widely used in trend analyses due to its accessible interface, free availability, and methodological robustness, although it has limitations, such as only accepting aggregated data with a normal distribution.

Ethical considerations

As this study was based on secondary data publicly available from DATASUS, it complied with the principles of Resolution No. 466/2012. Therefore, approval by the Research Ethics Committee of the Federal University of Rio Grande do Norte (CEP/UFRN) was waived.[10]

RESULTS

In 2008, the total number of live births in Rio Grande do Norte was 50,246 children. Since then, the state has shown a decreasing trend in four of the eight RS, with 40,542 births recorded in 2022 (Figure 1).
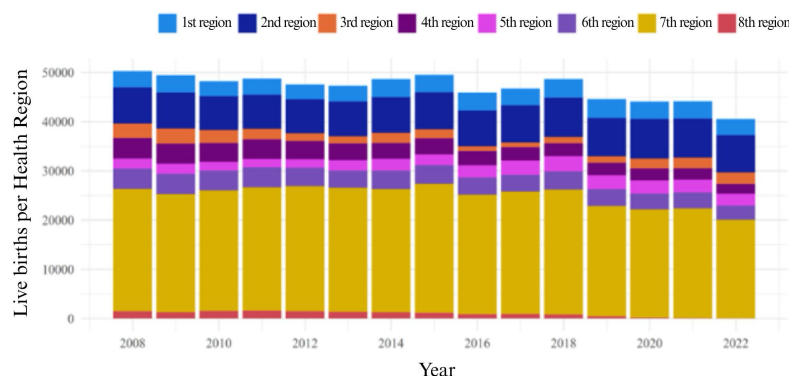
Figure 1. Live births per Health Region in Rio Grande do Norte, from 2008 to 2022. Rio Grande do Norte, 2023.

Despite the observed decline, the 7th Health Region (HR) maintained the highest absolute number of live births. Conversely, the 4th HR experienced a substantial decrease, with an approximate 50% reduction over the period, corresponding to 2,147 fewer births.

Regarding the incidence of congenital syphilis (CS) across the health regions, the 7th HR exhibited the highest rates, with a consistent upward trend throughout the years analyzed. Similar patterns were identified in the 1st, 2nd, 4th, and 8th HRs, which also demonstrated a gradual increase in reported cases. In contrast, the 3rd HR showed a decline in incidence during the last three years evaluated (2020–2022), while the 5th HR presented a significant reduction following a peak in 2020 (Figure 2).

In 2022, a total of 525 new cases of CS were reported in the state, approximately 100 fewer than in 2021 (Figure 3). Of this total, the 3rd Health Region (HR) accounted for 322 cases, exhibiting a markedly higher average rate than the other regions, at 25.51 cases per 1,000 live births. The lowest average rates were observed in the 6th, 4th, and 2nd HRs, with 1.04, 2.15, and 3.46 cases per 1,000 live births, respectively.
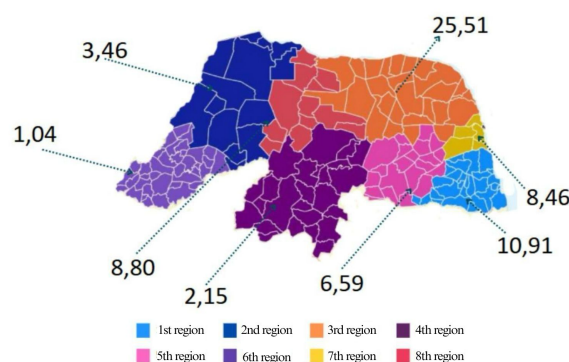
Figure 3. Average incidence of congenital syphilis cases per 1,000 live births in Rio Grande do Norte, from 2008 to 2022. Rio Grande do Norte, 2023.

Although the 3rd HR accounts for the fourth largest share of the population in Rio Grande do Norte, it maintained the highest average number of CS cases during the study period, followed by the 1st HR, with 10.91 cases per 1,000 live births. In 2016, the 3rd HR reached an alarming average of 67.91 cases per 1,000 live births, followed by a gradual decline in subsequent

Figure 2. Incidence of Congenital Syphilis Cases in Newborns per 1,000 Live Births, 2008 to 2022. Rio Grande do Norte, 2023.

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years and a sharp decrease during the Covid-19 pandemic.

Forecasts suggest that, starting in 2024, the 8th HR will surpass the 3rd HR, reaching the highest projected average of CS cases, estimated at 175.58 per 1,000 live births. By 2026, this figure is expected to rise to 245.19 cases per 1,000 live births, with a downward trend anticipated from 2027 onward (Figure 4h).
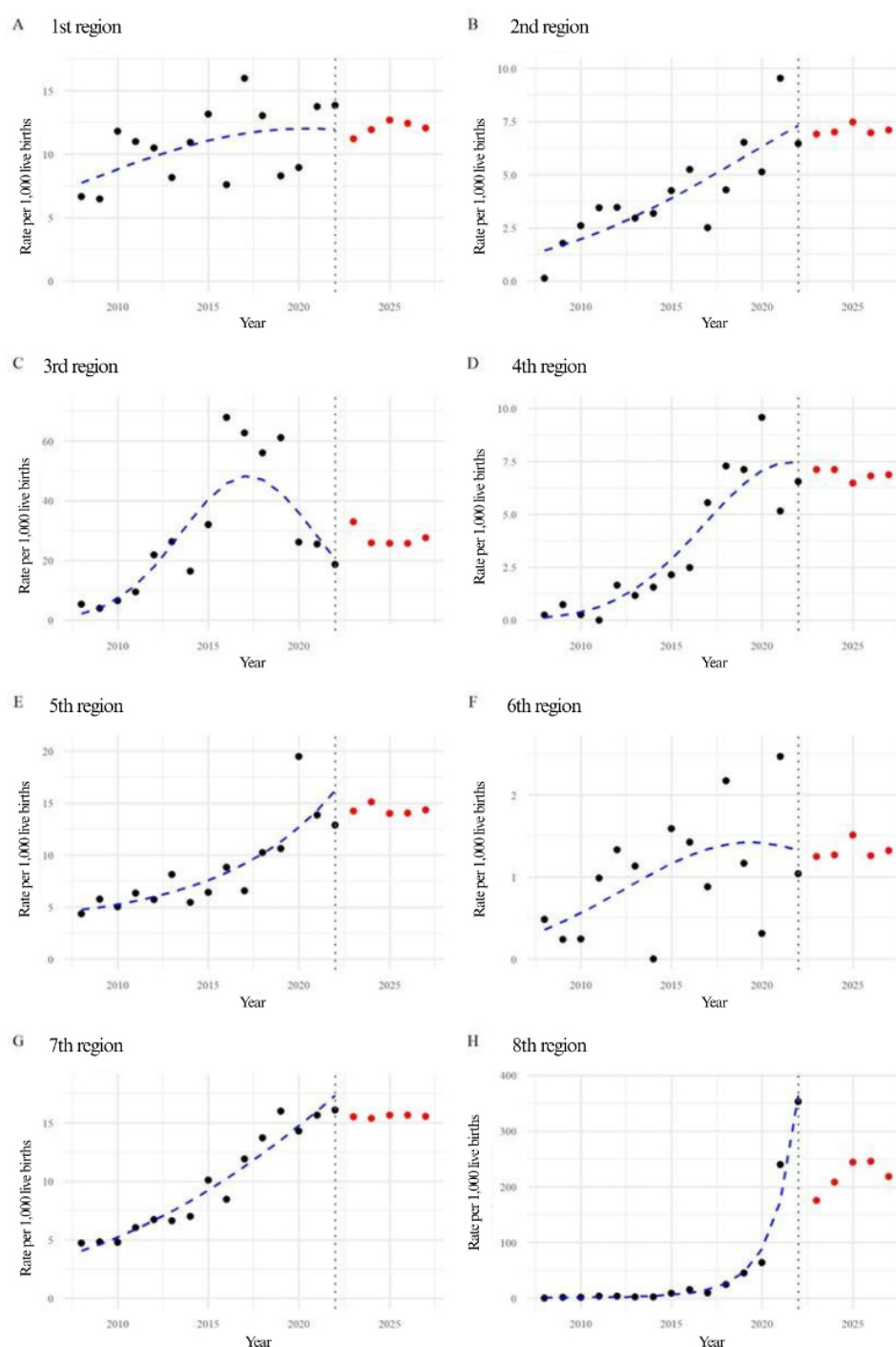
Figure 4. Forecast of the number of cases per 1,000 live births of congenital syphilis in the Health Regions of RN, from 2024 to 2027. Rio Grande do Norte, 2023.

DISCUSSION

The analysis of CS in Rio Grande do Norte revealed a high incidence of cases across the HR, with an upward trend over the study period, increasing from 168 cases in 2008 to 525 in 2022. According to the 2023 epidemiological bulletin, the state ranked fourth in the Northeast in absolute number of cases, with 527 notifications, and fifth in Brazil in incidence rate (13.2/1,000 live births).[7]

The Pan American Health Organization (PAHO) recommends that CS be reduced to ≤0.5 cases per 1,000 live births, a parameter considered indicative of low incidence.[3] In the absence of official thresholds,

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previous studies have proposed the following classifications: intermediate incidence (0.4–4.0), high (4.01–8.0), and very high (>8.0/1,000 live births).[11] Within this framework, none of the HRs in the state met the PAHO goal: the 2nd, 4th, and 6th HRs fell into the intermediate category; the 5th HR into the high category; and the 1st, 3rd, 7th, and 8th HRs into the very high category, as demonstrated in the results (Figure 4).

The HRs with very high incidence, except for the 8th, are part of Macroregion I, which concentrates the largest supply of maternal and child health services and technologies.[11] Of note is the 7th HR, corresponding to the metropolitan area, which, despite being the smallest in number of municipalities, has the largest population and recorded the highest incidence rates during the study period. This region includes the state capital, Natal, which in 2022 reported the third highest incidence rate among Brazilian capitals (27.0/1,000 live births).[7]

An ecological study conducted in the Northeast in 2022, using SINAN and SINASC data, found an association between higher CS incidence and geographic location, particularly in metropolitan and coastal municipalities. Another finding was the elevated risk of vertical transmission in Natal. This high detection rate may reflect both increased availability of health services and testing, as well as more structured notification systems.[12]

With regard to diagnosis, treponemal rapid tests, available in Primary Health Care, enable early identification and are incorporated into routine prenatal care in all three trimesters of pregnancy, as well as at hospital admission for delivery.[13] Nevertheless, the 3rd HR showed the highest incidence in the state (25.51/1,000 live births), despite having 98.72% coverage of the Family Health Strategy (FHS).[14] This finding suggests shortcomings in clinical management of pregnant women, corroborating studies that report increasing CS rates in the Northeast regardless of prenatal care uptake.[12] Another aggravating factor is the recurrent global shortage of benzathine penicillin.[1]

In 2021, the Brazilian Ministry of Health updated its technical manual for syphilis diagnosis, recommending the use of treponemal tests combined with clinical evaluation at the start of investigation due to their high sensitivity. However, because they induce a serological scar, treponemal tests should not be used to monitor therapeutic response; non-treponemal tests such as VDRL, RPR, and TRUST are required for follow-up.[13]

Despite the wide availability of diagnostic tests, a national study (2014) showed that fewer than 50% of municipalities in the Northeast and Southeast provided benzathine penicillin in more than half of their Primary Care teams.[2] Where the drug was available, vertical transmission was reduced. Administration requires physician support and availability of adrenaline to manage possible anaphylactic reactions, which may discourage municipalities from providing treatment, compounded by shortages of trained professionals.[15]

Conversely, the 2nd, 4th, and 6th HRs had the lowest CS incidence, reaching zero cases in the 4th HR in 2011. This reduction may be linked to improvements in maternal and child health care, particularly following the implementation of the Rede Cegonha program, care territorialization, and expansion of the FHS.[11] However, underreporting remains a challenge, especially in municipalities with limited technological capacity for data recording.[2] A previous study documented substantial underreporting of adverse outcomes such as fetal and infant deaths, even in areas with structured surveillance systems.[16]

Follow-up of exposed infants is the responsibility of Primary Care, which should refer them when necessary.[14] The protocol includes serial testing (at 1, 3, 6, 12, and 18 months) to avoid unnecessary invasive procedures.[1] Persistence or increased titers requires further investigation, including lumbar puncture.

Despite advances, a study conducted in Natal (2011–2015) revealed late diagnosis among pregnant women, often in the third trimester or only at delivery. Partner treatment was documented in just 10.9% of cases, favoring reinfection.[14,17] The epidemiological profile of pregnant women with syphilis has been linked to greater social vulnerability, low educational attainment, and brown skin color.[18-19]

Vertical transmission occurred in approximately 45% of pregnant women in the state in 2022.[7] It is estimated that 60% of children with CS develop neurosyphilis, particularly those symptomatic at birth.[14] However, a local study identified flaws in neonatal follow-up: 73.5% had no record of lumbar puncture and 47% did not undergo long-bone radiography, despite receiving treatment.[17]

Projections for 2024–2027 indicate an increase in cases, particularly in the 8th, 3rd, and 7th HRs. Spatial analysis, therefore, proves to be a crucial tool to guide regionally tailored interventions.[20]

Given these findings, it is clear that early diagnosis, timely treatment of pregnant women and their partners, assurance of essential supplies, and capacity building of FHS teams must be strengthened. Shortages of professionals and resources in Primary Care undermine the effectiveness of health care and hinder progress toward established goals.

Study limitations include the use of secondary data, subject to incomplete reporting and underreporting. Furthermore, the ecological design did not allow for identification of individual-level characteristics associated with case occurrence.

Finally, the expected rise in CS cases suggests a potential future burden on specialized health services.

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SPATIO-TEMPORAL ANALYSIS OF CONGENITAL SYPHILIS IN RIO GRANDE DO NORTE, BRAZIL, FROM 2008 TO 2022

Dhyanine Morais de Lima Raimundo, Rita de Cássia Azevedo Constantino, Richardson Augusto Rosendo da Silva, Angelo Maximo Soares de Araujo Filho, Ketyllem Tayanne da Silva Costa, Harlon França de Menezes, Ana Elza Oliveira de Mendonça

Investment in educational interventions, strengthening of Primary Care, and training of health professionals, especially nurses, must be prioritized to prevent new cases and reduce vertical transmission.

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AUTHORS' CONTRIBUTIONS

Dhyanine Morais de Lima Raimundo contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Richardson Augusto Rosendo da Silva** contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Rita de Cássia Azevedo Constantino** contributed to the literature review, abstract writing, introduction, methodology, discussion, interpretation and presentation of results, table development, conclusions, revision, and statistical analysis. **Angelo Maximo Soares de Araujo Filho** contributed to methodology, interpretation of results, conclusions, revision, and statistical analysis. **Ketyllem Tayanne da Silva Costa** contributed to abstract writing, introduction, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Harlon França de Menezes** contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Ana Elza Oliveira de Mendonça** contributed to methodology, interpretation of results, conclusions, revision, and statistical analysis.

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

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Original Article

Cost of antimicrobials associated with bacterial infections in hospitalized children and adolescents

Custos de antimicrobianos associados às infecções bacterianas em crianças e adolescente hospitalizados
Costo de antimicrobianos asociados a infecciones bacterianas en niños y adolescentes hospitalizados

Corresponding author:
E-mail: susany.franciely@uel.br
Address: Sidrak Silva Filho Street, 175, Londrina, Paraná, Brazil.

Susany Franciely Pimenta[1] iD
Rosângela Aparecida Pimenta[1] iD
Nayane Laine Paglione Dias[1] iD

[1]State University of Londrina, Londrina, Paraná, Brazil.

ABSTRACT

Background and Objectives: Healthcare-Associated Infections (HAIs) in hospitalized children and adolescents represent a significant challenge due to increasing bacterial resistance and the high costs associated with antimicrobial use. Understanding these factors is essential to optimizing antimicrobial use and reducing clinical and economic impacts. This study aims to describe the costs of antimicrobials associated with bacterial infections in hospitalized children and adolescents. **Methods:** This is an analytical cross-sectional study conducted in two philanthropic hospitals in northern Paraná, Brazil. A total of 234 children and adolescents with HAIs and positive cultures were included between January 2018 and December 2023. Demographic, clinical, and antimicrobial cost data were collected from electronic medical records. For statistical analysis, the Mann-Whitney U test and Spearman's correlation coefficient were used. Multiple linear regression was performed using the enter method. **Results:** Infections caused by resistant microorganisms occurred in 39.3% of cases. Age, length of hospital stay, and antimicrobial susceptibility profile were associated with higher antimicrobial costs. Patients with resistant microorganisms had antimicrobial costs approximately five times higher than those with susceptible microorganisms. Gram-negative bacteria were predominated, with *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* being multidrug-resistant species. The most frequently prescribed antimicrobials were aminoglycosides, followed by penicillins combined with beta-lactamase inhibitors, and cephalosporins. **Conclusion:** Age, length of hospital stay, and microbial resistance were significant predictors of antimicrobial costs in hospitalized children and adolescents. Infection control strategies and the rational use of antimicrobials are essential to reducing hospital costs and mitigating bacterial resistance.

Keywords: *Child. Adolescent. Drug Costs. Cross Infection. Drug Resistance Microbial.*

RESUMO

Justificativa e Objetivos: As Infecções Relacionadas à Assistência à Saúde (IRAS) em crianças e adolescentes hospitalizados representam desafio significativo devido à crescente resistência bacteriana e aos altos custos associados ao uso de antimicrobianos. Compreender esses fatores é essencial para otimizar o uso desses medicamentos e reduzir impactos clínicos e econômicos. O objetivo deste estudo é descrever os custos de antimicrobianos associados às infecções bacterianas em crianças e adolescentes hospitalizados. **Métodos:** Estudo transversal analítico, realizado em dois hospitais filantrópicos no norte do Paraná, Brasil. Foram incluídos 234 crianças e adolescentes com IRAS e culturas positivas entre janeiro de 2018 e dezembro de 2023. Foram coletados dados demográficos, clínicos e custos diretos dos antimicrobianos dos prontuários eletrônicos. Para análise estatística, foram utilizados os testes U de *Mann-Whitney* e o coeficiente de correlação de *Spearman*. A regressão linear múltipla foi realizada pelo método *enter*. **Resultados:** Infecções por microrganismos resistentes ocorreram em 39,3% da população. Idade, tempo de hospitalização e perfil de sensibilidade se associaram aos maiores custos com antimicrobianos. Pacientes com microrganismos resistentes tiveram custos com antimicrobianos aproximadamente cinco vezes maiores do que aqueles com microrganismos sensíveis. Prevaleceram as bactérias Gram-negativas, sendo *Klebsiella pneumoniae* e *Pseudomonas aeruginosa* multirresistentes. Entre antimicrobianos mais prescritos afiguram os aminoglicosídeos, seguidos pelas penicilinas associadas a inibidores de beta-lactamase e cefalosporinas. **Conclusão:** A idade, tempo de hospitalização e resistência microbiana foram preditores significativos de custos com antimicrobianos em crianças e adolescentes hospitalizados. Logo, estratégias de controle de infecções e uso racional de antimicrobianos são essenciais para reduzir custos hospitalares e mitigar a resistência bacteriana.

Descritores: *Criança. Adolescente. Custos de Medicamentos. Infecção Hospitalar. Resistência Microbiana a Medicamentos.*

RESUMEN

Justificación y Objetivos: Las Infecciones Relacionadas con la Atención de la Salud (IRAS) en niños y adolescentes hospitalizados representan un desafío significativo debido a la creciente resistencia bacteriana y a los altos costos asociados con el uso de antimicrobianos. Comprender estos factores es esencial para optimizar el uso de estos medicamentos y reducir los impactos clínicos y económicos. El objetivo de este estudio es describir los costos de los antimicrobianos asociados con las infecciones bacterianas en niños y adolescentes hospitalizados. **Métodos:** Estudio transversal analítico realizado en dos hospitales filantrópicos en el norte de Paraná, Brasil. Se incluyeron 234 niños y adolescentes con IRAS y cultivos positivos entre enero de 2018 y diciembre de 2023. Se recopilaron datos demográficos, clínicos y costos de los antimicrobianos a partir de los registros médicos electrónicos. Para el análisis estadístico se utilizaron la prueba U de *Mann-Whitney* y el coeficiente de correlación de *Spearman*. El análisis de regresión lineal múltiple se realizó mediante el método *enter*. **Resultados:** Las infecciones por microorganismos resistentes ocurrieron en el 39,3% de la población. La edad, el tiempo de hospitalización y el perfil de sensibilidad se asociaron con mayores costos de antimicrobianos. Los pacientes con microorganismos resistentes presentaron costos aproximadamente cinco veces mayores en comparación con aquellos con microorganismos sensibles. Predominaron las bacterias Gram negativas, siendo *Klebsiella pneumoniae* y *Pseudomonas aeruginosa* multirresistentes. Entre los antimicrobianos más prescritos se encontraron los aminoglucósidos, seguidos pelas penicilinas asociadas a inibidores de beta-lactamase y cefalosporinas. **Conclusión:** La edad, el tiempo de hospitalización y la resistencia microbiana fueron predictores significativos de los costos de antimicrobianos en niños y adolescentes hospitalizados. Las estrategias de control de infecciones y el uso racional de antimicrobianos son esenciales para reducir los costos hospitalarios y mitigar la resistencia bacteriana.

Palabras Clave: *Niño. Adolescente. Costos de Medicamentos. Infección Hospitalaria. Resistencia Microbiana a Medicamentos.*

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INTRODUCTION

Healthcare-associated infections (HAIs) represent one of the greatest challenges for health systems worldwide.[1,2,3] These infections are acquired by patients during hospitalization or in other health care settings. HAIs are caused by a variety of pathogens, including bacteria, viruses, and fungi, and are associated with significant increases in morbidity and mortality, especially when they occur in more vulnerable populations.[1,3]

Among these populations, hospitalized children and adolescents are particularly susceptible. The fragile immune systems of these age groups, combined with the need for invasive procedures and prolonged use of medical devices, make them particularly vulnerable to infections.[1,4,5] Studies have shown that this prevalence among children is alarming, and its impact on their health and well-being can result in serious complications and, in some cases, death.[3,5,6] Among the main complications is the development and spread of antimicrobial-resistant microorganisms, especially multidrug-resistant bacteria, which make treatment extremely challenging, given that dissemination in hospital settings has been a growing problem related, among other factors, to the excessive and inappropriate use of antibiotics, limiting therapeutic options.[1,2,4,6,8,9,10,11]

Infections caused by multidrug-resistant bacteria are associated with higher rates of morbidity and mortality, as well as high hospital costs.[1,4,7,10] Antimicrobial costs represent a significant portion of hospital expenditures, ranging from 15% to 30%, especially in Treatment of infections caused by resistant microorganisms. This high cost is attributed to the frequent use of broad-spectrum antimicrobials and the need for longer and more complex treatments required for these situations, which directly impacts overall treatment costs.[9] They also compromise the quality of care and hinder the efficient allocation of resources in the healthcare system. Therefore, effective prevention and control strategies are essential to improve clinical outcomes and reduce economic costs.[2,3,9,10,11]

Given the relevance of HAIs, the growing threat of antimicrobial resistance, and the high costs associated with treating these infections, this study aims to describe the antimicrobial costs associated with bacterial infections in hospitalized children and adolescents.

METHODS

This is an analytical cross-sectional study, guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) tool, conducted from January 2018 to December 2023.[12]

The study was conducted in two highly complex philanthropic hospitals, leading the Regional Health Department and other Regional Health Departments covering the state of Paraná and neighboring states. One specializes in the care of children up to 12 years old and has 30 beds, including 10 in the Neonatal ICU and 10 in the Pediatric ICU. The second, a general adult hospital, serves adolescents/young people over 12 years olde and has 274 beds, including 47 in the Intensive Care Unit (ICU). Both hospitals are located in the northern region of the state of Paraná, southern Brazil. The study population consisted of children and adolescents of both genders, aged 30 days up to 18 years old, diagnosed with HAIs, as assessed by the Hospital Infection Control Committee (HICC) of the hospitals, in the clinical, surgical, and/or intensive care units.

It is noteworthy that information on HAI diagnoses was included based on reports of all infections, whether or not associated with the presence of invasive devices, along with laboratory tests and clinical signs characteristic of each type. Those with a new episode of infection associated with invasive devices were considered a new case of infection only after a 14-day interval, with the occurrence of new signs and symptoms, and positive laboratory results.

Those with positive microbiological cultures, who received antimicrobial treatment, and whose total cost of these medications was accounted for during hospitalization were included.

During the study period, 253 children and adolescents who acquired HAIs and presented positive cultures with isolated microorganisms were evaluated. Of these, 10 were excluded for not meeting the antimicrobial cost variable, as they died before treatment began. Nine were excluded due to positive cultures for coagulase-negative Staphylococcus. This microorganism, although frequently identified in cultures, may merely represent colonization—that is, the presence of the agent on body surfaces or invasive devices without causing an inflammatory or clinical response. Unlike infection, which is characterized by tissue invasion with compatible clinical and laboratory manifestations. Given the impossibility of accurately distinguishing between these cases, exclusion was chosen. Thus, the final sample consisted of 234 children and adolescents.

Regarding blood cultures, urine cultures, and tracheal secretion cultures, the institution has a full-time microbiology laboratory. Microbial growth is detected using an automated method (BD BACTECT™), and positive samples are subsequently analyzed by the Siemens MicroScan® system, which identifies the microbial species.

Regarding the diagnostic criteria for HAIs, institutions adopt the guidelines of the Brazilian National Health Surveillance Agency (ANVISA), annually updated, to confirm infections. Microbiological confirmation is

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performed through a positive blood culture. Tracheal secretion culture, collected via a suction catheter, with a cutoff point of $\geq 10^6$ CFU/ml, is combined with clinical signs and radiological findings. VAP (Ventilator-Associated Pneumonia) is defined in patients who required mechanical ventilation for more than 48 hours, either by orotracheal intubation or tracheostomy.[10]

PSI (Primary Bloodstream Infection) is diagnosed in patients who had a central venous catheter in place for more than 48 hours and, at the time of infection, were using the device or it had been removed the previous day. The diagnosis was confirmed by clinical signs, laboratory tests, and isolation of the infectious agent in blood cultures. Blood cultures from both the central catheter and peripheral catheters were collected. Common skin contaminants and infections from other sources were not considered.[10]

CAUTI (Catheter-Associated Urinary Tract Infection) was diagnosed in patients with an indwelling urinary catheter for more than 48 hours, with clinical signs and quantitative urinary culture with $\geq 10^5$ CFU/ml, according to the criteria established by ANVISA.[10]

Positive cultures were defined as those that showed microbial growth. Microorganisms were classified according to antimicrobial resistance into two groups: resistant and susceptible.[10] The resistant group was subdivided into multidrug-resistant (MDR) bacteria, including Gram-negative bacilli resistant to 3rd and 4th generation cephalosporins, extended-spectrum β-lactamase (ESBL) producers, and carbapenem-resistant (CR) bacilli, as well as methicillin-resistant Staphylococcus (MRSA). The susceptible group comprised microorganisms that showed susceptibility to the tested antimicrobials.

For data collection, Microsoft Excel 2013® spreadsheets were provided by the institutions, containing information from electronic medical records extracted from the Business Intelligence® program. HAI diagnoses were obtained through individual forms, with HAI notifications completed by the Hospital Infection Control Committee (HICC) team, which evaluates patients with infectious diseases, in accordance with revised diagnostic criteria established by ANVISA.

Data were tabulated in Microsoft Excel® 2013 spreadsheets from February to April 2024. Demographic variables were categorized as follows: gender (female and male), age (≥ 30 days to ≤ 1 year, 2 to 6 years, 7 to 12 years, and 13 to <18 years), race (White and Black), and resident in the Health Region and other regions. Clinical variables included total hospitalization time (in days), ICU stay (yes or no), ICU length of stay (in days), reason for hospitalization (medical or surgical), presence of two or more HAIs, microbiological culture results, isolated microorganism, antimicrobial susceptibility profile (sensitive or resistant microorganism), antimicrobial therapy, days of

antibiotic therapy, and clinical outcome (discharge and death).

For the antimicrobial cost variable, values were calculated individually, considering the cost of the unit dose of each drug formulation and the period of use, according to records provided by the institution's financial department. The cost of antimicrobial therapy was presented as the average direct cost of antimicrobials, expressed in Brazilian Reais (R$). The analysis included exclusively the direct costs of antimicrobials used in the treatment of HAIs with positive cultures, after diagnostic confirmation according to the HICC criteria, regardless of the route of administration and including dosage variations. Antimicrobials used for prophylaxis were not included in the analysis. The values were subsequently converted to US dollars (USD) based on the exchange rate in effect on November 8, 2024, assuming a rate of R$5.76 per dollar.

The collected data were subjected to descriptive statistical analysis, with presentation of absolute and relative frequencies for categorical variables, and measures of central tendency (median) and dispersion (quartiles and Interquartile Range [IQR]; minimum and maximum) for continuous variables.

The distribution of quantitative variables was assessed using the Shapiro-Wilk normality test, which indicated that none of the variables were normally distributed. To compare continuous variables, such as total hospitalization time (in days), ICU stay (in days), and antimicrobial costs, according to the antimicrobial susceptibility profile (sensitive and resistant), the nonparametric Mann-Whitney U test for independent samples was used. Spearman's correlation coefficient was used to estimate bivariate correlations.

Effect size interpretations close to 0.10 were considered to indicate weak correlations, up to 0.30 moderate, and 0.50 strong.[13]

The models were evaluated using the Adjusted Coefficient of Determination (adjusted R^2), expressed as a percentage, to measure the correlation between the variables. To identify discrepancies in the observed distributions, the standardized adjusted residuals were analyzed. The model's multicollinearity was assessed using the Variance Inflation Factor (VIF), considering variables with scores greater than 10 as problematic. To detect outliers, Cook's D was used, considering scores >2 as a highly influential factor, indicating the presence of outliers. Bootstrapping procedures (BCA with 95% CI) were used to correct for possible deviations from the normality of the residuals.

After performing the multiple linear regression analysis, the enter method was used, in which all independent variables were entered simultaneously into the model, without prior selection or exclusion based on statistical criteria. This method was used to test the

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association between predictor variables (age in months, length of hospitalization (in days), length of ICU stay (in days), sensitivity profile (sensitive and resistant), and outcome (discharge and death)) and the response variable (antimicrobial costs). This model presented the regression coefficient estimates, their respective confidence intervals, and p-values. Furthermore, we considered unstandardized coefficients (β), which reflect the direct impact of each variable on antimicrobial costs, and standardized coefficients (βeta), which allow relative comparisons between the model variables. All analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 20.0, with a significance level of 5%.

This study is an excerpt from the research project entitled "Clinical and Economic Impact of Antimicrobial Resistance on Hospital Costs," approved by the Health Research Ethics Committee of the proposing institution, under No. 5,632,608, with Certificate of Approval for Ethical Assessment (CAAE) No. 24711718.8.0000.0099.

RESULTS

The study sample included 234 children and adolescents diagnosed with HAIs and positive microbial cultures, of which 142 (60.7%) were susceptible to microorganisms and 92 (39.3%) were resistant. Ages ranged from 29 days to 17 years, with a median of 12.5 months. They were also mostly females, ages 29 days to 1 year old, who were white (Table 1).

Regarding the reason for hospitalization, 65.4% of patients were admitted for surgical procedures, of which 70.5% were cardiac surgeries. This reflects the reality of one of the hospitals studied, a reference in pediatric cardiac surgeries.

It was found that 68.2% were from other municipalities and Regional Health Departments. Among the 54 deaths, 48.1% presented antimicrobial resistance.

Outcomes related to length of hospital stay and ICU stay were significantly higher among those with antimicrobial-resistant pathogens (Table 1).

Table 1. Comparison of antimicrobial sensitivity profiles among children and adolescents with sensitive and resistant microorganisms in high-complexity hospitals from 2018 to 2023. Paraná, Brazil.

Categorical variables	Infection by Sensitive Microorganisms* N (%)	Infection by Resistant Microorganisms** N (%)	Total N (%)
Total	142 (60.7)	92 (39.3)	234 (100.0)
Gender			
Female	76 (58.9)	53 (41.1)	129 (55.1)
Male	66 (62.9)	39 (37.1)	105 (44.9)
Age range			
1 month to 1 year	101 (60.8)	65 (39.2)	166 (71.0)
2 to 6 years	23 (62.2)	14 (37.8)	37 (15.8)
7 to 11 years	13 (68.4)	63 (1.6)	19 (8.1)
12 to ≤18 years	54 (1.7)	75 (8.3)	12 (5.1)
Race			
White	115 (62.2)	70 (37.8)	185 (79.1)
Black	27 (55.1)	22 (44.9)	49 (20.9)
Specialty			
Clinic	54 (66.7)	27 (33.3)	81 (34.6)
Surgery	88 (57.5)	65 (42.5)	153 (65.4)
Origin			
RS† residence	45 (62.5)	27 (37.5)	72 (31.0)
Other regions	97 (59.9)	65 (40.1)	162 (68.0)
Outcome			
Discharge	114 (63.3)	66 (36.7)	180 (76.9)
Death	28 (51.9)	26 (48.1)	54 (23.1)

Abbreviation: *Antimicrobial-sensitive microorganisms; **Antimicrobial-resistant microorganisms; †Regional Health.

Furthermore, antimicrobial costs were significantly higher for patients with resistant microorganisms, being approximately five times higher than the costs associated with sensitive microorganisms (Table 2). For the sensitive group, the 1st quartile cost R$43.19 (US$7.49) and the 3rd quartile cost R$1,277.03 (US$221.52), while for the resistant group, the 1st quartile cost R$441.49 (US$76.58) and the 3rd quartile cost R$4,899.37 (US$849.87).

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Table 2. Comparison of clinical variables and antimicrobial costs among children and adolescents with infections caused by sensitive and resistant microorganisms in highly complex hospitals from 2018 to 2023. Paraná, Brazil.

Continuous variables	Infection by Sensitive Microorganisms *	Infection by Resistant Microorganisms **	Total
	Median (IQR) ‡	Median (IQR) ‡	p-value[1]
ICU stay (in days)	16 (29.00)	26 (35.00)	< 0.001
Hospitalization time (in days)	27 (30.00)	36 (44.00)	< 0.001
Antimicrobial cost #	265,18 (1,242.02)	1.347,71 (4,523.67)	< 0.001
	45,99 (215.44) ##	233,68 (784.70) ##	

Abbreviation: *Antimicrobial-sensitive microorganisms; **Antimicrobial-resistant microorganisms; ‡IQR- Interquartile range; [1]p-value refers to the Mann-Whitney test; #Costs in Reais (R$); ##Costs in US dollars (US$).

When analyzing the sensitivity profile of the microorganisms, 328 bacterial strains were identified, of which 268 (81.7%) were Gram-negative. The most prevalent bacteria were *Klebsiella pneumoniae* (24.6%), *Pseudomonas aeruginosa* (23.8%), and *Escherichia coli* (12.6%). Among the Gram-positive bacteria, the most frequent was *Staphylococcus aureus* (70%), followed by *Enterococcus* spp. (28.3%).

Out of the identified microorganisms, 161 (49%) presented some resistance mechanism. Of these, 65.2% were MDR, 21.7% CR, and 5.6% MRSA. Regarding antimicrobial classes, aminoglycosides were the most commonly used, accounting for 207 (21.6%), followed by penicillins combined with beta-lactamase inhibitors, with 188 (19.6%), and cephalosporins, with 134 (14%).

The most commonly prescribed individual antimicrobials were amikacin, with 155 (16.2%); the piperacycline+tazobactam combination, with 127 (13.2%); and vancomycin, with 101 (10.5%). Almost all children and adolescents, 220 (94%), used more than one antibiotic, accounting for 957 antimicrobial cycles.

The results demonstrate that all variables in the multiple linear regression model, with an adjusted R², explain 44% of the variance in antimicrobial costs.

Age, length of hospital stay, and sensitivity profile demonstrated a statistically significant and positive association with antimicrobial costs (Table 3). However, length of ICU stay and outcome (discharge and death) did not show a significant association with antimicrobial costs.

Table 3. Multiple regression of demographic and clinical variables as predictors of antimicrobial costs for children and adolescents in high-complexity hospitals from 2018 to 2023. Paraná, Brazil.

Predictor variables	β*	Standardized βeta** coefficients	Antimicrobial Costs # CI 95% [1]	p-value
Age	16.5	0.176	7.20;25.8	< 0,001
Length of stay in the ICU	29.1	0.190	-13.4;71.7	0,180
Length of hospital stay	57.2	0.441	22.3;92.1	< 0,001
Sensitivity profile‡	539.5	0.119	171.6;1921.1	0,019
Outcome†	135.5	0.073	-349.0;1843.4	0,181

Abbreviation: ‡Sensitivity profile (Sensitive or resistant); †Outcome (discharge or death); β* Non-standardized coefficient; βeta Standardized coefficient; **CI[1] 95% confidence interval; #Costs in Reais (R$) and p-value refers to the multiple linear regression test.

DISCUSSION

The results of the study of children and adolescents with HAIs, confirmed by microbiological tests involving the isolation and identification of microorganisms in blood cultures, urine cultures, and/or respiratory secretion cultures, reveal several important nuances regarding the impacts of antimicrobial-resistant microorganisms compared to sensitive microorganisms. The main predictors of increased antimicrobial costs were age, length of hospital stay, and the sensitivity profile of the microorganisms. In contrast, length of ICU stay and the outcome of death did not show a statistically significant association with these costs.

It is noteworthy that, among children and adolescents with culture-positive HAIs, the distribution between the groups with resistant and sensitive microorganisms was relatively similar regarding demographic variables, with the majority of patients in the 1-month to 1-year age range, a predominance of females and White race, and a significant positive correlation between age and antimicrobial costs. Studies indicate that, in this age group, their still-developing immune systems may make them more susceptible to acquiring HAIs.[14,15,16,17] Furthermore, as children and adolescents age, treatment costs tend to increase. The importance of individualized management strategies to optimize treatment and reduce the costs associated with caring for patients with HAIs is highlighted, especially in more vulnerable age groups.[17,18]

In the present study, it was observed that most children and adolescents had prolonged hospital stays. In particular, those with resistant microorganisms had

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significantly longer ICU stays and total hospitalization days. This is similar to other studies, which strongly demonstrate the relationship between resistant microorganisms and increased hospital stays, therapeutic costs, and mortality. It is noteworthy, however, that other clinical conditions, such as congenital heart disease requiring surgical correction and other underlying comorbidities, may also have contributed to prolonged hospital stays.[17,18,20,21]

An epidemiological study conducted in a pediatric intensive care unit in China revealed that the prevalence of hospital-acquired infections in the PICU ranged from 10% to 25%. Furthermore, a series of risk factors were identified that could potentially be modified to reduce additional complications and minimize the need for more complex therapeutic interventions.[16]

Regarding the study results, there was no statistically significant association between the length of ICU stay and antimicrobial costs. Although several studies indicate that the transmission of multidrug-resistant microorganisms is most frequently reported in critical care units, such as ICUs, it is observed that all hospital sectors are impacted by the selection and spread of these microorganisms, consequently increasing costs.[16,17,18,22]

The presence of resistant infections increases the challenge for healthcare professionals, who must adopt rigorous infection control measures and consider therapeutic alternatives that are often limited due to antimicrobial resistance.[16,17] Therefore, it is crucial to implement effective hospital infection prevention and control strategies to mitigate these adverse impacts on pediatric health.[16,19]

It is noteworthy that results from national and international studies are similar in identifying the increasing difficulty in treating infections due to pathogen resistance to conventional antibiotics, highlighting the urgent need to develop new therapeutic strategies and prevent the irrational use of antimicrobials.[8,16,17,18,21,23,24,25]

The present study demonstrated that the susceptibility profile of microorganisms showed a statistically significant association with antimicrobial costs. Sensitive microorganisms tend to be associated with lower costs, while resistant microorganisms tend to be associated with higher costs. These findings corroborate the results of previous studies, which indicated that treatments for resistant infections generate substantially higher costs due to the need for more expensive antimicrobials and the prolonged treatment period.[18]

Regarding the microorganisms isolated in the cultures, Gram-negative bacteria predominated, with *Klebsiella pneumoniae* being the most common, followed by *Pseudomonas aeruginosa*. Both showed a high prevalence of resistance to multiple antibiotics, indicating the need for rigorous infection control measures and continuous monitoring for resistance.

Studies have identified *Klebsiella pneumoniae* as an opportunistic pathogen that frequently causes serious infections in hospital settings, especially in patients with compromised immune systems.[26]

A case-control study conducted in the Central-West region of Brazil found similar results, with a predominance of Gram-negative bacteria. However, in this study, *Pseudomonas* was the most common, followed by *Klebsiella pneumoniae* in HAI cases. Furthermore, infections were associated with significantly high hospital costs, longer hospital stays, and higher ICU mortality.[24]

A systematic review of the implementation and outcomes of antimicrobial stewardship programs in pediatrics globally identified that antimicrobials are frequently prescribed to children, and that, of these children, the high prescription rate raised concerns about their appropriateness and necessity, as it indicated that 20% to 50% of antimicrobials could be dispensable.[14]

The irrational use of this medication exposes children to antimicrobial resistance, significantly increasing the chances of complications, mortality, and associated healthcare costs.[6,14]

Mortality was 54 cases (23.1%), and the presence of resistant microorganisms correlated with greater disease severity, reflected in high death rates. The importance of controlling antimicrobial resistance to improve outcomes is highlighted.[10,18]

Direct antimicrobial costs varied considerably, being up to five times higher for resistant microorganisms compared to sensitive ones. This reflects the need for more complex and prolonged treatments to combat resistant infections. Therefore, understanding direct costs is crucial for hospitals, as it allows for efficient resource allocation, improved quality of care, and maintenance of the institution's financial viability, as argued by other authors.[24]

Authors highlight that the implementation of antimicrobial stewardship programs in pediatric hospitals has been shown to significantly reduce the costs associated with antimicrobial use. These programs focus on optimizing antimicrobial prescribing, avoiding inappropriate and excessive use, which are common contributors to increased healthcare costs.[14]

Consistent with other authors, this study highlights the importance of global cooperation, effective policies, and rigorous surveillance to mitigate the effects of antimicrobial resistance, emphasizing the need for a coordinated effort between governments, healthcare professionals, and the scientific community.[6,23] To mitigate these problems, it is essential to adopt strategies that promote the rational use of antimicrobials for this population and in various related areas.[6,14,23,25,26] These results reinforce the need for improvements in antimicrobial stewardship programs, especially in

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healthcare services, and investment in further research in this area.

This study highlights the need for rigorous infection control and rational antimicrobial prescribing to contain bacterial resistance and optimize costs. Measures such as epidemiological surveillance and rational use policies are essential to minimize the clinical and economic impacts associated with treating infections in hospitalized children and adolescents.

Although the multiple linear regression model explained 44% of the variance in antimicrobial costs, the results indicate potential limitations related to the influence of other predictor variables not included in the model. Factors such as individual characteristics of children and adolescents, institutional prescribing patterns, and unmeasured clinical variables may impact observed costs. Future studies should explore these aspects to deepen understanding of the determinants of antimicrobial costs and improve management strategies.

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AUTHORS' CONTRIBUTIONS

Susany Franciely Pimenta contributed to the bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review and statistics. **Rosângela Aparecida Pimenta** contributed to project management, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, review and statistics. **Nayane Laine Paglione Dias** contributed to writing the abstract, methodology, interpretation 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

Prevalence of tuberculosis notifications at a university hospital between 2010 and 2022

Prevalência das notificações de tuberculose em um hospital universitário, entre 2010 e 2022
Prevalencia de notificaciones de tuberculosis en un hospital universitario entre 2010 y 2022

Corresponding author:
E-mail: sribeiro25@unifesp.br
Address: 754 Napoleão de Barros Street, Vila Clementino, São Paulo, São Paulo, Brazil.

Stephanie Ribeiro[1] (ID)
Claudia Susana Pérez Guerrero[1] (ID)
Suely Miyuki Yashiro[2] (ID)
Nivia Aparecida Pissaia Sanches[2] (ID)
Marina Doreto Castilho[1] (ID)
Hugo Fernandes[1] (ID)
Giselle Lima de Freitas[3] (ID)
Meiry Fernanda Pinto Okuno[1] (ID)
Paula Hino[1] (ID)

[1]Federal University of São Paulo, São Paulo, São Paulo, Brazil.
[2]São Paulo Hospital, São Paulo, São Paulo, Brazil.
[3]Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

ABSTRACT

Background and Objectives: Tuberculosis remains a significant public health challenge. This study aimed to describe the sociodemographic and clinical-epidemiological profiles of tuberculosis cases and identify factors associated with loss to follow-up between 2010 and 2022 at a university hospital in São Paulo-SP, Brazil. **Methods:** This cross-sectional study analyzed secondary data from mandatory tuberculosis notifications in a tertiary health service in São Paulo. Descriptive statistics and measures of central tendency were applied. Poisson regression with robust variance was used to calculate prevalence ratios for loss to follow-up. **Results:** A total of 2,076 cases were reported during the study period, with 39% identified in urgent or emergency settings, and 10.6% classified as loss to follow-up. Higher prevalence of treatment discontinuation was associated with unemployment, diagnosis in urgent/emergency care or hospitalization, retreatment cases, alcohol use, and positive serology for human immunodeficiency virus. **Conclusion:** Many cases were reported in the urgent care and/or emergency sector, and treatment interruption was high. This scenario underscores the necessity for a comprehensive approach to tuberculosis, with a focus on cases diagnosed in tertiary care and those undergoing retreatment.

Keywords: *Tuberculosis. Health Profile. Lost to Follow-Up. Tertiary Healthcare. Public Health Surveillance.*

RESUMO

Justificativa e Objetivos: A tuberculose persiste como um importante problema de saúde pública. Dessa forma, objetivou-se descrever o perfil sociodemográfico e clínico-epidemiológico dos casos de tuberculose e identificar as características associadas à perda de seguimento, entre 2010 e 2022 em um hospital universitário do município de São Paulo - SP, Brasil. **Métodos:** Estudo transversal, com base em dados secundários referentes às notificações compulsórias de tuberculose de um serviço de saúde terciário do município de São Paulo. Na análise foram reportadas as medidas descritivas e de tendência central e, pela regressão de Poisson com variância robusta, a razão de prevalência para a perda de seguimento do tratamento. **Resultados:** Foram notificados 2.076 casos durante o período do estudo, dos quais 39% foram descobertos no setor de urgência/emergência e 10,6% foi encerrado por perda de seguimento. A maior prevalência para interrupção do tratamento esteve associada as pessoas que se encontravam desempregadas, com descoberta em serviços de urgência/emergência ou durante a internação hospitalar, em retratamento, que relataram uso de álcool e com sorologia positiva para o vírus da imunodeficiência humana. **Conclusão:** Muitos casos foram notificados no setor de urgência e/ou emergência e a interrupção do tratamento foi elevada. Esse cenário reforça a necessidade de enfrentamento amplo da tuberculose, com atenção aos casos diagnosticados na atenção terciária e que se encontram em retratamento.

Descritores: *Tuberculose. Perfil de saúde. Perda de Seguimento. Atenção Terciária à Saúde. Vigilância em Saúde Pública.*

RESUMEN

Justificación y Objetivos: La tuberculosis sigue siendo un desafío significativo para la salud pública. Este estudio tuvo como objetivo describir el perfil sociodemográfico y clínico-epidemiológico de los casos de tuberculosis e identificar los factores asociados a la pérdida de seguimiento entre 2010 y 2022 en un hospital universitario de São Paulo-SP, Brasil. **Métodos:** Se realizó un estudio transversal utilizando datos secundarios de notificaciones obligatorias de tuberculosis provenientes de un servicio de salud terciario en São Paulo. Se aplicaron estadísticas descriptivas y medidas de tendencia central. La regresión de Poisson con varianza robusta se utilizó para calcular las razones de prevalencia de la pérdida de seguimiento. **Resultados:** Durante el período de estudio, se notificaron 2.076 casos, de los cuales el 39% fueron detectados en servicios de urgencias o emergencias, y el 10,6% se clasificaron como pérdida de seguimiento. Una mayor prevalencia de interrupción del tratamiento se asoció con el desempleo, el diagnóstico en urgencias o durante la hospitalización, los casos en retratamiento, el consumo de alcohol y la serología positiva para el virus de la inmunodeficiencia humana. **Conclusión:** Se notificaron muchos casos en el sector de urgencias y/o emergencias y la interrupción del tratamiento fue elevada. Este escenario refuerza la necesidad de abordar la tuberculosis de manera integral, prestando atención a los casos diagnosticados en la atención terciaria y que se encuentran en retratamiento.

Palabras Clave: *Tuberculosis. Perfil de Salud. Pérdida de seguimiento. Atención Terciaria de Salud. Vigilancia en Salud Pública.*

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INTRODUCTION

Tuberculosis (TB) remains a major global public health problem, despite the availability of treatment and cure; in 2023, more than 10 million people worldwide were affected, resulting in 1.2 million deaths.[1] As it is a socially determined disease, it is more prevalent in developing countries, such as Brazil, which is among the countries with the highest burden of disease and co-infection, TB-Human Immunodeficiency Virus (HIV), in the world.[1]

Given the magnitude of the damage caused by the disease, the 2030 Agenda for Sustainable Development established by the United Nations (UN) aims to eliminate TB by that year. In addition, as a global and national effort, guidelines have been developed by the World Health Organization (WHO), with the End TB Strategy, and by the Ministry of Health, with the National Plan to End Tuberculosis as a Public Health Problem, seeking to reduce the incidence and mortality of cases by 2035.[1,2]

Although there is a commitment to achieve the agreed targets, more than 80,000 new cases were recorded in Brazil in 2023, representing an incidence rate of 37/100,000 inhabitants.[3] The state of São Paulo accounts for the highest absolute number of notifications in the country, covering 24.4% of new cases, and its capital has a higher rate than the national average, with 58.3 cases per 100,000 inhabitants. In addition to this high incidence, approximately 14% of cases in the country are closed due to treatment interruption, with a proportion of 16% for the state of São Paulo, which makes the elimination process more challenging.[3]

Through the Unified Health System (SUS), TB care is organized around Primary Health Care (PHC), which is the priority gateway for diagnosing the disease and monitoring treatment with a basic regimen and/or with fewer adverse effects.[2] However, the identification of TB cases in the hospital network is still a reality in the country.[4-6]

A study that aimed to understand the motivation for seeking diagnosis and treatment in urgent and emergency care units rather than in PHC services close to home revealed issues related to fear of prejudice and stigma, severe clinical manifestations due to delays in seeking care, the perception of rapid resolution at this level of health care, and gaps in PHC in terms of organization and human resources.[4]

A previous population-based study conducted in the state of São Paulo found that TB was diagnosed in emergency departments in 45% of cases.[5] In the state capital, the proportion of cases detected in specialized services was 50.2% in two regions of the municipality.[6] Furthermore, cases diagnosed in medium- or high-complexity settings, via urgent/emergency care or diagnostic clarification during hospitalization, had worse outcomes for TB.[5]

This scenario reveals weaknesses in the organization of TB control services, highlighting the importance of understanding the epidemiological situation of the disease based on cases reported in secondary and tertiary health care services. Thus, the objective of the study was to describe the sociodemographic and clinical-epidemiological profile of TB cases and identify the characteristics associated with loss to follow-up between 2010 and 2022 in a university hospital in the city of São Paulo, SP, Brazil.

METHODS

This is a cross-sectional study with a quantitative approach, referring to TB cases reported in a university hospital in the city of São Paulo, SP, Brazil, from 2010 to 2022. The study was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) tool.

The study setting was the Epidemiology Center of a large teaching hospital. This hospital is classified as tertiary and provides outpatient, inpatient, and urgent/emergency care, in addition to working in conjunction with teaching, research, and extension activities at a public higher education institution. The study population consisted of all TB cases reported at that health institution, regardless of age, over a 12-year period (2010 to 2022), excluding duplicate cases.

The data were collected from notification forms and TB-WEB, which is a TB case monitoring system in the state of São Paulo. A semi-structured instrument containing the items that make up the TB Notification/Investigation and Follow-up Form was used for this purpose, with both sociodemographic and TB-related variables.

The variables collected were: gender (female; male), age group (≤15; 15 to 29; 30 to 59; ≥60 years), color/race/ethnicity (white; brown; black; yellow or indigenous; unknown or not filled in), years of schooling (no schooling; 1-7; 8-11; 12 or more; unknown or not filled in), marital status (single; married; separated; widowed; not filled in), occupational status (employed/self-employed; unemployed; retired; homemaker; student; unknown or not filled in), year of notification (2010-2022), place of discovery (outpatient demand; urgency/emergency; diagnostic clarification during hospitalization; contact investigation; active search; unknown or not filled in), type of admission (new case; recurrence; retreatment), clinical form (pulmonary; extrapulmonary; pulmonary + extrapulmonary), if extrapulmonary (pleural; peripheral lymph node; meningeal; miliary; multiple organs; bone; other), associated diseases and conditions (Aids; diabetes; mental illness; alcoholism; smoking; drug use;

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others), HIV serology (positive; negative; ongoing; not performed; no information; not filled in), antiretroviral therapy (yes; no; not applicable; unknown or not filled in), and outcome/closure (cure; loss to follow-up; death from TB; death from other causes; failure; undergoing treatment or not started; change in diagnosis; transfer or not filled in).

For descriptive analyses, absolute frequencies (n) and relative frequencies (%) of qualitative and quantitative variables were reported; and mean, standard deviation (SD), minimum, maximum, and 95% confidence interval (95% CI) for quantitative variables. In addition, a line graph was created showing notifications over time.

For the association, loss to follow-up was defined as the dependent variable and occupational status, place of discovery, type of entry, clinical form, associated diseases and conditions, HIV serology, and antiretroviral therapy were defined as predictor variables; while the covariates were gender, color/race/ethnicity, age group, and years of schooling. In addition, for this analysis, the groups "no information" and "ignored or not filled in" were removed, and the following variables were regrouped: outcome (cure; loss to follow-up); occupational status (employed/self-employed; unemployed; retired; other) and place of discovery (outpatient demand; urgency/emergency; diagnostic clarification in interaction; other).

To verify the Prevalence Ratio (PR) between the outcomes "loss to follow-up" and "cure," a Poisson regression with robust variance was performed, reporting the PR, its respective 95% CI, and p-value,

adopting 5% (p ≤ 0.05) as the minimum level of statistical significance. In addition, the assumption of collinearity was verified by the variance inflation factor (VIF) and pseudo-R^2 as an indicator of model quality.

Initially, a bivariate analysis was performed, followed by the selection of variables for multivariate analysis using backward stepwise regression, i.e., variables with a p-value < 0.20 in the first analysis for the likelihood ratio test were included in the second analysis. subsequently, the variables were removed one by one until those with a p-value < 0.05 remained in the final model.

The data were analyzed using Jamovi version 2.3.28 (Sydney, NSW, Australia) and RStudio version 4.1.3 (Boston, MA, USA).

In accordance with the recommendations of Resolutions No. 466/12, 510/16, and 580/18 of the National Health Council of the Ministry of Health, the study was approved by the Research Ethics Committee of the Federal University of São Paulo under opinion No. 6,183,627 and Certificate of Ethical Review No. 41064920.4.0000.5505, on July 14, 2023.

RESULTS

During the 12-year period (2010 to 2022), after excluding 29 duplicate cases, 2,076 cases of TB were reported by the Epidemiology Center of the university hospital, with an average of 159.6 cases (SD ± 26.8), with a minimum of 107 and a maximum of 200 notifications in 2022 and 2019, respectively (Figure 1).
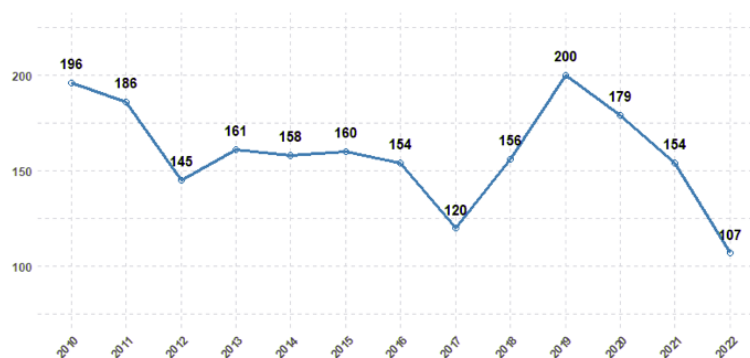
Figure 1. Distribution of tuberculosis case notifications by year (2010–2022).

Regarding the sociodemographic characteristics of the cases, most were male (63.4%), aged between 30 and 59 years (54.7%) and with a mean age of 41.3 years (SD ± 17.41), ranging from a minimum of 0 to a maximum of 92 years (Table 1). The majority were black (51.5%), single (53.8%), employed or self-employed (40.3%), and had eight to 14 years of schooling (40.6%), followed by one to seven years (35.6%).

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Table 1. Distribution of sociodemographic and clinical-epidemiological characteristics of tuberculosis cases reported at a university hospital in the city of São Paulo, Brazil, between 2010 and 2022.

Sociodemographic characteristics	N (%)
Gender	
Women	759 (36.6)
Men	1317 (63.4)
Age group (years)	
< 15	88 (4.2)
15 to 29	501 (24.1)
30 to 59	1136 (54.7)
≥ 60	351 (16.9)
Race/color/ethnicity	
White	911 (43.9)
Black	282 (13.6)
Brown	786 (37.9)
Yellow/Indigenous	66 (3.2)
Ignored or not filled in	31 (1.4)
Years of study	
No education	69 (3.3)
1 to 7	739 (35.6)
8 to 11	695 (33.5)
12 or more	229 (11.0)
Ignored or not filled in	344 (16.6)
Marital status	
Single	1117 (53.8)
Married	501 (24.1)
Separated	133 (6.4)
Widowed	92 (4.4)
No entry	233 (11.2)
Employment status	
Employed/self-employed	836 (40.3)
Unemployed	232 (11.2)
Retired	238 (11.5)
Housewife	195 (9.4)
Student	131 (6.3)
Ignored or not filled in	444 (21.4)
Clinical and epidemiological characteristics	N (%)
Place of discovery	
Outpatient demand	640 (30.8)
Urgency/Emergency	809 (39.0)
Diagnostic clarification during hospitalization	520 (25.0)
Contact tracing	7 (0.3)
Active search	11 (0.5)
Ignored or not filled out	89 (4.3)
Input type	
New case	1797 (86.6)
Recurrence	170 (8.2)
Retreatment	106 (5.1)
No information	3 (0.1)
Clinical form	
Pulmonary	1150 (55.4)
Extrapulmonary	647 (31.2)
Pulmonary + Extrapulmonary	279 (13.4)
Extrapulmonary	
Pleural	244 (26.2)
Peripheral lymph nodes	145 (15.6)
Meningeal	108 (11.6)
Miliary	80 (8.6)
Multiple organs	80 (8.6)
Bone	50 (5.4)
Other	224 (24.0)
Associated diseases and conditions present	
Aids	387 (18.6)
Diabetes	153 (7.4)
Mental illness	40 (1.9)
Alcoholism	235 (11.3)
Smoking	236 (11.4)
Drug use	160 (7.7)
Other	669 (32.2)
Serology	
Positive	401 (19.4)
Negative	1237 (59.6)
In progress	3 (0.1)
Not completed	389 (18.7)
No information	39 (1.9)
Not filled out	7 (0.3)

Antiretroviral therapy	
Yes	88 (4.2)
No	21 (1.0)
Not applicable	1623 (78.2)
Ignored or not filled in	344 (16.6)
Outcome/Closure	
Cure	1221 (58.8)
Loss to follow-up	221 (10.6)
Death from tuberculosis	128 (6.2)
Death from other causes	197 (9.5)
Bankruptcy	39 (1.9)
Undergoing treatment or treatment not started	35 (1.7)
Change in diagnosis	155 (7.5)
Transfer or no information provided	80 (3.9)

Regarding TB characteristics, most cases were detected in the emergency room (39%), followed by outpatient care (30.8%), with new cases (86.6%), pulmonary clinical form (55.4%), and cure outcome (58.8%). Regarding associated diseases and conditions, the prevalence of Aids between the years was 18.6%, smoking and alcoholism was about 11.3%, drug addiction and diabetes was 7.5%, mental illness was 1.9%, and others was 32.3%, which includes immunosuppression and sexually transmitted infections, as well as cardiovascular, renal, neurological, and pulmonary diseases, cancers, and others.

Most HIV serology tests were negative (59.6%), followed by positive (19.4%) and not performed (18.7%). Regarding antiretroviral therapy (ART), when separating cases that did not apply, only 19.4% of individuals were receiving ART, and for 75.9% of cases, this information was unknown or not filled in.

Among the associations with sociodemographic and clinical-epidemiological characteristics and loss to follow-up in the univariate model (Table 2), statistical significance was observed for occupational status (<0.001), place of discovery (<0.001), type of admission (<0.001), Aids (<0.001), mental illness (0.004), alcoholism (<0.001), smoking (0.042), drug use (<0.001), HIV serology (<0.001), and antiretroviral therapy (0.018).

In the adjusted multivariate model (Table 2), only the following variables remained significant: occupational status (0.024), place of discovery (0.004), type of admission (<0.001), alcoholism (0.033), and HIV serology (<0.001).

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Table 2. Association between sociodemographic and clinical-epidemiological characteristics and loss to follow-up in tuberculosis treatment, using bivariate and multivariate models. São Paulo-SP, Brazil, 2010-2022.

Characteristics	Loss of follow-up			
	PR (IC95)	p-value	aPR (95%CI)*	p-value
Employment status		< 0.001		0.024
Employee/self-employed	0.38 (0.28-0.53)		0.64 (0.44-0.93)	
Unemployed	refererence		reference	
Retired	0.14 (0.05-0.28)		0.49 (0.19-1.08)	
Other	0.48 (0.32-0.71)		1.08 (0.65-1.79)	
Place of discovery		< 0.001		0.004
Outpatient demand	reference		reference	
Urgent/Emergency care	2.16 (1.57-3.03)		1.80 (1.20-2.76)	
Diagnostic clarification during hospitalization	2.44 (1.72-3.49)		2.06 (1.35-3.2)	
Other	2.51 (0.69-6.42)		2.66 (0.72-7.17)	
Admit		< 0.001		< 0.001
New case	reference		reference	
Recurrence	1.8 (1.19-2.63)		1.19 (0.70-1.9)	
Retreatment	4.74 (3.40-6.46)		2.59 (1.71-3.85)	
Clinical form		0.074		
Pulmonary	reference		-	
Extrapulmonary	0.74 (0.55-0.99)		-	
Pulmonary + Extrapulmonary	1.09 (0.77-1.52)		-	
Aids		< 0.001		
Yes	3.15 (2.45-4.04)		-	
No	reference		-	
Diabetes		0.087		
Yes	0.6 (0.3-1.06)		-	
No	reference		-	
Mental illness		0.004		
Yes	2.68 (1.41-4.59)		-	
No	reference		-	
Alcoholism		< 0.001		0.033
Yes	2.19 (1.62-2.91)		1.54 (1.03-2.26)	
No	reference		reference	
Smoking		0.042		
Yes	1.44 (1.01-2)		-	
No	reference		-	
Drug use		< 0.001		
Yes	2.97 (2.19-3.96)		-	
No	reference		-	
HIV serology		< 0.001		< 0.001
Positive	reference		reference	
Negative	0.31 (0.24-0.4)		0.4 (0.29-0.56)	
Not achieved	0.22 (0.14-0.33)		0.51 (0.3-0.85)	
Antiretroviral therapy		0.018		
Yes	reference		-	
No	2.45 (1.17-4.93)		-	

Abbreviations: *Robust Poisson regression model adjusted for gender, age group, race/color/ethnicity, and years of schooling; regarding model adjustment, it presented a VIF between 1.1 and 1.02, which corresponds to non-collinearity, and a pseudo-R^2 0.201, that is, it has the capacity to explain 20.1% of the variation in the dependent variable data.

Employment status was a sociodemographic characteristic associated with the outcome, with a lower prevalence of loss to follow-up among employed or self-employed individuals (OR = 0.64; 95% CI = 0.44-0.93) compared to those who were unemployed. This aspect was also observed for HIV serology, which had a lower prevalence of the outcome in cases with negative results (aRP = 0.4; 95% CI = 0.29-0.56) as opposed to positive tests.

The highest prevalences of loss to follow-up were associated with clinical-epidemiological aspects. For the place of discovery, both urgent/emergency care and diagnostic clarification during hospitalization were associated with discontinuation of treatment, with 1.8 times (95% CI = 1.20-2.76) higher prevalence in urgent/emergency care and 2 times (95% CI = 1.35-3.20) more prevalent in diagnostic clarification when compared to outpatient demand.

For the type of admission, retreatment after loss to follow-up showed a 2.5-fold (95% CI = 1.71-3.85) higher prevalence of a new treatment interruption when compared to admission classified as a new case. Among the diseases and conditions present, only alcoholism showed an association, with a prevalence 1.54 times (95% CI = 1.03-2.26) higher in the loss to follow-up outcome.

DISCUSSION

Analysis of the epidemiological situation of TB based on cases identified in a large university hospital over a 12-year period showed that detection of the disease in this service corresponds to approximately 2% of the municipality's reported cases.

TB notifications over the years showed a similar trend to that observed in the municipality of São Paulo, except for the Covid-19 pandemic period, which went from a reduction in 2020 to a gradual increase in 2022, contrasting with the decrease in cases detected in the hospital over these three years. These changes may be linked to the respiratory symptoms present in both

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diseases and the reorganization of services to contain Covid-19.[7-9]

It should be noted that public calamities are circumstances that intensify social inequalities, as experienced in the Covid-19 pandemic and its implications for TB control in the health sector.[8] From this perspective, with regard to the goals agreed upon by the UN, the pandemic has led to significant setbacks, given the increase in deaths after two decades of decline, posing new challenges for containing the burden of the disease.[10]

The sociodemographic characteristics present in most cases are similar to those found in Brazil and in the municipality of São Paulo, with a predominance of males, black people, of working age, and with low levels of education.[3,7] Another aspect observed is that almost half of the individuals had an occupation, either as an employee or self-employed, and this was a protective factor against loss to follow-up. In fact, the occupational profile found corroborates the findings in a TB reference center, characterizing these individuals as having occupations that require a lower degree of specialization and remuneration.[11]

The sociodemographic profile found in this study, as well as that reported in the literature, reinforces that vulnerability to TB has a social character, being inherent to living and working conditions, given that social groups in less favorable socioeconomic conditions account for the highest proportion of cases of the disease.[12-16]

Regarding the organization of TB control services, the place of discovery is a strategic aspect to be analyzed in order to understand access to the health care network and the actions promoted for disease detection. The study found that 64% of diagnoses were made in the emergency room/emergency department and during hospitalization, with these factors being associated with higher prevalence of loss to follow-up.

In the state of São Paulo, one in four people were diagnosed with TB in emergency departments between 2010 and 2013, with these cases presenting a higher risk of death, discontinuity, and treatment failure compared to those detected in PHC/outpatient clinics. 6 In fact, there is less resolution when seeking initial care in PHC, with a longer time elapsed for TB diagnosis, which motivates patients to seek more complex services based on the perception of rapid resolution of the problem.[5,17,18]

These circumstances indicate the need to strengthen PHC in its role in the healthcare network in order to enhance its capacity for resolution in the face of diseases that require hospitalization, such as TB, considering the cultural motivators of the therapeutic pathway.[5,17,18] To this end, it is imperative to involve other government segments and civil society in the process of addressing and controlling the disease, which is marked by social and health inequalities.[5,15]

One challenge in reducing the chain of disease transmission is cases involving re-treatment after loss to follow-up, as they present a higher chance of recurrence of this unfavorable outcome.[19] Corroborating the findings of the cases under study, which show that retreatment has a 150% higher prevalence of new interruption, a national study that aimed to analyze the factors associated with TB treatment interruption also identified a higher prevalence of these patients repeating the treatment outcome due to discontinuity.[13] Since loss to follow-up is an obstacle to be overcome, special attention is required for the group that includes individuals undergoing retreatment, both in the design and implementation of TB control actions, seeking to provide opportunities for engagement, bonding, and adherence to treatment.[19]

Diseases and associated conditions are established factors influencing loss to follow-up in TB treatment.[12,14,16] In the notifications analyzed, the most common were TB-HIV coinfection and tobacco and alcohol use. However, alcoholism was the only condition that showed a significant association, with a 54% higher prevalence for loss to follow-up. Alcohol use in individuals with TB impairs immunity and increases the possibility of liver damage and, consequently, adverse events. From this perspective, the relationship between substance use and TB infection is harmful, making treatment adherence more difficult and, consequently, increasing treatment interruption and mortality.[12,14,20,21]

Brazilian municipalities face operational difficulties in controlling TB, such as low HIV testing rates.[22] Regarding this test, almost 20% of notifications were HIV-positive, which is a factor of higher prevalence for loss to follow-up; a condition also observed for unfavorable outcomes in a tertiary service in the municipality of Rio de Janeiro.[23] Given the complexity involved in TB-HIV coinfection, ranging from health issues with dual therapy management, leading to adverse events, to social aspects of stigma, this group is more vulnerable to death and loss to follow-up.[24,25]

Therefore, it is worth highlighting the need to strengthen TB control actions, investing in PHC through human and material resources, training that promotes early diagnosis and adherence to treatment, together with social incentives and awareness about TB, considering sociocultural aspects related to stigma and motivation for choosing the service, in addition to addressing social inequalities.

The topic studied and the results found are relevant to the journey towards TB eradication in the municipality of São Paulo, although the limitations present in this investigation are related to the use of secondary data, conditioned by the quality and completeness of the

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notification forms, and having a single health service as the investigation setting, exposing the local reality and, thus, restricting its generalization.

The study made it possible to determine the prevalence of TB cases reported in a university hospital between 2010 and 2022, in terms of their sociodemographic and clinical-epidemiological profile, as well as the factors associated with loss to follow-up, reaffirming a process of illness marked by social determination.

Unemployment, discovery in emergency services/emergency rooms and hospitalization, retreatment, alcohol use, and testing positive for HIV were factors identified with an increased prevalence of loss to follow-up for treatment to be prioritized in the involvement of actions.

Consequently, tackling TB requires a comprehensive approach, through political commitment from public entities and engagement from civil society, in order to transform living conditions and achieve the elimination of the disease.

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AUTHORS' CONTRIBUTIONS

Stephanie Ribeiro contributed to project management, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Claudia Susana Pérez Guerrero** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and review. **Suely Miyuki Yashiro** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and revision. **Nivia Aparecida Pissaia Sanches** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and revision. **Marina Doreto Castilho** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and revision. **Hugo Fernandes** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and revision. **Giselle Lima de Freitas** contributed to project management, bibliographic research, methodology, interpretation of results, conclusions, and revision. **Meiry Fernanda Pinto Okuno** contributed to project management, literature review, methodology, interpretation of results, conclusions, and revision. **Paula Hino** contributed to project management, literature review, writing of the abstract, introduction, methodology, discussion, interpretation 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

Epidemiological profile of leptospirosis in Brazil from 2018 to 2023

Perfil epidemiológico da leptospirose no Brasil de 2018 a 2023
Perfil epidemiológico de la leptospirosis en Brasil de 2018 a 2023

Corresponding author:
E-mail: julucascastellobranco@gmail.com
Address: Dr. José Rocha Junqueira Street, 13, Ponte
Preta, Campinas, São Paulo, Brazil.

Lucas Charuri de Andrade Castello Branco[1]
Barbara Zorzi Sanfins[1]
Fernanda Emanoeli Souza[2]
Amanda Caixeta Campos[1]
Victhor Luiz Senna de Moraes[3]
Guilherme de Andrade Ruela[4]

[1]São Leopoldo Mandic Faculty, Campinas, São Paulo, Brazil.
[2]Paranaense University, Umuarama, Paraná, Brazil.
[3]Federal University of the Jequitinhonha and Mucuri Valleys, Diamantina, Minas Gerais, Brazil.
[4]Federal University of Juiz de Fora - Governador Valadares Advanced Campus, Governador Valadares, Minas Gerais, Brazil.

ABSTRACT

Background and Objectives: Leptospirosis is caused by the bacterium *Leptospira*, which is transmitted in rainy weather. The disease has different manifestations depending on how it develops, and can lead to death. Early detection can prevent serious developments, but there is limited information and standardization of the most affected profile. The objective of this study was to identify the epidemiological profile of leptospirosis from 2018 to 2023 in Brazil. **Methods:** a quantitative study, ecological, with secondary data collection from the Notifiable Diseases Information System (SINAN) and the SUS Hospital Admissions System, using Tabnet/DATASUS, using the following variables: gender, age group, race, schooling, disease progression, years and region of notification. **Results:** there were 16,866 notifications and 1,586 deaths from leptospirosis in Brazil in the period analyzed, with 56.03% of cases progressing to hospitalization and 9.40% to death. The profile most affected was male, aged between 20 and 59, brown, with completed high school. Incidence and mortality rates prevailed in the South, but the fatality rate was higher in the Northeast. **Conclusion:** Although more than half of leptospirosis cases progress to hospitalization, patients have more than an 80% chance of cure. Therefore, this study helped in the more current recognition of leptospirosis cases, in order to contribute to policies to prevent and control the disease.
Keywords: *Health Profile. Epidemiology. Leptospirosis. Deaths. Brazil.*

RESUMO

Justificativa e Objetivos: A leptospirose é causada pela bactéria *Leptospira*, que possui transmissão associada e intensificada por climas chuvosos. A doença apresenta diferentes manifestações a depender da evolução, podendo levar ao óbito do portador. A detecção precoce pode prevenir evoluções graves, porém há limitações de informações e padronização do perfil mais acometido. O objetivo deste estudo foi identificar o perfil epidemiológico da leptospirose de 2018 a 2023 no Brasil. **Métodos:** estudo quantitativo, ecológico, com coleta de dados secundários no Sistema de Informação de Agravos de Notificação (SINAN) e no Sistema de Internações Hospitalares do SUS (SIH/SUS), por meio do Tabnet/DATASUS, utilizando-se as variáveis: sexo, faixa etária, raça, escolaridade, evolução, anos e região de notificação. **Resultados:** ocorreram 16.866 notificações e 1.586 mortes por leptospirose no Brasil no período analisado, com evolução para internação em 56,03% dos casos e óbitos em 9,40%. O perfil mais afetado foi pacientes do sexo masculino, de 20 a 59 anos, pardos, com ensino médio completo. As taxas de incidência e mortalidade prevaleceram no Sul, porém a taxa de letalidade foi maior no Nordeste. **Conclusão:** Apesar de mais da metade dos casos de leptospirose evoluírem para internação, os pacientes apresentam mais de 80% de probabilidade de cura. Portanto, este estudo auxiliou no reconhecimento mais atual dos casos de leptospirose, a fim de contribuir com políticas de prevenção e controle da doença.
Descritores: *Perfil de Saúde. Epidemiologia. Leptospirose. Morte. Brasil.*

RESUMEN

Justificación y Objetivos: La leptospirosis es causada por labacteria *Leptospira*, que tiene asociada una transmisión que se intensifica en climas lluviosos. La enfermedad tiene distintas manifestaciones según su evolución y puede conducir a la muerte. La detección precoz puede evitar una evolución grave, pero la información y la normalización del perfil más afectado son limitadas. El objetivo de este estudio fue identificar el perfil epidemiológico de la leptospirosis de 2018 a 2023 en Brasil. **Métodos:** estudio cuantitativo, ecológico, con recolección de datos secundarios del Sistema de Información de Enfermedades de Declaración Obligatoria (SINAN) y del Sistema de Internación Hospitalaria del SUS, utilizando Tabnet/DATASUS, con las siguientes variables: sexo, grupo de edad, raza, escolaridad, evolución, años y región de notificación. **Resultados:** Hubo 16.866 notificaciones y 1.586 muertes por leptospirosis en Brasil durante el período analizado, con 56,03% de los casos evolucionando a hospitalización y 9,40% a muerte. El perfil más afectado fue hombres, de entre 20 y 59 años, morenos, con estudios secundarios completos. Las tasas de incidencia y mortalidad prevalecieron en el Sur, pero la tasa de mortalidad fue mayor en el Noreste. **Conclusión:** Aunque más de lamitad de los casos de leptospirosis requieren hospitalización, los pacientes tienen más del 80% de posibilidades de curarse. Por lo tanto, este estudio ayudó a reconocerlos casos de leptospirosis de forma más actualizada, con el fin de contribuir a las políticas de prevención y control de la enfermedad.
Palabras Clave: *Perfil de Salud. Epidemiología. Leptospirosis. Muertes. Brasil.*

INTRODUCTION

Leptospirosis is a zoonosis with a global distribution and is endemic throughout Brazil.[1] Caused by the bacterium *Leptospira*, the disease is typically transmitted through direct contact with the mucous membranes or broken skin of humans, who are accidental hosts, or indirectly through water or food contaminated with the urine of rodents infected with the microorganism.[2] Studies indicate that the incidence of infection is strongly associated with tropical and subtropical climates, due to frequent rainy periods that favor the transmission cycle. Brazil is particularly prone to the development of the disease, especially in regions with high rainfall and densely populated urban centers characterized by poor social, environmental, and sanitary conditions.[3,4]

Recent studies estimate the occurrence of approximately 1.03 million new cases and 58,900 deaths from leptospirosis each year worldwide. Despite these alarming figures, leptospirosis remains a neglected disease of major global importance.[5] In Brazil, between 2016 and 2019, an average of 3,926 cases were reported annually, with a fatality rate of 8.9%. The high incidence results in significant public health expenditures, including hospital costs and productivity losses due to workers' absences, thereby affecting individual and household incomes.[6]

The clinical presentation of the disease is variable, ranging from asymptomatic or subclinical forms to severe cases that may result in death. The Brazilian Ministry of Health reported that the overall case fatality rate for leptospirosis is approximately 9%, rising to over 50% in cases that progress to pulmonary hemorrhage.[7]

Furthermore, several complications may occur, including electrolyte imbalances, pancreatitis, anemia, aseptic meningitis, myocarditis, acute respiratory failure, neurological disorders, vascular lesions, and acute renal failure, which, in advanced stages, can lead to acute tubular necrosis.[5,7]

Leptospira comprises hundreds of infectious serovars, each with distinct pathogenicity. Consequently, symptom severity may vary depending on the infecting serovar, with some strains causing more aggressive disease manifestations.[8] Recent studies have shown that the serovars Icterohaemorrhagiae, Copenhageni, Canicola, and Pomona are the most prevalent in Brazil, with the first two being most commonly associated with severe clinical outcomes.[9]

The progression of the disease is commonly associated with late diagnosis and inadequate treatment, causing the condition to worsen rapidly.[10] Therefore, early and accurate detection can prevent deaths from leptospirosis.[11] Management is not always correct due to limited information or lack of standardization of clinical investigation.[12]

Leptospirosis is known to be an occupational disease, very common among workers in cattle, rice, sugarcane, sewage, and other at-risk groups, all of whom perform activities in highly humid environments that favor the transmission of the pathogen.[13] However, there is currently no predictive or scoring model that indicates which patients are most likely to develop the severe form.[5] To assist in identifying the most susceptible individuals during clinical diagnosis and identify the regions with the greatest need for more effective prevention and control measures, new, updated studies addressing this topic at the national level are necessary, as these are fundamental for public health management in Brazil. Targeted searches of the PubMed and SciELO databases were conducted in May 2025, using the descriptors "leptospirosis," "epidemiology," "Brazil," and "profile," filtered for the period 2018–2023. The search yielded 14 studies, none of which addressed the national context, demonstrating the need for further study on this topic.

Given the lack of recent research on the most affected regions and population groups, this study aims to identify the epidemiological profile of leptospirosis from 2018 to 2023 in Brazil.

METHODS

This is a quantitative, ecological study, collecting secondary data on the epidemiological profile of leptospirosis in Brazil from 2018 to 2023. Data were collected from the Notifiable Diseases Information System (SINAN) and the SUS Hospital Admissions System (SIH/SUS), managed by the Health Surveillance Secretariat in conjunction with state and municipal health departments. These data are available on the website of the Unified Health System Information Technology Department (DATASUS), accessed on August 6, 2024.

The study population comprises all reported cases and hospitalizations for leptospirosis during the period and throughout the country analyzed.

Data collection used the variables sex, age group, race, education level, progression, years, and region of notification, which were extracted from SINAN, and the variables region and year of care, which were extracted from SIH/SUS. Reported cases were used in the SINAN database, and hospitalizations for icterohemorrhagic leptospirosis, other forms of leptospirosis, and unspecified leptospirosis were used in the SIH/SUS database. The inclusion criteria were all reported cases of leptospirosis in the SINAN database and all hospitalizations for icterohemorrhagic leptospirosis, other forms of leptospirosis, and unspecified leptospirosis in the SIH/SUS database. There were no exclusion criteria.

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Subsequently, a descriptive statistical analysis of the variables was performed using Microsoft Excel® (version 2504), presented as proportions and absolute numbers in the results. The indicators calculated and presented were incidence, incidence rate, mortality rate, and case-fatality rate. Furthermore, the denominator used to calculate the rates was the population from the 2022 census, conducted by the Brazilian Institute of Geography and Statistics (IBGE). No association or significance tests were used, as this is a descriptive study.

Because the study was conducted using secondary, public domain data sources, with the individuals' identities protected, submission to the Research Ethics Committee was not required, in accordance with Resolution No. 510/2016 of the National Health Council.

RESULTS

A total of 16,866 cases of leptospirosis were recorded in Brazil during the analyzed period. The South and Southeast regions had the highest number of cases in total, with 5,516 and 5,387 cases, respectively, followed, in decreasing order, by the Northeast (3,348), North (2,263) and Central-West, with 352 (Figure 1).
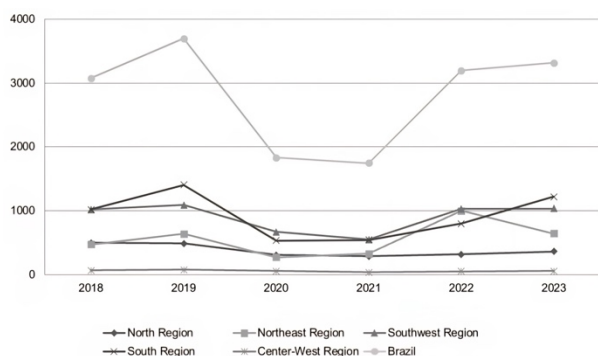
Figure 1. Leptospirosis cases by region and year of notification, Brazil, 2018-2023.

The regions that presented the highest incidence rates of leptospirosis per 100,000 inhabitants, in the period analyzed, were the South (18.42) and North (13.03), with the Central-West being the region that presented the lowest rate (2.16) (Table 1).

Table 1. Incidence rate of leptospirosis per 100,000 inhabitants from 2018 to 2023.

	Incidence per 100,000 inhabitants
Country	
Brazil	8.30
Regions	
North	13.03
Northeast	6.12
Southeast	6.34
South	18.42
Central-west	2.16

The highest number of cases occurred in 2019, with 3,698 cases, and in 2023, with 3,318. The lowest number occurred in 2021, with 1,744 cases. Despite the reduction in cases at the beginning of the years studied, there was an increase in cases in 2022 and 2023 (Figure 2).

There were 11,466 hospitalizations due to leptospirosis in Brazil during the period analyzed, suggesting that 67.98% of cases likely progressed to hospitalization, although the percentage is uncertain due to data being taken from different databases and possibly inconsistent in some records. The South and Southeast regions had the highest total hospitalizations, with 3,981 and 3,318, respectively, followed, in descending order, by the Northeast (2,731), North (1,263), and Central-West (173). The highest number of hospitalizations occurred in 2019, with 2,666, and the lowest in 2021, with 1,159 (Figure 2).

Regarding disease progression, 80.03% of cases were cured and 9.40% resulted in death from the reported condition (Table 4). The Southeast and Northeast regions had the highest number of deaths from the disease in total, with 665 and 438 deaths, respectively, followed, in decreasing order, by the South (304), North (150) and Central-West, with 29. The highest number of deaths from the reported disease occurred in 2019, with 325 deaths and 2022, with 320. The lowest number occurred in 2021, with 181 deaths (Figure 2).
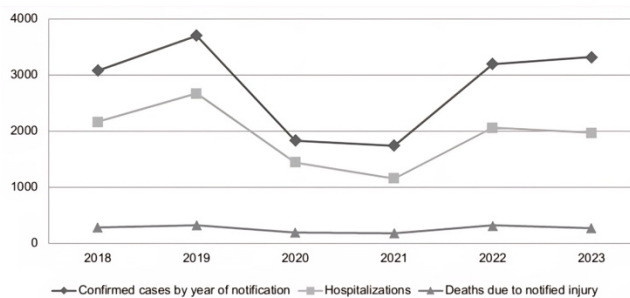
Figure 2. Leptospirosis cases, hospitalizations, and deaths by year of notification, Brazil, 2018-2023.

The regions that presented the highest mortality rates due to leptospirosis per 1,000,000 inhabitants, in the period analyzed, were the South (10.15) and North (8.64), with the Central-West region presenting the lowest rate (1.78) (Table 2).

Table 2. Leptospirosis mortality rate per 1,000,000 inhabitants from 2018 to 2023.

	Deaths per 1,000,000 inhabitants
Country	
Brazil	7.80
Regions	
North	8.64
Northeast	8.01
Southeast	7.83
South	10.15
Central-west	1.78

The regions with the highest fatality rates for leptospirosis in Brazil were the Northeast and Southeast, with 13.08% and 12.34%, respectively, while the South region had the lowest rate, with 5.51% (Table 3). The highest fatality rate occurred in 2020 (10.58%) and the lowest in 2023 (8.31%).

Table 3. Leptospirosis fatality rate from 2018 to 2023.

	Fatality rate
Country	
Brazil	9.40%
Regions	
North	6.62%
Northeast	13.08%
Southeast	12.34%
South	5.51%
Central-west	8.23%

Cases were more frequent in males, with 13,846 cases (82.09%), in the age group of 20 to 39 years, with 6,391 notifications (37.89%) and in individuals of mixed race, with 7,160 cases (42.45%). Although most notifications of leptospirosis ignored or left blank the field of education of the patients, it was noted that, when this variable was informed, patients with complete secondary education were the most affected, with 2,363 cases (14.01%) (Table 1).

Table 4. Demographic profile of confirmed cases of leptospirosis in Brazil, 2018-2023 (n=16.866).

	N (%)
Gender	
Ignored	1 (0.01)
Female	3.019 (17.90)
Male	13.846 (82.09)
Age range	
Blank/Ignored	2 (0.01)
<1 year	101 (0.60)
1-4 years	67 (0.40)
5-9 years	279 (1.65)
10-14 years	613 (3.63)
15-19 years	1.234 (7.32)
20-39 years	6.391 (37.89)
40-59 years	6.061 (35.94)
60-64 years	949 (5.63)
65-69 years	560 (3.32)
70-79 years	505 (2.99)
>80 years	104 (0.62)
Race	
Indigenous	69 (0.41)
Yellow	101 (0.60)
Black	1.074 (6.37)
Ignored/White	1.489 (8.83)
White	6.973 (41.34)
Brown	7.160 (42.45)
Education	
Unknown/Blank	7.226 (42.84)
Illiterate	180 (1.07)
Incomplete 1st to 4th grade of elementary school	1.130 (6.70)
Complete 4th grade of elementary school	688 (4.08)
5th to 8th grade of elementary school	1.988 (11.79)
Complete elementary school	1.168 (6.93)
Incomplete high school	1.148 (6.81)
Complete high school	2.363 (14.01)

	N (%)
Incomplete higher education	215 (1.27)
Complete higher education	491 (2.91)
Not applicable	269 (1.59)
Outcome	
Unknown/Blank	1.581 (9.37)
Cure	13.498 (80.03)
Death due to the notified cause	1.586 (9.40)
Death due to another cause	201 (1.20)

DISCUSSION

Leptospirosis is considered the most widespread zoonotic disease worldwide.[15] According to studies analyzing leptospirosis prevalence data, Brazil ranks third among countries in the Americas.[16] However, this study examined incident cases of the disease reported in the Notifiable Diseases Information System (SINAN), which revealed the presence of leptospirosis in all Brazilian regions, although in varying proportions.

It is important to note that data on leptospirosis-related deaths were obtained from SINAN, not from the Mortality Information System (SIM), as the focus of this study was specifically on the outcome variable, not solely on deaths. In other words, we analyzed the number of incident cases, the number of recovered cases, deaths from the notified disease, and deaths from other causes.

Leptospirosis was initially described in rural environments; however, with globalization, it has become increasingly common in urban areas—particularly in less developed nations with low socioeconomic conditions and inadequate sanitation.[16] In this context, understanding the spatial distribution of leptospirosis is crucial for the effective planning of preventive measures.

The incidence of infection is strongly associated with tropical and subtropical climates, as well as regions with high rainfall.[16] The tropical climate predominates in the Southeast and Central-West regions, while the subtropical climate occurs mainly in the South of Brazil.[17] When considering incidence rates per 100,000 inhabitants, this study observed that the South region presented the highest rate in the country, followed by the North and Southeast regions—consistent with the association between the infection and areas of high rainfall. However, a divergence was identified in the Central-West region, which had the lowest incidence rate among all regions. This contrasts with expectations for a predominantly tropical region, given its climatic association with the disease. This lower-than-expected reporting pattern may indicate an actual reduction in cases due to lower population density, reporting delays, underreporting, or clinical similarities with other diseases that lead to underdiagnosis.[18]

A study analyzing the prevalence of leptospirosis in the Americas found a higher concentration of cases in

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countries with tropical and subtropical climates, such as Colombia and Brazil, with prevalence rates of 29% and 21%, respectively.[13] Although these data cannot be directly compared to the findings of the present study—which focuses on the incidence of reported cases—they align in showing a greater occurrence of leptospirosis in hot and humid regions. Nevertheless, it is important to emphasize that each country exhibits distinct epidemiological characteristics related to the disease's behavior. For instance, a study revealed differences in seasonal patterns between São Paulo, where hospitalizations due to leptospirosis were seasonal and peaked during the rainy season, and Colombia, which showed no seasonality despite having a bimodal precipitation regime across most of its territory.[19]

Similarly, a study analyzing the spatial and temporal incidence of leptospirosis in northeastern Argentina found that warmer, more humid climates were most frequently associated with the disease. In Argentina, leptospirosis is seasonal, with the highest number of cases and outbreaks recorded during warmer seasons with moderate temperatures, and flooding events emerging as the main risk factor.[12] Therefore, understanding both the similarities and differences in leptospirosis patterns across regions is essential to correctly identify risk factors and the epidemiological profile for each location, enabling more targeted and effective preventive measures.

Regarding the temporal evolution of leptospirosis cases, one study found that climate change—driven by rising global surface temperatures—poses a major challenge to public health, contributing to the emergence and reemergence of many communicable diseases, including waterborne diseases such as leptospirosis. In this context, the present study showed a considerable increase in leptospirosis cases in Brazil between 2018 and 2023, except in 2020 and 2021, when the numbers declined compared to previous years. Thus, the increasing incidence of leptospirosis in Brazil from 2018 to 2023 is a reality. However, establishing a causal relationship with climate change would require the analysis of specific environmental data, which was beyond the scope of this study.[20]

This study also demonstrated that approximately 68% of reported leptospirosis cases with monitored outcomes progressed to hospitalization, highlighting the high hospital morbidity associated with the disease in Brazil.

A comparison with a study that analyzed leptospirosis in Brazil and Alagoas between 2009 and 2019 revealed cure and mortality rates similar to those found in the present study (2018–2023): approximately 83.1% of patients recovered, while 8.6% died from the disease.[21] These findings suggest a possible pattern of stability in cure and mortality rates over time. Another study from 2005 reported an average case fatality rate of 12% in Brazil, a value close to that observed in the regions with

the highest fatality rates in the current study.[22] Together, these observations indicate a relative stability in the cure and mortality rates of leptospirosis over the years, suggesting that despite regional variations, there is a temporal trend toward homogeneity between the most affected regions and the country as a whole.

Comparing the epidemiological profile of leptospirosis cases in Brazil with a previous study covering the years 2007 to 2015, sex and age criteria were evaluated. Regarding sex, in the 2007 to 2015 study, men were more affected by human leptospirosis than women, with the most affected age group being 20 to 59 years old. This data remained unchanged for the period evaluated in this study (2018-2023).[23]

The age group affected is directly related to individuals of working age, with this disease having a strong association with occupational activities, especially in the agricultural sector and waste collection and separation, which can lead to economic losses for the country.[24] The greater incidence among males is due to their greater propensity and vulnerability to acquiring diseases due to their greater exposure to risk factors, whether environmental, behavioral, or cultural. Associated with this, they often do not seek health services until the disease worsens.[25]

Other variables that can be compared between the two studies are the categories of race/ethnicity and education. In a study that addressed leptospirosis as a doubly neglected disease in Brazil, Martins identified that between 2007 and 2015, the most prevalent color/race in leptospirosis cases were, in decreasing order of number of cases: white, brown, black, yellow and indigenous, while the classification of education of the most affected individuals, in decreasing order, by leptospirosis, were cases in which education was ignored, incomplete 5th to 8th grade, and complete high school. The two educational levels with the lowest number of leptospirosis cases were complete higher education and incomplete higher education.[23]

Compared to the present study, the only change observed in the color/race item was the inversion of white for brown, so that the latter became the predominant color among leptospirosis cases.[23] The variation in the disease incidence among brown individuals is also due to the increase in the number of cases, especially in the Central-West region, where this race predominates.[26] Regarding educational level, when comparing the profile from 2007 to 2015, it was found that the three previously mentioned categories remain the most prevalent in the population profile of leptospirosis. However, only an inversion was observed among individuals who had incomplete 5th to 8th grades and completed high school.[23] This can be interpreted as an improvement in the evolution of educational development in Brazil, reflecting the data indicated in

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The country's education levels.[27] The education levels with the lowest number of cases remained the same.

Based on these analyses, it can be seen that there were no significant changes in the epidemiological profile of leptospirosis between 2007 and 2015 and 2018 and 2023. Therefore, according to the results of this study, the people most affected by this disease are men, aged between 20 and 59, of mixed race, and with less education.[23] The limited variation in this profile allows for the continuation of prevention efforts without the need for major changes in planning in the most affected areas. Furthermore, it facilitates the development of control measures in regions that have seen an increase in cases compared to previous years.

However, it is important to emphasize that this study has certain limitations. The first is that it is an ecological study, therefore not suitable for identifying cause-and-effect relationships. Other limitations include possible underreporting, as data were collected only from DATASUS. Therefore, not considering information about supplementary services, including health plans, insurance, and private services, may reduce the true number of leptospirosis cases. It is worth noting that potential errors were avoided through careful analysis of the information generated in tables by DATASUS, allowing more than one participating member to make observations and checks to avoid potential biases. Furthermore, the SIH only records SUS hospitalizations, meaning the number of hospitalizations may be even higher than reported in the system. Finally, we used the 2022 demographic census conducted by IBGE as the denominator for calculating leptospirosis incidence and mortality rates. However, the analysis covered the period from 2018 to 2023, so the population in other years is not necessarily the same as in the 2022 census.[27]

According to the results obtained in the study, it is concluded that the epidemiological profile of leptospirosis cases in Brazil, during the analyzed period, was male patients, aged between 20 and 59 years old, of mixed race, and with a high school diploma. The incidence and mortality rates prevailed in the South and North, but the fatality rate was higher in the Northeast and Southeast. Although leptospirosis has an incidence of 8.30 per 100,000 inhabitants, its fatality rate is only 7.30 per 1,000,000 inhabitants, demonstrating a high cure rate among those affected. Because leptospirosis is more prevalent in certain climatic and socioeconomic conditions, the studies presented demonstrate that it follows a specific pattern of affected patients and regional distribution over time in Brazil. This suggests that it will likely continue this trend in the coming years. Therefore, further studies analyzing the distribution of leptospirosis and its relationship with climate factors are necessary to continually update information about this disease in the country and thus enable the development of effective measures to contain it.

Therefore, despite its limitations, it is believed that this study helped identify individuals most susceptible to the disease and identify the regions with the highest cases and morbidity and mortality outcomes, contributing to more multidisciplinary public policies for disease prevention and control, as well as health education strategies for the national population.

Although the data were collected in DATASUS, a platform that gathers information on a wide range of diseases and procedures performed in the country, the literature indicates deficiencies in the quantity, accuracy, and integration of the data. A study evaluated and compiled the limitations of using DATASUS as a data source in research and found that there are absences of clinical and individual information that are not collected from patients or entered into the platform, a reliance on filling out forms in hospitals, and underreporting due to the lack of data from private resources or regional coverage limitations due to differences in population densities and access to the health system, in addition to the period of the Covid-19 pandemic, which may have reduced the number of reported cases in 2020 and 2021.

However, DATASUS is an important tool for data collection in ecological quantitative research, as it integrates data at the national level, gathers information from various databases, and is widely used for calculating indicators, population trends, disease distribution, and planning for the country's public health policies.

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AUTHORS' CONTRIBUTIONS

Lucas Charuri de Andrade Castello Branco contributed to the abstract, methodology, interpretation and description of results, conclusions, review, and statistics. **Barbara Zorzi Sanfins** contributed to the abstract, methodology, interpretation and description of results, conclusions, review, and statistics. **Fernanda Emanoeli Souza** contributed to the bibliographic research, abstract writing, introduction, discussion, table preparation, figures, and review. **Amanda Caixeta Campos** contributed to the bibliographic research, introduction, discussion, and review. **Victhor Luiz Senna de Moraes** contributed to the bibliographic research, discussion, and review. **Guilherme de Andrade Ruela** contributed to the supervision, writing, and review of the article.

All authors have 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

Vulvovaginal candidiasis: prevalence and antifungal susceptibility of species isolated from women living in recôncavo baiano

Candidíase vulvovaginal: prevalência e suscetibilidade antifúngica de espécies isoladas de mulheres residentes no recôncavo baiano

Candidiasis vulvovaginal: prevalencia y susceptibilidad antifúngica de especies aisladas en mujeres residentes en recôncavo baiano

Corresponding author:
E-mail: caulordelo@hotmail.com
Address: Anísio Teixeira Street, Dona Rosa Condominium 213, Downtown, Cruz das Almas, Bahia, Brazil.

Cássia Vargas Lordêlo[1] (ID)
Jakeline Souza Torres[2] (ID)
Alexsandra dos Santos Campos[3] (ID)
Manuela Fraga Fernandes e Silva[3] (ID)
Ricardo David Couto[1] (ID)
Tânia Fraga Barros[1] (ID)

[1]Federal University of Bahia, School of Pharmacy, Graduate Program in Pharmacy, Salvador, Bahia, Brazil.
[2]Maria Milza University Center, Regional Development and Environment Program, Governador Mangabeira, Bahia, Brazil.
[3]Federal University of Bahia, School of Pharmacy, Institutional Scientific Initiation Scholarship Program, Salvador, Bahia, Brazil.

ABSTRACT

Background and Objectives: *Candida albicans* is the species most implicated in vulvovaginal candidiasis, but its adaptive and virulence characteristics have contributed to the increase in *non-albicans* yeast species. Resistance mechanisms make drug treatment difficult. The aim of the study was to evaluate the prevalence of vulvovaginal candidiasis, its etiological agents and antifungal susceptibility profiles. **Methods:** This was an observational, cross-sectional study involving 358 women living in the Recôncavo Baiano. Molecular tests were used to identify the isolated species and antifungal analysis to determine the antifungal susceptibility profile. Fisher's exact test was used to calculate associations. **Results:** The prevalence of vulvovaginal candidiasis was 10,89% (39/358). *C. albicans* was most common (64%-37/58), followed by 12% (7/58) each of *Nakaseomyces glabratus* and *C. parapsilosis*, 7% (4/58) *C. tropicalis*, 3% (2/58) *Meyerozyma guilliermondii* and 2% (1/58) *Pichia kudriavzevii*. Pruritus and bleeding were associated with vulvovaginal candidiasis caused by *C. albicans*. Itraconazole and miconazole showed greater variability in the susceptibility profile. Resistance to itraconazole was reported in *N. glabratus*. **Conclusion:** The results obtained indicate that *C. albicans* continue to be the predominant species in cases of VVC and, together with other species, may present resistance to the antifungals tested.
Keywords: *Fungi. Vulvovaginitis. Antimycotics. Vulvar Pruritus. Resistance.*

RESUMO

Justificativa e Objetivos: *Candida albicans* é a espécie mais comumente implicada na candidíase vulvovaginal, mas suas características adaptativas e de virulência contribuíram para o aumento de espécies de leveduras *não-albicans*. Mecanismos de resistência eficientes e sofisticados têm dificultado a terapia farmacológica e preocupado a comunidade científica, uma vez que o número de antifúngicos é limitado. O objetivo do estudo foi avaliar a prevalência da candidíase vulvovaginal, dos seus agentes etiológicos e perfis de suscetibilidades antifúngicas. **Métodos:** Estudo observacional, de corte transversal, envolvendo 358 mulheres residentes no Recôncavo Baiano. Testes moleculares foram utilizados para identificação das espécies isoladas, bem como antifungigrama para determinar o perfil de sensibilidade antifúngica. O Teste exato de Fisher foi utilizado para calcular associações. **Resultados:** A prevalência de candidíase vulvovaginal foi de 10,89% (39/358). *C. albicans* foi mais prevalente (64%-37/58), seguida de 12% (7/58) cada de *Nakaseomyces glabratus* e *C. parapsilosis*, 7% (4/58) *C. tropicalis*, 3% (2/58) de *Meyerozyma guilliermondii* e 2% (1/58) de *Pichia kudriavzevii*. Prurido e sangramento foram associados à candidíase vulvovaginal por *C. albicans*. Itraconazol e miconazol apresentaram maior variabilidade no perfil de sensibilidade. Resistência foi relatada por *N. glabratus* ao itraconazol. **Conclusão:** Os resultados obtidos indicam que *C. albicans* continua sendo a espécie predominante em casos de candidíase vulvovaginal e, juntamente com outras espécies, pode apresentar resistência aos antifúngicos testados.
Descritores: *Fungos. Vulvovaginite. Antimicóticos. Prurido Vulvar. Resistência.*

RESUMEN

Justificación y Objetivos: *Candida albicans* es la especie más comúnmente implicada en la candidiasis vulvovaginal, pero sus características adaptativas y de virulencia han contribuido al aumento de especies de levaduras *no albicans*. Mecanismos de resistencia han dificultado el tratamiento farmacológico. El objetivo del estudio fue evaluar la prevalencia de candidiasis vulvovaginal, sus agentes etiológicos y los perfiles de susceptibilidad antifúngica. **Métodos:** estudio observacional transversal donde participaron 358 mujeres residentes en el Recôncavo Baiano. Para identificar las especies aisladas se utilizaron pruebas moleculares y, para determinar el perfil de susceptibilidad antifúngica, pruebas antifúngicas. Se utilizó la prueba exacta de Fisher para calcular las asociaciones. **Resultados:** prevalencia de candidiasis vulvovaginal fue del 10,89 % (39/358). *C. albicans* fue la más prevalente (64%), seguida de un 12% (7/58) de *Nakaseomyces glabratus* y *C. parapsilosis*, un 7% (4/58) de *C. tropicalis*, un 3% (2/58) de *Meyerozyma guilliermondii* y un 2% (1/58) de *Pichia kudriavzevii*. Prurito y sangrado se asociaron a la candidiasis vulvovaginal causada por *C. albicans*. El itraconazol y el miconazol mostraron una mayor variabilidad en el perfil de sensibilidad. Se registró resistencia a itraconazol en *N. glabratus*. **Conclusiones:** Los resultados obtenidos indican que *C. albicans* sigue siendo la especie predominante en los casos de VVC y, junto con otras especies, puede presentar resistencia a los antifúngicos ensayados.
Palabras Clave: *Hongos. Vulvovaginitis. Antimicóticos. Prurito Vulvar. Resistencia.*

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Cássia Vargas Lordêlo, Jakeline Souza Torres, Alexsandra dos Santos Campos, Manuela Fraga Fernandes e Silva, Ricardo David Couto, Tânia Fraga Barros

INTRODUCTION

Vulvovaginal candidiasis (VVC) is a common, non-life-threatening fungal infection of the female reproductive tract. This condition is the second leading cause of vulvovaginitis worldwide and has a significant impact on women's physical and mental health and overall functioning.[1] Several risk factors, signs, symptoms, diagnostic methods, microorganism species, virulence factors, and treatment options are relevant to understanding and effectively addressing VVC.[2]

Approximately 75% of women will experience at least one episode of VVC in their lifetime, with Candida albicans responsible for approximately 80% to 90% of cases.[3] However, other species, such as *Nakaseomyces glabratus* (*Candida glabrata*), *Candida tropicalis*, *Pichia kudriavzevii* (*Candida krusei*), and *Candida parapsilosis*, may also be involved. Each species has unique characteristics that influence its virulence, response to treatment, and propensity to cause recurrent infections.[4]

As microorganisms of the vaginal microbiota, yeasts of the albicans and non-albicans species commonly colonize the vaginal lumen asymptomatically. However, symptomatic infection results from their excessive growth, followed by epithelial invasion and production of virulence factors that result in mucosal inflammation.[5]

Common symptoms may vary in intensity and frequency, including hyperemia, pruritus, and burning in the genital region. In addition, pain may occur during sexual intercourse and urination. These symptoms are often accompanied by thick, white vaginal discharge, consisting of desquamated epithelium, immune cells, yeast, and vaginal fluid. The recurrent presence of these signs and symptoms, with episodes more than four times throughout the year, characterizes recurrent candidiasis.[6]

Several factors increase women's susceptibility to fungal vulvovaginitis. One of the main risk factors is the indiscriminate use of antibiotics, which can alter the balance of the vaginal microbiota, favoring the overgrowth of *albicans* and *non-albicans* species. Other factors include pregnancy, uncontrolled diabetes mellitus, compromised immune system, prolonged use of corticosteroids, oral contraceptives, smoking, and the use of synthetic underwear that promotes moisture.[7]

The diagnosis of VVC is usually clinical, based on symptoms and physical examinations. Laboratory diagnosis can be made presumptively by identifying the presence of yeast through direct Gram and Papanicolaou staining tests and confirmatory mycological tests, such as culture or molecular tests.[2,8]

Although the Papanicolaou test plays an important role in women's health by identifying inflammatory processes and yeast-like structures, it is not able to distinguish the species of fungus involved in vulvovaginitis or assess the sensitivity profile to antifungal agents. Thus, mycological diagnosis is essential because it covers these particularities.[9]

Treatment of VVC usually involves drug therapy with antifungal agents, which can be administered orally, topically, or intravaginally. The most commonly prescribed drugs are azoles, which include compounds such as ketoconazole, miconazole, clotrimazole (imidazoles), fluconazole, and itraconazole (triazoles) and polyene agents such as nystatin. However, sensitivity to antifungals varies between species, and resistance mechanisms have compromised drug therapy, highlighting the need for specific identification of the yeast and sensitivity testing to establish appropriate therapy.[10,11]

Considering the scarcity of scientific studies related to VVC in the state of Bahia, the objective of this study was to evaluate the prevalence of vulvovaginal candidiasis, its etiological agents, and antifungal susceptibility profiles. We hope that the results will have a positive impact on the health of women in this region by providing clinical and laboratory information that can help in safe diagnosis and a more effective therapeutic approach against this infection.

METHODS

An observational, cross-sectional study conducted between August 2021 and November 2023, comprising women aged between 18 and 65 years old, residing in the Recôncavo Baiano region: Governador Mangabeira, Cruz das Almas, and Sapeaçu. The municipalities were chosen based on their proximity to the Maria Milza University Center (UNIMAM) laboratory, where the initial microbiological tests were carried out, at distances of approximately 5, 8, and 20 km, respectively. Three Primary Care Center, one in each municipality, were selected because they had better physical structures in the collection rooms, a higher flow of patients, and the availability of nurses to perform the collections.

Women who spontaneously sought public health services to undergo a Pap smear participated in the study, agreeing to sign the Free and Informed Consent Form. Pregnant women, postpartum women, women with no history of sexual activity, and women who had undergone treatment for any urogenital tract pathology in the last 12 months were excluded. Cervical-vaginal samples were collected at the time of the cytopathological examination of the cervix, using a sterile swab containing Amies transport medium.

Cervical samples

The cervicovaginal samples collected were cultured in Sabouraud Dextrose Agar (SDA) (ACUMEDIA, USA)

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VULVOVAGINAL CANDIDIASIS: PREVALENCE AND ANTIFUNGAL SUSCEPTIBILITY OF SPECIES ISOLATED FROM WOMEN LIVING IN RECÔNCAVO BAIANO

Cássia Vargas Lordêlo, Jakeline Souza Torres, Alexsandra dos Santos Campos, Manuela Fraga Fernandes e Silva, Ricardo David Couto, Tânia Fraga Barros

supplemented with chloramphenicol and, after 48 hours of incubation at 35±1°C, positive cultures were subjected to Gram staining to confirm yeast. Direct examination of the sample by Gram staining was not used to assess the presence of yeast, but rather a Papanicolaou cytological examination. Hyphae or pseudo-hyphae morphology was not considered a criterion for pathogenicity, since non-albicans yeast species, even if they do not produce them, can be responsible for infectious processes because they present several other virulence factors.[12]

Species identification was performed using the molecular technique PCR-RFLP (Polymerase Chain Reaction - Restriction Fragment Length Polymorphism) technique, where the intergenic spacer region (ITS) of rDNA was amplified with the primers ITS1 (5´TCCGTAGGTGAACCTGCGG3´) and ITS4 (5´TCCTCCGCTTATTGATAGC3´) with GoTaq® Green Master Mix (PROMEGA). The reaction was performed in a MyCycler thermocycler (Bio Rad) under the following conditions: 2 min at 94°C, 35 cycles of 1 min at 95°C, 1 min at 51°C, 2 min at 72°C, and 10 min at 72°C. The negative control was performed with Mili-Q water and the positive control with the standard strain *C. albicans* ATCC 90028. The PCR product was used in restriction with *Hpa* II and *FspB* I enzymes (Thermo Fisher Scientific), separately.[13]

Antifungal susceptibility tests were performed based on the disk diffusion technique as described in protocol M44, using disks of fluconazole (25 μg), itraconazole (10 μg), miconazole (50 μg), nystatin (100 IU), clotrimazole (50 μg), and ketoconazole (50 μg) - CECON).[14]

Signs and symptoms of vaginal bleeding after sexual intercourse, itching and burning in the vaginal region, presence of thick white vaginal discharge (leucorrhea), and changes in the cervix/vagina, including edema, hyperemia, excoriations, fissures, and/or lesions, were evaluated based on information recorded by the nurse responsible for collecting the cytopathological examination request.

The diagnosis of VVC was defined when study participants simultaneously presented a positive yeast culture and any of the signs/symptoms described above.

Data were analyzed using GraphPad InStat version 3.05. Fisher's exact test, with a significance level of 5%, was performed to determine the association of VVC with possible risk factors, clinical signs, and symptoms. Descriptive statistics were presented in the form of tables and graphs.

This study is part of a project and was approved by the Research Ethics Committee (REC) of Maria Nilza University (UNIMAM), opinion No. 7,281,350, CAAE No. 36887120.6.0000.5025. During the study, strict patient confidentiality was maintained.

RESULTS

The study consisted of 358 women, with a mean age of 41 ± 11.8 years, years old, with 10.9% (39/358) between 18 and 24 years old, 53.3% (191/358) between 25 and 45 years old, and 35.8% (128/358) between 46 and 65 years old. Clinical signs and symptoms were described in 56.7% (203/358) of the study participants, while 43.3% (155/358) of the women were asymptomatic.

Smoking, multiparity (two or more pregnancies), and hormone therapy use were reported by 5.6% (20/358), 68.4% (255/358), and 0.84% (3/358) of the study participants, respectively. Among the contraceptive methods evaluated, oral contraceptives, regardless of the route of administration, were the most widely used (24.9% - 89/358), while intrauterine devices (IUDs) were the choice of only one participant.

Yeasts were isolated in 15.6% (56/358) of the participants. However, 58 species were identified, as two participants had positive cultures for two different yeast species. The distribution of species showed a frequency of 63.8% (37/58) of C. albicans and 36.2% (21/58) of non-albicans yeasts (Table 1).

Table 1. Frequency of yeast isolated from women in the Recôncavo Baiano region, from 2021 to 2023.

Yeast species	N (%)
Candida albicans	37 (63.8)
Nakaseomyces glabrata	7 (12.1)
Candida parapsilosis	7 (12.1)
Candida tropicalis	4 (6.9)
Meyerozyma guilliermondii	2 (3.4)
Pichia kudriavzevii	1 (1.7)

The prevalence of VVC in this study was 10.89%, with the diagnosis established in 39 of the 358 participants who simultaneously presented a positive mycological culture for yeast and any of the clinical signs/symptoms evaluated. Cases of colonization were described in 4.75% (17/358) of asymptomatic participants. Although signs and symptoms were associated with VVC (p=0.0227), the association remained only when the isolated yeast was of the albicans species (p=0.0098) as opposed to non-albicans species (p=0.5554). The signs/symptoms and their associations with VVC are described below (Table 2).

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VULVOVAGINAL CANDIDIASIS: PREVALENCE AND ANTIFUNGAL SUSCEPTIBILITY OF SPECIES ISOLATED FROM WOMEN LIVING IN RECÔNCAVO BAIANO

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Table 2. Clinical signs and symptoms associated with vulvovaginal candidiasis in women from the Recôncavo Baiano region, 2021 to 2023.

Variable	Total N (%)	*p* value	*Candida albicans* N (%)	*p* value	Non-albicans yeasts N (%)	*p* value
Leukorrhea						
Yes	23 (59.0)	0.8423	18 (64.3)	0.5314	05 (45.5)	0.1773
No	16 (41.0)		10 (35.7)		06 (54.5)	
Altered cervix/vagina						
Yes	11 (28.2)	0.4720	07 (25.0)	0.5201	04 (36.4)	0.3291
No	28 (71.8)		21 (75.0)		07 (63.6)	
Bleeding after sexual intercourse						
Yes	05 (12.8)	0.0143	04 (14.3)	0.0226	01 (9.0)	0.4006
No	34 (87.2)		24 (85.7)		10 (91.0)	
Itching						
Yes	24 (61.5)	0.0026	20 (71.4)	0.0004	04 (36.4)	0.5216
No	15 (38.5)		08 (28.6)		07 (63.6)	
Burning sensation						
Yes	11 (28.2)	0.5325	07 (25.0)	0.3960	04 (36.4)	0.4023
No	28 (71.8)		21 (75.0)		07 (63.6)	
Odor						
Yes	04 (10.3)	0.4116	04 (14.3)	0.4982	0 (0.0)	-
No	35 (89.7)		24 (85.7)		11 (100)	

Considering possible risk factors for VVC, age was not associated with this pathology in this population (*p*=0.3001), but women between 18 and 24 years of age had a lower prevalence (13%) of VVC, followed by the group aged 46 to 65 years (26%). The 25-45 age group had the highest number of VVC cases (61%). Smoking was also not associated with VVC; however, the results suggest that women who smoke may be 2.1 times more likely to develop fungal vulvovaginitis (*p*=0.1308, RR 2.123, 95% CI 0.8211; 5.490), especially when the isolated pathogen is of the non-albicans species (*p*=0.0838, R.R. 3.185, 95% CI 0.9877; 10.269).

Analyzing the antifungal sensitivity profile, *C. albicans* isolates did not show resistance to the antifungals tested, but showed intermediate sensitivity to fluconazole in 3% (1/37), itraconazole in 19% (7/37), miconazole in 16% (6/37), and clotrimazole in 3% (1/37); all remaining isolates were sensitive to the antifungals tested.

When the analysis was performed on non-albicans yeasts, resistance was detected in only 4.76% (1/21) of the isolates, which were of the species *N. glabrata*, against itraconazole. Still with regard to itraconazole, 4.76% (1/21) of *C. tropicalis* and 9.52% (2/21) of *M. guilliermondii* showed intermediate sensitivity, while 9.52% (2/21) of *C. tropicalis* and 4.76% (1/21) of *P. kudriavzevii* showed intermediate sensitivity to miconazole. The remaining isolates were sensitive to the antifungals tested.

DISCUSSION

Information on the prevalence of VVC in the Recôncavo Baiano region is lacking in academic literature. Therefore, understanding the epidemiological profile of this pathology and its causative agents in this population can help public managers and the scientific community to direct actions for prevention, early diagnosis, and appropriate treatment.

Although the Recôncavo Baiano is located in a tropical region, where the combination of high temperatures and relative humidity usually favors yeast growth, the findings of this study revealed a prevalence of VVC lower than the national average estimated at 18%.[15] This discrepancy may be related to methodological variations employed in studies, especially when based on self-reports or only on clinical criteria.[2,9,16] Robust methodologies, with VVC diagnosis defined by the presence of signs/symptoms and mycological tests, including molecular tests, as used in this study, may have allowed a more precise distinction between asymptomatic colonization and active infection, avoiding an overestimation of VVC frequency.

Additionally, environmental, behavioral, and cultural factors specific to the studied population may have contributed to the lower prevalence observed. The Recôncavo Baiano region has semi-urban and rural characteristics, which may favor protective habits, such as the predominant use of light and cotton clothing and less exposure to urban factors associated with VVC, such as stress, obesity, and industrialized diets.[7,11,16]

Furthermore, data on the fungal species responsible for VVC cases in the study are similar to scientific studies that indicate a predominance of the species *C. albicans*, with an increasing number of *non-albicans* clinical yeasts, the most frequently isolated remaining *C. tropicalis*, *N. glabratus*, *C. parapsilosis*, and *P. kudriavzevii*.[3,7,17,18]

In this context, the predominance of *C. albicans* as the etiological agent of VVC, as well as its association with the presence of clinical signs and symptoms, can be

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explained by the intrinsic virulence characteristics of this yeast. *C. albicans* has a high capacity for adhesion to the vaginal epithelium, formation of hyphae and pseudohyphae, production of hydrolytic enzymes (proteases and phospholipases), and the ability to invade the immune system and cause an intense inflammatory response. These factors favor not only colonization but also the transition to the pathogenic form, resulting in more evident clinical manifestations.[5,11,12]

In contrast, *non-albicans* clinical yeasts tend to be less aggressive and cause less immune inflammatory stimulation, which may explain their lower frequency as causative agents of VVC and the absence of association with the clinical signs and symptoms investigated. However, the greater involvement of these species in fungal vulvovaginitis represents a significant epidemiological change and may be a warning sign for the possible impact of self-medication, prolonged use of azoles, or changes in the immunological profiles of patients.[4,12,19,20]

The findings of the present study, which identified vulvar pruritus as a symptom associated with fungal vulvovaginitis, contrast with the current clinical guidelines in Brazil. The Brazilian Protocol for Sexually Transmitted Infections recommends empirical treatment of VVC based on signs such as white, lumpy vaginal discharge and/or vulvar erythema, not considering pruritus as a criterion for therapeutic conduct.[8] However, growing evidence reiterating pruritus as the only independent predictor for VVC strengthens the implementation of a newly proposed algorithm, in which this clinical symptom is included in the differential diagnosis of vulvovaginitis in women with abnormal vaginal discharge, including VVC.[1,2,21,22]

A unique finding in this study was the association between vaginal bleeding after sexual intercourse and the presence of VVC caused by *C. albicans*. Although this symptom does not commonly occur in the typical clinical presentation of VVC, it can be pathophysiologically justified when considering the invasive and inflammatory power of this species, which, combined with local hypervascularization induced by inflammation, makes the vaginal epithelium more susceptible to microtrauma, especially after sexual intercourse. This manifestation may also be exacerbated in contexts of hypoestrogenism, use of vaginal douches, or vigorous sexual intercourse, factors not evaluated in the present study, but which may act as additional modulators of the tissue response.[18]

Although age and smoking do not represent risk factors for VVC in this population, the observation that women between 18 and 45 years of age are more affected by fungal vulvovaginitis is consistent with the literature. It is believed that increased hormone levels, common in this age group, as well as contraceptive use and pregnancy, may promote a reduction in the inhibitory activity of epithelial cells against yeasts, which explains increase in candidiasis in women of reproductive age.[23]

With regard to smoking, it is important to note that the research data suggest that participants who smoke are more likely to develop fungal vulvovaginitis. This observation is justified by the fact that nicotine, present in tobacco, is responsible for altering the local immunomodulatory response, which can lead to changes in the genital tract microbiota, favoring the development of candidiasis.[24]

The evaluation of *C. albicans* isolates revealed an in vitro susceptibility profile without resistance determination, although cases of intermediate sensitivity were observed. The presence of intermediate phenotypes may indicate a possible adaptive process related to repeated, prolonged, or inappropriate use of topical or systemic antifungals. In addition, mutations in the *ERG11* gene and biofilm formation capacity have been documented as relevant mechanisms in reducing susceptibility to azoles.[4,20] This finding highlights the importance of considering epidemiological surveillance strategies, even in community settings, especially in cases of recurrent infection.

Analysis of the in vitro susceptibility profile of non-albicans clinical yeasts showed greater phenotypic heterogeneity compared to *C. albicans* isolates, although resistance was detected in only one case, corresponding to the species *N. glabratus* against itraconazole. This finding is consistent with the literature, which describes *N. glabratus* as a yeast that is naturally less susceptible to azoles due to characteristics such as low membrane permeability and constitutive activation of efflux pumps.[19,20,25]

Because it is not a notifiable infection, few health professionals request diagnostic tests for VVC to distinguish between the causes of vaginitis, which can lead to excessive prescription of antifungals and misuse of antibacterials. This inappropriate use favors the resistance of opportunistic pathogens, which makes antifungal susceptibility testing essential, both for accurate treatment and for the detection of possible antifungal resistance.[4,20]

The changes in the in vitro susceptibility profile for the antifungals tested in this study require attention in light of current therapeutic recommendations for the management of VVC. In cases of a single episode of VVC, local treatment (vaginal ovules), usually based on imidazole, or oral treatment with fluconazole is indicated. In the therapeutic approach to recurrent VVC, systemic use of fluconazole or itraconazole and local application of imidazoles are recommended. In primary care, the antifungals miconazole, in the form of a vaginal cream, and fluconazole, itraconazole, and nystatin, for oral administration, are available for the treatment of VVC. [3,10]

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The finding of strains with resistance or intermediate sensitivity to antifungals, even in an outpatient population such as that in this study, has significant implications for epidemiological surveillance and clinical practice. This reality is especially concerning in tropical regions with low regulation of access to medicines, as is often the case in inland areas of Brazil, including the Recôncavo Baiano.

Although the data do not indicate established clinical resistance, they may reflect an early stage of fungal adaptation to the drugs, which would compromise the response to treatment, especially in patients with recurrent VVC. Therefore, the integration of epidemiological surveillance, accurate mycological diagnosis, and rationalization of antifungal use would be essential to contain emerging cases of resistance and ensure the effectiveness of recommended therapies.

The findings of this study conclude that, although the prevalence of VVC in the outpatient population of the Recôncavo Baiano was lower than the national average, Candida albicans remains the main etiological agent associated with signs and symptoms, while non-albicans species showed no clinical association. Detection of isolates with reduced sensitivity, even outside the hospital environment, reinforces the importance of mycological monitoring and rationalization of antifungal use in primary care, contributing to the prevention of resistance and the adequacy of therapeutic approaches.

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AUTHORS' CONTRIBUTIONS

Cássia Vargas Lordêlo contribuiu para a concepção, delineamento do estudo, coleta, análise e interpretação dos dados; redação, revisão crítica relevante do conteúdo intelectual do manuscrito. **Jakeline Souza Torres** contribuiu para a realização das coletas, análises e interpretação dos dados. **Alexsandra dos Santos Campos** contribuiu para a realização das análises e interpretação dos dados. **Manuela Fraga Fernandes e Silva** contribuiu para a realização das análises e interpretação dos dados. **Ricardo David Couto** contribuiu para a realização das análises e interpretação dos dados; revisão crítica relevante do conteúdo intelectual do manuscrito. **Tânia Fraga Barros** contribuiu para a concepção e delineamento do estudo, análise e interpretação dos dados; revisão crítica relevante do conteúdo intelectual do manuscrito.

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

Analysis of the resistance profile of microorganisms in the pre-pandemic and Covid-19 pandemic period

Análise do perfil de resistência de microrganismos em Unidades de Terapia Intensiva do Amazonas no período pré-pandêmico e pandêmico de Covid-19

Análisis del perfil de resistencia de microorganismos en el periodo prepandémico y pandemia de Covid-19

Corresponding author:
E-mail: adb.med23@uea.edu.br
Address: Cosme Ferreira Avenue, 5787, São José Operário, Manaus, Amazonas, Brazil.

Esther Pereira Abensur[1] iD
Adriany da Rocha Pimentão[1] iD
Vinícius Moura de Araújo[1] iD
Albe Dias Batista[1] iD
Eidie Souza de Queiroz[1] iD
Maria Luiza Silva dos Santos[1] iD
Pedro Eduardo Garcia de Andrade[1] iD
Elielza Guerreiro Menezes[1] iD
Evelyn Cesar Campelo[2] iD
Timóteo Tadashi Watanabe[2] iD

[1]University of the State of Amazonas, Manaus, Amazonas, Brazil.

[2]Amazonas Health Surveillance Foundation "Dr. Rosemary Costa Pinto", Manaus, Amazonas, Brazil.

ABSTRACT

Background and Objectives: With the pandemic caused by SARS-CoV-2, the intense empirical use of antibiotic therapy endorsed selective pressure driving microbial resistance. Understanding the profile of this resistance in the hospital environment generates support for the rational use of antimicrobials. This study aimed to analyze the resistance profile of microorganisms in patients admitted to intensive care units of Amazonas before and during the Covid-19 pandemic. **Methods:** This is a quantitative, observational, and retrospective study conducted between 2019 and 2021. Based on the database provided by Dr. Rosemary Costa Pinto Health Surveillance Foundation, it was possible to identify the isolated microorganisms, compare the microbial resistance profile during the research period, and relate it to the main types of mandatory notification infections found in blood cultures and urine cultures. The data were organized in Microsoft Excel® spreadsheets and subjected to a descriptive analysis according to their epidemiological significance. **Results:** 26 microorganisms were classified over the three years, with a higher prevalence of carbapenem-resistant and cephalosporin-resistant gram-negative bacteria; however, there was a higher incidence of oxacillin-resistant gram-positive bacteria. **Conclusion:** Empirical antimicrobial treatment was used to minimize the high mortality in health services during the coronavirus pandemic, but its approach lacked good clinical reasoning from the professionals of the multidisciplinary team. By avoiding the indiscriminate use of antibiotics, the cost and expenses of unnecessary public and private resources are also avoided, also slowing down the speed of spread of microbial resistance.

Keywords: *Drug Resistance. Covid-19. Cross Infection. Intensive Care Units.*

RESUMO

Justificativa e Objetivos: Com a pandemia causada pelo SARS-CoV-2, o intenso uso da antibioticoterapia endossou uma pressão seletiva impulsionando a resistência microbiana. Compreender o perfil dessa resistência no ambiente hospitalar fornece subsídios para o uso racional de antimicrobianos. O presente estudo teve como objetivo analisar o perfil de resistência dos microrganismos em pacientes internados em Unidades de Terapia Intensiva do Amazonas antes e durante a pandemia de Covid-19. **Métodos:** Trata-se de um estudo quantitativo, observacional e retrospectivo, realizado entre 2019 e 2021. A partir do banco de dados disponibilizado pela Fundação de Vigilância em Saúde Drª Rosemary Costa Pinto, foi possível identificar os microrganismos isolados, comparar o perfil de resistência microbiana durante o período da pesquisa e relacionar com os principais tipos de infecção de notificação obrigatória encontrados em hemoculturas e uroculturas. Os dados foram organizados em planilhas do *Microsoft Excel*® e submetidos a uma análise descritiva de acordo com sua importância epidemiológica. **Resultados:** Foram classificados 26 microrganismos durante os três anos, com maior prevalência das bactérias gram-negativas resistentes a carbapenêmicos e a cefalosporinas, entretanto houve maior incidência das bactérias gram-positivas resistentes à oxacilina. **Conclusão:** O tratamento empírico de antimicrobianos visou minimizar a alta mortalidade nos serviços de saúde durante a pandemia do coronavírus, mas sua abordagem careceu de um bom raciocínio clínico dos profissionais da equipe multidisciplinar. Evitando o uso indiscriminado de antibióticos, evita-se também o custo e despesas de recursos públicos e privados desnecessários, desacelerando também a velocidade de propagação da resistência microbiana.

Descritores: *Resistência Microbiana. Covid-19. Infecção Hospitalar. Unidades de Terapia Intensiva.*

RESUMEN

Justificación y Objetivos: Con la pandemia causada por el SARS-CoV-2, el uso empírico intensivo de la terapia antibiótica respaldó una presión selectiva que impulsó la resistencia microbiana. Entender el perfil de esta resistencia en el ámbito hospitalario genera subsidios para el uso racional de los antimicrobianos. El presente estudio tuvo como objetivo analizar el perfil de resistencia de microorganismos en pacientes ingresados en unidades de cuidados intensivos del estado de Amazonas antes y durante la pandemia de Covid-19. **Métodos:** Se trata de un estudio cuantitativo, observacional y retrospectivo, realizado entre los años 2019 y 2021. A partir de la base de datos puesta a disposición por la Fundación de Vigilancia de la Salud Dra. Rosemary Costa Pinto, fue posible identificar los microorganismos aislados, comparar el perfil de resistencia microbiana durante el período de investigación y relacionarlos con los principales tipos de infecciones de notificación obligatoria encontradas en hemocultivos y urocultivos. Los datos se organizaron en hojas de cálculo de Microsoft Excel® y se sometieron a un análisis descriptivo de acuerdo con su importancia epidemiológica. **Resultados:** Se clasificaron un total de 26 microorganismos a lo largo de los tres años, con mayor prevalencia de bacterias gramnegativas resistentes a carbapenémicos y cefalosporinas, sin embargo, hubo una mayor incidencia de bacterias grampositivas resistentes a oxacilina. **Conclusión:** El tratamiento empírico de antimicrobianos se utilizó para minimizar la alta mortalidad en los servicios de salud durante la pandemia del coronavirus, pero su enfoque careció de un buen razonamiento clínico por parte de los profesionales del equipo multidisciplinario. Al evitar el uso indiscriminado de antibióticos, también se evitan costos y gastos innecesarios de recursos públicos y privados, desacelerando además la velocidad de propagación de la resistencia microbiana.

Palabras Clave: *Farmacorresistencia Microbiana. Covid-19. Infección Hospitalaria. Unidades de Cuidados Intensivos.*

Esther Pereira Abensur, Adriany da Rocha Pimentão, Vinícius Moura de Araújo, Albe Dias Batista, Eidie Souza de Queiroz, Maria Luiza Silva dos Santos, Pedro Eduardo Garcia de Andrade, Elielza Guerreiro Menezes, Evelyn Cesar Campelo, Timóteo Tadashi Watanabe

INTRODUCTION

Since the beginning of the Covid-19 pandemic caused by SARS-CoV-2, along with the evolution of technology, there has been an acceleration in the transmission of information around the world about treatment possibilities, and the impact of empirical treatment has been a proven problem.[1] This challenge was also experienced in the state of Amazonas, which experienced two waves of exponential growth in infections in early and late 2020, totaling more than 10,400 deaths from the beginning of the pandemic until February 2021.[2] The widespread use of antibiotic therapy has caused selective pressure so that the most resistant strains have persisted, accumulated resistance mechanisms, and spread.[1]

On the other hand, research involving the development of new antibiotics has not progressed at the same speed as pathogens have developed resistance mechanisms, compromising treatment options for some infections.[3,4]

According to the Pan American Health Organization (PAHO), Microbial Resistance (MR) occurs when microorganisms undergo changes when exposed to antimicrobials, acquiring resistance to a wide range of drugs, thus jeopardizing the effectiveness of prevention and treatment of an increasing number of infections.[5,6]

With the possible increase in multidrug-resistant (MDR) microorganisms in hospital services with a wider range of resistance to the most used antimicrobials and increasingly restricted therapeutic treatments due to the lack of rapid development of new drugs, it is becoming increasingly difficult to treat and recover patients affected by MDR.[4]

It is illusory to believe that the development of new drugs will keep pace with the development of MR, so it is necessary to understand the resistance profile of microorganisms present in hospitals to have subsidies for the rational use of antimicrobials, in addition to emphasizing preventive measures.

Given the above, the objective of this study was to analyze the resistance profile of microorganisms in Intensive Care Units (ICUs) in the state of Amazonas during the pre-pandemic and pandemic periods of Covid-19.

METHODS

This is a quantitative, observational, retrospective study conducted using data provided by the Amazonas Health Surveillance Foundation – Rosemary Costa Pinto. The research involved the analysis of microorganisms isolated in blood cultures and urine cultures, as well as their antimicrobial resistance profiles, in all ICUs in the state of Amazonas, from 2019 to 2021, considering January 2019 to December 2021.

Sample

All blood cultures and urine cultures from intensive care units (ICUs) in the state of Amazonas were processed by the Central Public Health Laboratory (LACEN). This laboratory strictly follows the criteria established by Technical Standards No. 01, 02, and 03 of the Health Services Surveillance and Monitoring Management (GVIMS) of the National Health Surveillance Agency (ANVISA), regarding the diagnosis of Healthcare-Associated Infections (HAIs) subject to mandatory national notification for the year 2023.

The standards define the diagnostic criteria according to the type of infection, with specific categorization for adult, pediatric, and neonatal patients. After processing, the data were forwarded to the State Commission for Infection Prevention and Control in Health Services, of the Amazonas Health Surveillance Foundation – Dr. Rosemary Costa Pinto (CECISS/FVS-RCP), where they created the annual database.[7-9]

Selection criteria

To define the types of infection considered in the study, the classifications established by the Technical Standards of the Health Services Surveillance and Monitoring Management of the National Health Surveillance Agency (GVIMS/ANVISA), 2023 edition, were adopted. The following healthcare-associated infections were included in the scope of the study: Laboratory Primary Bloodstream Infection (LPBI) associated with the use of Central Venous Catheters (CVC); Urinary Tract Infection (UTI) associated with the use of Indwelling Urinary Catheters (IUC).

These infections were selected based on their epidemiological relevance and the availability of consolidated blood and urine culture data in the surveillance system of the Amazonas Health Surveillance Foundation – Rosemary Costa Pinto (FVS-RCP). On the other hand, the following conditions were excluded from the study: Ventilator-Associated Pneumonia (VAP); Surgical Site Infections (SSI); Infections associated with dialysis services. Both are also described in ANVISA's Technical Standards and are included in the records of the State Coordination of Infection Control in Health Services (CECISS/FVS-RCP), but were not considered in this analysis because they did not fit the specific objectives of this study.[7-9]

Data collection instruments

Initially, a comprehensive literature review was conducted using the Scientific Electronic Library Online (SciELO), Virtual Health Library (VHL), National Center for Biotechnology Information (NCBI), and

PubMed databases between August 2022 and June 2023.

The purpose of the review was to contextualize local findings within the national and international landscape, identify patterns and trends related to MR in intensive care settings, and provide a theoretical basis for the choice of microorganisms and infections prioritized in the research. In addition, it allowed the identification of gaps in the scientific literature that justify and reinforce the relevance of the present study to the Amazonian reality.

At the same time, between November 2022 and March 2023, secondary data were collected from the MR database on Healthcare-Associated Infections (HAIs), made available by the State Commission for Infection Prevention and Control in Health Services of the Health Surveillance Foundation – Dr. Rosemary Costa Pinto (CECISS/FVS-RCP). These data include records from ICUs in the state of Amazonas related to blood cultures and urine cultures and were used as the main analysis tool in this study.

Although data collection began in 2022, the 2023 ANVISA guidelines were adopted as a normative reference because they were the most current and consolidated version at the time of analysis and interpretation. The use of these standards was essential to ensure greater methodological rigor, standardization of diagnostic criteria, and alignment with the latest epidemiological surveillance practices in the country.

Data organization and analysis

The collected data were digitized and organized in spreadsheets using Microsoft Excel® software. They were then subjected to descriptive statistical analysis to identify patterns of occurrence of microorganisms and their MR profile in ICUs in the state of Amazonas from 2019 to 2021.

The data were separated to allow comparisons between the isolated microorganisms, the years of occurrence, and the types of infection observed in different age groups (adults, pediatric, and neonatal).

The study allowed the identification of the main microorganisms isolated according to their epidemiological relevance, as well as a comparative analysis of the antimicrobial resistance profile over the three years of investigation. In addition, the data were stratified by type of infection, enabling a detailed assessment of microbiological behavior in the different population groups admitted to ICUs.

Ethical considerations

The research followed the ethical precepts of Resolution No. 466 of the National Health Council (CNS) of December 12, 2012. As this was a study using secondary data and did not involve participants, the project was not submitted to the Research Ethics Committee, requiring only submission for review and obtaining consent.

RESULTS

Analysis of data from 2019 to 2021 reveals important changes in the MR profile in ICUs in the state of Amazonas, particularly when comparing the pre-pandemic period with the Covid-19 pandemic context. Initially, there was a significant increase in the frequency of microorganism isolation in blood and urine cultures throughout the period evaluated.

During the research period, 26 microorganisms were identified in blood and urine cultures from ICU patients in Amazonas, classified as Gram-negative bacteria (57.7%), Gram-positive bacteria (23.1%), fungi (11.5%), atypical microorganisms (3.8%), and unlisted microorganisms (3.8%).

A total of 1,508 microorganisms were isolated in ICU blood cultures, with gram-negative bacteria such as K. pneumoniae (16.84%) and Acinetobacter spp. (6.23%) being the most prevalent. On the other hand, Gram-positive bacteria had a higher incidence when comparing the three years, with emphasis on coagulase-negative Staphylococcus (CNS) (37.53%) and S. aureus (14.46%), which were the main microorganisms of LPBI-CVC (Table 1).

Table 1. Microorganisms isolated in adult, pediatric, and neonatal blood cultures in Amazonas during the period from 2019 to 2021.

Isolated Microorganisms	2019			2020			2021		
	Adult	Pediatric	Neonatal	Adult	Pediatric	Neonatal	Adult	Pediatric	Neonatal
Acinetobacter spp.	10	4	13	8	12	2	36	6	3
Alcaligenes faecalis	0	1	0	0	0	0	0	0	0
Burkholderia cepacia	2	1	0	5	3	0	13	13	7
Escherichia coli	3	2	6	11	2	7	13	2	3
Enterococcus faecalis	6	2	3	7	2	7	0	3	9
Enterococcus faecium	0	3	0	1	0	0	4	0	0
Enterobacter cloacal	0	0	0	0	0	0	0	0	0
Enterobacter spp.	6	7	4	10	5	4	16	3	10
Enterococcus spp.	0	0	1	3	1	3	6	3	1

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Isolated Microorganisms	2019			2020			2021		
	Adult	Pediatric	Neonatal	Adult	Pediatric	Neonatal	Adult	Pediatric	Neonatal
Klebsiella sp.	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	17	19	63	18	13	45	32	13	34
Other enterobacteria	3	2	0	4	1	0	5	0	0
Pseudomonas aeruginosa	12	1	2	12	10	2	34	3	4
Proteus spp.	0	0	0	0	0	0	0	0	0
Ralstonia spp.	0	0	0	0	0	0	0	0	1
Ralstonia picketti	0	1	0	0	0	0	0	0	0
Streptococcus pneumoniae	0	1	0	0	0	0	0	0	0
Staphylococcus aureus	24	10	29	30	11	18	57	18	21
Stenotrophomonas maltophilia	0	2	0	2	4	0	6	0	2
Staphylococcus Coagulase Negative	31	40	113	53	41	69	151	26	42
Serratia spp.	2	11	0	2	5	0	11	2	5

Microorganisms such as SCN and S. aureus stand out for being consistently among the most frequently isolated, with SCN increasing from 113 isolates in 2019 to 219 in 2021, predominantly in adult patients. Similarly, K. pneumoniae, a pathogen widely associated with severe hospital infections, had a high number of isolates, particularly in adult and neonatal patients. Also noteworthy is the significant growth in isolates of Acinetobacter spp., which increased from 27 in 2019 to 45 in 2021, predominantly in adults.

For CAUTI data in urine cultures during the study period, a total of 768 isolated microorganisms were identified, the most frequent being Enterobacter spp. (41.80%) and E. coli (20.31%). There was a 3% decrease in the rate of indwelling urinary catheter use and consequent CAUTI in urine cultures of patients admitted to pediatric ICUs compared to 2019 (Table 2). In addition, although the focus of this study was microorganisms belonging to Prokaryota, it is important to mention that there was also a high incidence of fungi such as Candida albicans and non-albicans Candida. Data on these microorganisms were not presented because they belong to the Eukaryota group, and the emphasis of this study was on the resistance profile without addressing antifungals.

Table 2. Microorganisms isolated in adult and pediatric urine cultures in Amazonas during the period from 2019 to 2021.

Isolated Microorganisms	2019		2020		2021	
	Adult	Pediatric	Adult	Pediatric	Adult	Pediatric
Acinetobacter spp.	1	0	5	0	20	2
Alcaligenes faecalis	0	0	0	0	0	0
Burkholderia cepacia	0	0	2	0	7	0
Escherichia coli	25	22	31	9	64	5
Enterococcus faecalis	2	1	3	0	15	1
Enterococcus faecium	0	0	0	0	2	1
Enterobacter cloacal	0	0	0	0	1	0
Enterobacter spp.	65	3	77	7	168	1
Enterococcus spp.	0	0	1	0	4	1
Klebsiella sp.	0	0	0	0	1	0
Klebsiella pneumoniae	11	12	19	10	40	2
Other enterobacteria	0	0	0	0	4	0
Pseudomonas aeruginosa	20	8	16	7	22	2
Proteus spp.	6	0	3	0	5	0
Ralstonia spp.	0	0	0	0	0	0
Ralstonia picketti	0	0	0	0	0	0
Streptococcus pneumoniae	0	0	0	0	0	0
Staphylococcus aureus	0	0	0	1	1	1
Stenotrophomonas maltophilia	0	0	0	1	4	0
Staphylococcus Coagulase Negative	4	1	7	0	3	0
Serratia spp.	0	1	2	2	5	1

Regarding the resistance profile of microorganisms in blood cultures from adult, pediatric, and neonatal patients, as well as in urine cultures, these data can be seen in Tables 3, 4, and 5, divided by year.

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Table 3. Resistance profile of microorganisms in blood cultures and urine cultures in Amazonas during 2019.

Microrganisms	AM	Car	CP	CAZ	MP	OX	PO	TS	VA
Acinetobacter spp.	0	10	0	0	0	0	0	0	0
Alcaligenes faecalis	0	0	0	0	0	0	0	0	0
Burkholderia cepacia	0	0	0	1	0	0	0	0	0
Escherichia coli	0	10	35	0	0	0	0	0	0
Enterococcus faecalis	0	0	0	0	0	0	0	0	0
Enterococcus faecium	0	0	0	0	0	0	0	0	0
Enterobacter cloacal	0	0	0	0	0	0	0	0	0
Enterobacter spp.	0	5	16	0	0	0	0	0	0
Enterococcus spp.	0	0	0	0	0	0	0	0	0
Klebsiella sp.	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	0	13	52	0	0	0	0	0	0
Other enterobacteria	0	1	6	0	0	0	0	0	0
Pseudomonas aeruginosa	0	5	0	0	0	0	0	0	0
Proteus spp.	0	0	0	0	0	0	0	0	0
Ralstonia spp.	0	0	0	0	0	0	0	0	0
Ralstonia picketti	0	0	0	0	0	0	0	0	0
Streptococcus pneumoniae	0	0	0	0	0	0	0	0	0
Staphylococcus aureus	0	0	0	0	0	31	0	0	0
Stenotrophomonas maltophilia	0	0	0	0	0	0	0	0	0
Staphylococcus Coagulase Negative	0	0	0	0	0	132	0	0	0
Serratia spp.	0	1	1	0	0	0	0	0	0

Abbreviation: AM = ampicillin; Car = carbapenems; CP = third- and/or fourth-generation cephalosporins; CAZ = ceftazidime; MP = meropenem; OX = oxacillin; PO = polymyxin; TS = sulfamethoxazole/trimethoprim; VA = vancomycin.

Table 4. Resistance profile of microorganisms in blood cultures and urine cultures in Amazonas during 2020.

Microrganisms	AM	Car	CP	CAZ	MP	OX	PO	TS	VA
Acinetobacter spp.	0	12	0	0	0	0	3	0	0
Alcaligenes faecalis	0	0	0	0	0	0	0	0	0
Burkholderia cepacia	0	0	0	1	3	0	0	1	0
Escherichia coli	0	2	29	0	0	0	2	0	0
Enterococcus faecalis	0	0	0	0	0	0	0	0	0
Enterococcus faecium	0	0	0	0	0	0	0	0	0
Enterobacter cloacal	0	0	0	0	0	0	0	0	0
Enterobacter spp.	0	4	8	0	0	0	1	0	0
Enterococcus spp.	0	0	0	0	0	0	0	0	2
Klebsiella sp.	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	0	19	58	0	0	0	1	0	0
Other enterobacteria	0	1	6	0	0	0	0	0	0
Pseudomonas aeruginosa	0	8	0	0	0	0	0	0	0
Proteus spp.	0	0	0	0	0	0	0	0	0
Ralstonia spp.	0	0	0	0	0	0	0	0	0
Ralstonia picketti	0	0	0	0	0	0	0	0	0
Streptococcus pneumoniae	0	0	0	0	0	0	0	0	0
Staphylococcus aureus	0	0	0	0	0	29	0	0	0
Stenotrophomonas maltophilia	0	0	0	0	0	0	0	2	0
Staphylococcus Coagulase Negative	0	0	0	0	0	146	0	0	0
Serratia spp.	0	4	4	0	0	0	0	0	0

Abbreviation: AM = ampicillin; Car = carbapenems; CP = third- and/or fourth-generation cephalosporins; CAZ = ceftazidime; MP = meropenem; OX = oxacillin; PO = polymyxin; TS = sulfamethoxazole/trimethoprim; VA = vancomycin.

There was an 8.46% increase in the number of resistant microorganisms in 2020 (n=346) compared to 2019 (n=319) and a 56% increase in 2021 (n=540) compared to 2020 (Table 5).

Table 5. Resistance profile of microorganisms in blood cultures and urine cultures in Amazonas during the period of 2021.

Microrganisms	AM	Car	CP	CAZ	MP	OX	PO	TS	VA
Acinetobacter spp.	0	36	0	0	0	0	2	0	0
Alcaligenes faecalis	0	0	0	0	0	0	0	0	0
Burkholderia cepacia	0	0	0	7	7	0	0	1	0
Escherichia coli	0	14	62	0	0	0	0	0	0
Enterococcus faecalis	0	0	0	0	0	0	0	0	0
Enterococcus faecium	0	0	0	0	0	0	0	0	0
Enterobacter cloacal	1	0	0	0	0	OX	0	TS	0
Enterobacter spp.	0	7	20	0	0	0	1	0	0

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Microorganisms	AM	Car	CP	CAZ	MP	OX	PO	TS	VA
Enterococcus spp.	0	0	0	0	0	0	0	0	1
Klebsiella sp.	0	0	0	0	0	0	0	0	0
Klebsiella pneumoniae	0	26	80	0	0	0	0	0	0
Other enterobacteria	0	1	11	0	0	0	0	0	0
Pseudomonas aeruginosa	0	6	0	0	0	0	0	0	0
Proteus spp.	0	0	0	0	0	0	0	0	0
Ralstonia spp.	0	0	0	1	0	0	0	0	0
Ralstonia picketti	0	0	0	0	0	0	0	0	0
Streptococcus pneumoniae	0	0	0	0	0	0	0	0	0
Staphylococcus aureus	0	0	0	0	0	65	0	0	0
Stenotrophomonas maltophilia	0	0	0	0	0	0	0	4	0
Staphylococcus Coagulase Negative	0	0	0	0	0	164	0	0	0
Serratia spp.	0	11	12	0	0	0	0	0	0

Abbreviation: AM = ampicillin; Car = carbapenems; CP = third- and/or fourth-generation cephalosporins; CAZ = ceftazidime; MP = meropenem; OX = oxacillin; PO = polymyxin; TS = sulfamethoxazole/trimethoprim; VA = vancomycin.

In summary, the results indicate that the Covid-19 pandemic had a direct impact on the increase in MR in ICUs in Amazonas. This scenario reinforces the importance of strengthening microbiological surveillance programs, implementing effective policies for the rational use of antimicrobials, and continuously investing in the training of healthcare teams and rigorous hospital infection control practices. The adoption of these measures is essential to contain the spread of MR and preserve the effectiveness of available antimicrobials.

DISCUSSION

Empirical antibiotic therapy was used during the Covid-19 pandemic. Severely ill patients hospitalized for coronavirus developed Acute Respiratory Distress Syndrome and underwent mechanical ventilation, which caused various cases of lung injury and, more rarely, VAP coinfection due to secondary bacterial colonization. Such indiscriminate use of antibiotics certainly increased the generalized selective pressure on these drugs, which probably explains the increase in resistance profile found in our results during the Covid-19 pandemic.[10,11]

Additionally, it is reported that during the coronavirus pandemic, 88.3% of patients hospitalized for Covid-19 in health services were treated with broad-spectrum antibiotics, including third-generation cephalosporins, generating a weekly growth of 0.6% in antibiotic consumption. This scenario contributed to the intensification of selective pressure and favored the growth of multidrug-resistant strains, which was also reflected in the data presented here.[12,13]

Similarly, the high occurrence of SCN identified in our results in pediatric and neonatal units stands out, since this microorganism is an important nosocomial agent, often related to SSI in premature or low birth weight newborns undergoing invasive procedures, such as central venous catheters and prosthetic devices. In

these vulnerable populations, immunological immaturity potentiates the severity of infections, especially when associated with inappropriate antibiotic use.[5,14]

In the findings of this study, K. pneumoniae stood out as one of the main agents isolated in ICUs, especially in cases of primary bloodstream infection (PBSI). This Gram-negative bacterium, recognized as the second leading cause of this type of infection, has a high resistance capacity due to the production of carbapenemases, enzymes capable of degrading carbapenems, limiting the available therapeutic options. Its higher occurrence among patients undergoing long periods of catheterization observed in the results is consistent with evidence linking prolonged use of invasive devices with the selection and spread of multidrug-resistant strains.[3,15]

There was also an increase in the gram-positive bacterium S. aureus, classified by the World Health Organization as a high priority for epidemiological surveillance, research, and development of new antimicrobials. In addition, there was a high incidence of fungi such as Candida albicans and non-albicans Candida, found in neonatal blood cultures and adult urine cultures. Although these fungi are commonly found in adult patients in ICUs, these infections increase the length of stay with a mortality rate ranging from 35% to 50%.[2,16]

According to Technical Standard No. 3 GVIMS/GGTES/DIRE/ANVISA, it is mandatory to separate data from hospitalized pediatric and neonatal patients, considering the diagnosis of neonatal patients when they are younger than 28 days or when they are older than 28 days but born prematurely and/or with low birth weight. In the context of the research, it was observed that the number of isolated microorganisms found in both blood cultures and urine cultures of adult patients was higher than in pediatric and neonatal patients admitted to ICUs. One possible cause could be that one of the risk factors for complications and

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consequent hospitalizations due to Covid-19 is age equal to or greater than 60 years.[17]

Another study conducted in Minas Gerais performed a microbiological analysis of indwelling urinary catheters and concluded that the prophylactic use of antibiotics had no influence on the growth or decrease of bacterial colonies. In addition, their inappropriate use favored bacterial resistance, and their use prior to urine cultures led to false-negative results.[18]

Extended-spectrum β-lactamase (ESBL)-producing enterobacteria are resistant to a wide range of antibiotics effective against gram-positive and gram-negative bacteria. These antimicrobials have proven increasingly ineffective in treating infections caused by *A. baumannii*, *P. aeruginosa*, and *S. maltophilia* due to the progressive increase in resistance of these pathogens related to ESBL.[19]

P. aeruginosa is a gram-negative bacterium considered epidemiologically important only when it is resistant to at least 3 of 5 antibiotics in cultures, which was not observed in the present study.

Overall, it can be observed that the increase in the quantity and profile of MR in the state of Amazonas coincided directly during the Covid-19 pandemic with the indiscriminate use of antibiotics.

This study had limitations because it was retrospective in nature and only used secondary data collected by the Amazonas Health Surveillance Foundation, which may be subject to underreporting.

It is concluded that empirical treatment with antimicrobials was used to minimize high mortality in health services during the coronavirus pandemic, but its approach lacked adequate clinical reasoning by multidisciplinary team professionals to conduct therapy only in more severe patients. Avoiding the indiscriminate use of antibiotics reduces unnecessary public and private costs and expenses, in addition to slowing down the speed of RM propagation.

ACKNOWLEDGEMENTS

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AUTHORS' CONTRIBUTIONS

Esther Pereira Abensur contributed to the literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Adriany da Rocha Pimentão** contributed to project management, literature review, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, review, and statistics. **Vinícius Moura de Araújo** contributed to writing the abstract, revision, and statistics. **Albe Dias Batista** contributed to the revision and organization of the sections of the article. **Eidie Souza de Queiroz** contributed to project management, fund acquisition, bibliographic research, revision, and statistics. **Maria Luiza Silva dos Santos** contributed to writing the abstract, revision, and statistics. **Pedro Eduardo Garcia de Andrade** contributed to the writing of the abstract, revision, and statistics. **Elielza Guerreiro Menezes** contributed to the writing of the abstract, methodology, conclusions, and revision. **Evelyn Cesar Campelo** contributed to project management, bibliographic research, writing of the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, revision, and statistics. **Timóteo Tadashi Watanabe** 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 Chagas disease in the North and Northeast regions of Brazil (2018-2022)

Perfil epidemiológico da doença de Chagas nas regiões norte e nordeste do Brasil (2018-2022)
Perfil epidemiológico de la enfermedad de Chagas en las regiones Norte y Nordeste de Brasil (2018-2022)

Corresponding author:
E-mail: mayronhadsd@gmail.com
Address: Vitorino Orthiges Fernandes Street, 6123, Uruguai, Teresina, Piauí, Brazil.

Mayron Henrique Alves De Sá Dantas[1] iD
Gustavo Fonseca de Moura[1] iD

[1]Uninovafapi AFYA University Center, Teresina, Piauí, Brazil.

ABSTRACT

Background and Objectives: Chagas disease is a parasitic infection caused by the protozoan *Trypanosoma cruzi* and a public health problem in Brazil. Transmission occurs through the triatomine vector, oral, vertical, transfusional, and accidental routes. This study aims to outline the epidemiological profile of the disease in the North and Northeast regions between 2018 and 2022, analyzing case distribution and sociodemographic factors. **Methods:** This is an epidemiological and descriptive study. Data on confirmed cases of acute Chagas disease in the North and Northeast regions between 2018 and 2022 were collected using secondary data from the Notifiable Diseases Information System (SINAN). The variables analyzed include sex, age group, race/color, and mode of transmission. The data were processed using *Microsoft Excel*® and TABNET. **Results:** The state of Pará accounted for 78.29% of cases. The sex distribution was 52.26% for men and 47.74% for women. The most affected age group was 20 to 39 years (34.69%), and most cases occurred in brown individuals (83.51%). The primary transmission route was oral, associated with the consumption of contaminated food. **Conclusion:** The distribution of cases highlights the predominance of oral transmission, mainly in Pará. The epidemiological profile indicates a higher incidence among young adults and men, reflecting occupational and socioeconomic factors. The reduction recorded in 2020 suggests an impact of the Covid-19 pandemic on case reporting. The study reinforces the need for oral transmission control and expanded epidemiological surveillance.
Keywords: *Chagas disease. Epidemiology. Public Health.*

RESUMO

Justificativa e Objetivos: A doença de Chagas é uma infecção parasitária causada pelo protozoário *Trypanosoma cruzi* e um problema de saúde pública no Brasil. A transmissão ocorre por meio do vetor triatomíneo, via oral, vertical, transfusional e acidental. O estudo tem o objetivo de traçar o perfil epidemiológico da doença nas regiões Norte e Nordeste entre 2018 e 2022, analisando a distribuição dos casos e fatores sociodemográficos. **Métodos:** O estudo é epidemiológico e descritivo. Foram coletadas informações sobre casos confirmados de doença de Chagas aguda nas regiões Norte e Nordeste entre 2018 e 2022, utilizando dados secundários do Sistema de Informação de Agravos de Notificação (SINAN). As variáveis analisadas incluem sexo, faixa etária, raça/cor e modo de transmissão. Os dados foram processados no *Microsoft Excel*® e TABNET. **Resultados:** O estado do Pará concentrou 78,29% dos casos. A distribuição por sexo foi de 52,26% para homens e 47,74% para mulheres. A faixa etária mais acometida foi de 20 a 39 anos (34,69%), e a maioria dos casos ocorreu em indivíduos de raça parda (83,51%). A principal via de transmissão foi a oral, associada ao consumo de alimentos contaminados. **Conclusão:** A distribuição dos casos evidencia a predominância da transmissão oral, principalmente no Pará. O perfil epidemiológico indica maior incidência em adultos jovens e homens, refletindo fatores ocupacionais e socioeconômicos. A redução registrada em 2020 sugere impacto da pandemia de Covid-19 na notificação de casos. O estudo reforça a necessidade de controle da transmissão oral e ampliação da vigilância epidemiológica.
Descritores: *Doença de Chagas. Epidemiologia. Saúde Pública.*

RESUMEN

Justificación y Objetivos: La enfermedad de Chagas es una infección parasitaria causada por el protozoo *Trypanosoma cruzi* y un problema de salud pública en Brasil. La transmisión se produce a través del vector triatomino, vía oral, vertical, transfusional y accidental. Este estudio tiene como objetivo delinear el perfil epidemiológico de la enfermedad en las regiones Norte y Nordeste entre 2018 y 2022, analizando la distribución de los casos y los factores sociodemográficos. **Métodos:** Se trata de un estudio epidemiológico y descriptivo. Se recopilaron datos sobre casos confirmados de enfermedad de Chagas aguda en las regiones Norte y Nordeste entre 2018 y 2022, utilizando datos secundarios del Sistema de Información de Enfermedades de Notificación Obligatoria (SINAN). Las variables analizadas incluyen sexo, grupo de edad, raza/color y modo de transmisión. Los datos fueron procesados en *Microsoft Excel*® y TABNET. **Resultados:** El estado de Pará concentró el 78,29% de los casos. La distribución por sexo fue del 52,26% para hombres y 47,74% para mujeres. El grupo de edad más afectado fue de 20 a 39 años (34,69%), y la mayoría de los casos ocurrieron en individuos pardos (persona de ascendencia mixta) (83,51%). La principal vía de transmisión fue la oral, asociada con el consumo de alimentos contaminados. **Conclusión:** La distribución de los casos evidencia el predominio de la transmisión oral, principalmente en Pará. El perfil epidemiológico indica una mayor incidencia en adultos jóvenes y hombres, lo que refleja factores ocupacionales y socioeconómicos. La reducción registrada en 2020 sugiere un impacto de la pandemia de Covid-19 en la notificación de casos. El estudio refuerza la necesidad de controlar la transmisión oral y ampliar la vigilancia epidemiológica.
Palabras Clave: *Enfermedad de Chagas. Epidemiología. Salud Pública.*

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INTRODUCTION

Chagas disease, also known as American trypanosomiasis, is caused by the protozoan *Trypanosoma cruzi* and has two phases: acute and chronic. The acute phase is characterized by nonspecific symptoms, such as fever, dysphagia, diarrhea, and abdominal pain, or may be asymptomatic. The chronic phase may also be asymptomatic or manifest with cardiac and/or digestive complications, such as cardiomyopathy, heart failure, megacolon, and megaesophagus. The vector of T. cruzi, the protozoan that causes Chagas disease, is the triatomine bug, popularly known as the "kissing bug", and is frequently found throughout South and Central America. Because of this, the disease is endemic in 21 Latin American countries, including Brazil.[1-3]

Globally, approximately 6 to 8 million people are infected with *T. cruzi*. Although its incidence and mortality rates have declined globally, Chagas disease remains among the four leading causes of death from infectious and parasitic diseases in Brazil. Therefore, it constitutes a significant public health problem and is a mandatory reportable disease in the Notifiable Diseases Information System (SINAN).[3,4]

One reason for the difficult to control of American trypanosomiasis in Brazil is its varied transmission methods. The main route of infection is through the contaminated feces of the "kissing bug", which enters the bloodstream through the bite. However, cases through vertical and oral transmission are increasing. The latter occurs when an individual ingests food or drinks contaminated by the infected vector (açaí or sugarcane juice, for example) and is the main mechanism of transmission in the Amazon region. Therefore, epidemiological studies are highly relevant for supporting preventive and treatment measures against the disease.[5]

This study was motivated by several critical factors related to Chagas disease's persistence and impact in the North and Northeast regions. One of these is the significant presence of precarious housing conditions, such as brick or wattle and daub houses with partially coated walls (or even no coating). These homes often have attached chicken coops, which are also linked to the proliferation of the vector. Furthermore, activities such as deforestation and livestock farming, very common in such areas, promote environmental changes that interfere with the triatomine's natural habitat, resulting in a higher risk of infection. Therefore, the North and Northeast regions constitute areas of high epidemiological concern.[6]

Given that Chagas disease is categorized as a neglected pathology, establishing a comprehensive epidemiological understanding of its presence in the North and Northeast regions is essential for developing effective control strategies.[4] Consequently, the main objective of this study is to outline the epidemiological profile of Chagas disease in these regions between 2018 and 2022, analyzing the distribution of cases and associated sociodemographic factors. Our study seeks to contribute to public health in these regions by addressing specific challenges, such as oral transmission and the presence of native triatomines, and improving detection. This includes intensifying the active search for insect vectors, essential for identifying foci of infestation and preventing new cases, especially in more vulnerable areas, as well as improving disease management.[7]

METHODS

This is a descriptive epidemiological study. Reported cases of acute Chagas disease were collected in the North and Northeast regions of Brazil from 2018 to 2022. The combined population of these locations is 72,013,399 inhabitants.[8]

Information on the epidemiological profile of patients was obtained through SINAN, a system provided by the Ministry of Health. The data underlying this information were collected with the use of investigation forms completed by the local health service. Subsequently, data were stored in TABNET, a table generator developed by the Department of Information Technology of the Unified Health System (DATASUS), accessed on September 15, 2024.[22]

The variables of state of infection, year of infection, race, sex, and age group were evaluated after data collection.

The variables were analyzed using Microsoft Excel to perform stratified descriptive statistics. This quantitative approach focused on calculating the frequency of variables and presenting the results in the form of proportions.

Incidence rates were calculated using TABNET to obtain the number of cases, and the Brazilian Institute of Geography and Statistics (IBGE) demographic census to obtain the resident population. TABWIN was used for this calculation.[8]

Because this is a survey using secondary data publicly available on the DATASUS and SINAN platforms, linked to the Ministry of Health, evaluation for review and approval by the Research Ethics Committee (CEP) is not required, as per Resolution No. 510/16 of the National Health Council.

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RESULTS

The study analyzed the annual incidence of Chagas disease in the North and Northeast regions of Brazil between 2018 and 2022. Data over the study period show significant variation in incidence, marked by notable fluctuations (Graph 1).

Graph 1. Incidence of Chagas disease per 100,000 inhabitants in states of the North and Northeast regions, 2018-2022.
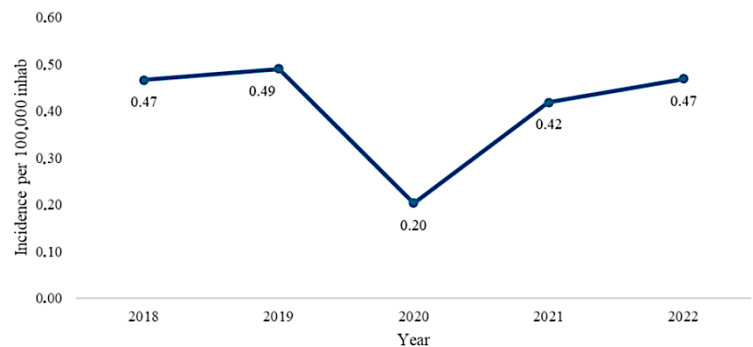
Among the metrics obtained, the peak in 2019 (0.49/100,000 population) and the reduction in 2020 (0.20/100,000 population) stand out. This suggests a decrease in the number of new cases, possibly related to the Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-COV-2) pandemic, which causes Coronavirus Disease 2019 (Covid-19). Furthermore, the fact of the incidence returning to pre-pandemic levels in the following two years reinforces the hypothesis of underreporting to the detriment of an actual decrease in new cases.

The distribution of confirmed cases of Chagas disease varied between states of the North and Northeast regions. The state of Pará accounted for most cases, highlighting the relevance of environmental and socioeconomic conditions (Table 1).[10]

Table 1. Absolute distribution of confirmed cases of Chagas disease by Brazilian state, 2018-2022.

State	Confirmed cases
Rondônia	4
Acre	41
Amazonas	88
Roraima	2
Pará	1,230
Amapá	103
Tocantins	25
Maranhão	28
Piauí	4
Rio Grande do Norte	1
Paraíba	14
Pernambuco	29
Alagoas	1
Bahia	1

The geographic distribution of the disease was heterogeneous across the states of both regions. Pará accounted for 78.29% (n=1,230) of confirmed cases during the analyzed period, followed by Amapá with 6.56% (n=103) and Amazonas with 5.60% (n=88). In the Northeast, the states of Maranhão with 1.78% (n=28) and Pernambuco with 1.85% (n=29) stood out,

although with a smaller proportion of cases compared to the North region.

Regarding the sociodemographic profile of American trypanosomiasis carriers between 2018 and 2022, a slight majority of cases occurred in males, accounting for 52.26% (n=821), while women represented 47.74% (n=750). There was a predominance of individuals aged 20 to 39 years (34.69%) and of brown race (83.51%). This pattern indicates that the economically active group, more involved in rural activities and more exposed to the vector, is the most affected by the disease (Table 2).

Table 2. Sociodemographic profile (sex, age group, and race) of confirmed cases of Chagas disease in the North and Northeast regions of Brazil, 2018-2022 (n=1,571).

Variables	N = 1,571
Sex	
Male	821
Female	750
Age range	
<1 year	20
1 to 4	68
5 to 9	98
10 to 14	144
15 to 19	136
20 to 39	545
40 to 59	394
60 to 64	55
65 to 69	43
70 to 79	51
80 and +	17
Race	
Ignored	24
White	119
Black	92
Yellow	3
Brown	1312
Indigenous	21

Furthermore, the analysis revealed a significant distribution of cases among children and adolescents under 14 years of age, with 21.01% of cases in this age

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group. This finding may be related to vertical transmission (from mother to child) and oral transmission, especially in Amazonian regions, where consumption of contaminated foods such as açaí and sugarcane juice is common (Graph 2).

Graph 2. Modes of transmission recorded in confirmed cases of Chagas disease in Brazil, 2018-2022.

Number of cases

■ Ignored ■ Vector ■ Vertical ■ Accidental ■ Oral
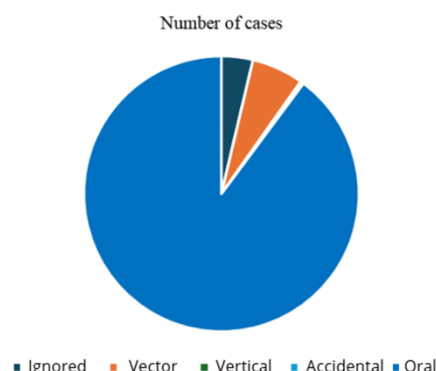
Oral transmission was significant during the study period, and the main route of infection. This type of transmission occurs when infected kissing bugs release parasites (*Trypanosoma cruzi*) into food or beverages that are later ingested by humans.

DISCUSSION

The number of new cases of Chagas disease is affected by several factors, such as socioeconomic status, geographic location, housing conditions, and access to health services. Therefore, a detailed study of its epidemiology is important.[2,10]

A decrease in the incidence rate can be observed during 2020. There were changes in the organization of society in this year caused by the Covid-19 pandemic, such as the lockdown, as well as greater awareness of the health-disease process. Therefore, hospital services dedicated most of their financial resources to combating the pandemic, expanding hospital beds and treating a growing number of suspected Covid-19 cases. However, this funding was distributed unevenly, with the minority of resources allocated to the North and Northeast regions. As a result, endemic diseases in these areas — such as American trypanosomiasis — suffered from budgetary constraints, which may have led to underreporting.[11-13]

The state of Pará accounted for the majority of cases (1,230 cases, 78.29% of the total) during the analyzed period. This high percentage is intrinsically related to the açaí cultivation in the region, since Para is the largest producer of this fruit in all of Brazil, with an average production of 120,127.10 tons from 2011 to 2017. During the harvesting and processing of açaí into pulp, there are several stages where contamination by the infected triatomine can occur. For example,

nighttime harvesting can render the vector undetectable, generating a cascade of contagion. Therefore, proper sanitary handling of food is essential to reduce the spread of Chagas disease.[10,14]

Regarding the socioeconomic profile of the disease, there was a predominance of male individuals (52.26%) aged between 20 and 39 years (34.69%). Furthermore, 394 cases were recorded in the 40-59 years age group, corresponding to 25.08% of the total. These data confirm a pattern found in the literature: the older the age, the longer the exposure time and consequently, the greater the chance of acquiring American trypanosomiasis. This study also corroborates studies that find a higher prevalence in people of working age (20 to 59 years). Given the above, it is clear that Chagas disease is closely related to a specific pattern of demographic variables.[18,19]

In turn, brown race is the most affected, represented by 83.51% of cases, which may be due to the high percentage of people of this ethnicity in the North and Northeast regions (61.40% of the total population). The white group is the second most affected, as well as the second most self-reported race/color in these areas (25.23% of the total population). Therefore, there is no correlation between a specific ethnicity and more cases of acute Chagas disease, only a simple census.[8]

Oral transmission is also associated with outbreaks of the disease, both in and outside endemic regions. In 2015, 18 new cases occurred in the municipality of Marcelino Vieira (RN), an incidence 17 times higher than the regional average. All those involved reported having consumed sugarcane juice from the same source. This beverage was responsible for another outbreak, this time in Navegantes (SC), in 2005. Finally, the largest outbreak ever recorded, with 103 individuals affected, occurred in Caracas, Venezuela, due to contaminated guava juice. This shows that the range of foods susceptible to contamination goes far beyond açaí, although this is the main one.[15-17]

Another prominent method is vector-borne transmission, in which the triatomine insect inoculates contaminated feces into the individual's bloodstream. The first recorded case of this transmission — and also the first recorded case of the disease — occurred in 1909, in the city of Lassance, state of Minas Gerais. The first suspected case of oral transmission occurred only in 1969, in Belém, Pará, precisely in the state most affected by the disease. This reinforces the data and demonstrates a shift in the pattern of Chagas disease spread: once vector-driven, it is now linked to food.[20]

Finally, vertical transmission is emerging. Although this form of transmission is statistically insignificant, it poses an important public health concern, as the infected fetus will experience consequences after birth. This form of transmission is associated with endemic regions, where prenatal screening for American

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trypanosomiasis is recommended. Furthermore, the drug used to treat Chagas disease (benznidazole) is highly toxic, and its administration is recommended only to pregnant women with severe disease and in the acute phase. An existing infection increases the risk of premature birth, premature rupture of membranes, and low birth weight. Given this difficult-to-treat condition with a severe prognosis, preventive measures are essential, both in relation to the vector and food consumption.[4,21]

Chagas disease is a neglected disease in Brazil, and this study highlights the importance of developing a well-defined epidemiological profile to provide data to the appropriate bodies.

Despite the relevant results, limitations were identified in the use of secondary data from SINAN, such as the possibility of underreporting and inconsistencies in records, especially in regions with less infrastructure. Furthermore, the analysis is limited to the acute phase of the disease and may not fully reflect the full picture of the chronic phase. To reduce these limiting factors, it is recommended to strengthen notification systems, train professionals in active search, locate vectors, and expand diagnostic coverage, especially in endemic areas.

It is important to emphasize that public health depends on other factors, such as education and infrastructure. Therefore, the information contained in this study can be used by Health Departments to plan Primary Care actions against American trypanosomiasis. Entomological monitoring and surveillance are also strengthened with a focus on combating the triatomine in the North and Northeast regions. Finally, the research data can inform public policies, favoring the allocation of financial resources to areas that most need it. In this way, it may be possible to reduce the incidence and morbidity and mortality of Chagas disease in the North and Northeast regions.

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AUTHORS' CONTRIBUTIONS

Mayron Henrique Alves De Sá Dantas was responsible for data collection and table preparation, and contributed to writing the introduction, methodology, results presentation, discussion, and reference formatting. **Gustavo Fonseca de Moura** was responsible for defining the title, project layout and graph preparation, and contributed to writing the introduction, methodology, results presentation, discussion, and reference formatting.

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

Impact of Covid-19 on the profile of mycoses reported in a public hospital in Paraíba, Brazil

Impacto da Covid-19 no perfil das micoses reportadas em um hospital público da Paraíba, Brasil

Impacto de la Covid-19 en el perfil de las micosis notificadas en un hospital público de Paraíba, Brasil

Mariana de Assis Valverde[1] ID
Natan Gomes Emmanuel[1] ID
Ana Paloma Tavares de Araújo[2] ID
Wallace Felipe Blohem Pessoa[1] ID

[1]Department of Biomedical Sciences, Health Sciences Center, Federal University of Paraíba, João Pessoa, Brazil.
[2]Mycology Sector, Clinical Analysis Laboratory Unit, Lauro Wanderley University Hospital, João Pessoa, Brazil.

ABSTRACT

Background and Objectives: Covid-19 can lead to critical immunological conditions, requiring hospitalization in intensive care units. The risk of fungal co-infections increases in these patients, especially if they are on mechanical ventilation, using invasive devices and/or broad-spectrum antibiotics. Secondary fungal infections can worsen the symptoms of the disease, make prognosis and treatment more difficult, and increase mortality and hospital stay rates. Thus, the objective of the present study was to evaluate the influence of the Covid-19 pandemic on the distribution of fungal infections in patients admitted to a university hospital in Paraíba during the period from 2020 to 2022. **Methods:** A total of 456 medical records from the period between March 2020 and July 2022 sent to the Mycology department with suspected fungal infection were analyzed. **Results:** Of the medical records evaluated, 120 presented infection by some fungus. Only 17 medical records came from the Covid ICU and 14 of them were positive for some mycosis. The *Candida* genus stood out as the most prevalent. It was identified in more than 90% of patients evaluated in the general group and in 85.7% of patients admitted to the Covid ICU. *Aspergillus* spp., *Rhizopus* spp. and *Mucor* spp. were also reported to a lesser extent. **Conclusion:** The profile of hospital fungal infections was impacted by the pandemic, since a high percentage of Covid ICU patients affected by mycoses was observed in comparison to patients in other departments.

Keywords: *Fungal Infections. Co-infection. Intensive Care Unit. Healthcare-Associated Infection.*

RESUMO

Justificativa e Objetivos: A Covid-19 pode levar a uma condição imunológica crítica, com necessidade de internação em unidades de terapia intensiva. O risco de coinfecções fúngicas aumenta nesses pacientes, sobretudo se estiverem sob ventilação mecânica, fazendo uso de dispositivos invasivos e/ou antibióticos de largo espectro. Infecções fúngicas secundárias podem agravar os sintomas da doença, dificultar o prognóstico e o tratamento e elevar as taxas de mortalidade e permanência hospitalar. Dessa forma, o objetivo do presente trabalho foi avaliar a influência da pandemia de Covid-19 na distribuição de infecções fúngicas em pacientes internados em um hospital universitário na Paraíba no período de 2020 a 2022. **Métodos:** Foram analisados 456 prontuários do período entre março de 2020 e julho de 2022 encaminhados ao setor de Micologia com suspeita de infecção fúngica. **Resultados:** Dos prontuários avaliados, 120 apresentavam infecção por algum fungo. Apenas 17 prontuários advinham da UTI Covid e 14 deles foram positivos para alguma micose. O gênero *Candida* destacou-se como o mais prevalente, sendo identificado em mais de 90% dos pacientes avaliados no conjunto geral, e em 85,7% dos pacientes internados na UTI Covid. Também foram reportados, em menor frequência, *Aspergillus* spp., *Rhizopus* spp. e *Mucor* spp. **Conclusão:** O perfil das infecções fúngicas hospitalares foi impactado pela pandemia, visto que foi observada uma alta porcentagem de pacientes da UTI Covid acometidos por micoses, em comparação com os pacientes dos demais setores.

Descritores: *Infecções Fúngicas. Coinfecção. Unidade de Terapia Intensiva. Infecção Relacionada à Assistência à Saúde.*

RESUMEN

Justificación y Objetivos: La Covid-19 puede provocar estados inmunológicos críticos que requieren hospitalización en unidades de cuidados intensivos. El riesgo de coinfecciones fúngicas aumenta en estos pacientes, especialmente si reciben ventilación mecánica, utilizan dispositivos invasivos y/o antibióticos de amplio espectro. Las infecciones fúngicas secundarias pueden agravar los síntomas de la enfermedad, dificultar el pronóstico y el tratamiento y aumentar las tasas de mortalidad y la estancia hospitalaria. Así, el objetivo del presente estudio fue evaluar la influencia de la pandemia de Covid-19 en la distribución de las infecciones fúngicas en pacientes ingresados en un hospital universitario de Paraíba durante el período de 2020 a 2022. **Métodos:** Se analizaron 456 historiales médicos del período comprendido entre marzo de 2020 y julio de 2022 enviados al departamento de Micología con sospecha de infección fúngica. **Resultados:** De los historiales evaluados, 120 presentaron infección por algún hongo. Sólo 17 historias clínicas procedían de la UCI Covid y 14 de ellas fueron positivas para alguna micosis. El género *Candida* se destacó como el más prevalente, identificándose en más del 90% de los pacientes evaluados en el grupo general, y en el 85,7% de los pacientes ingresados en la UCI Covid. También se reportaron, en menor medida, *Aspergillus* spp. y *Rhizopus* spp. y *Mucor* spp. **Conclusión:** El perfil de las infecciones fúngicas hospitalarias fue impactado por la pandemia, ya que se observó un alto porcentaje de pacientes de la UCI Covid afectados por micosis en comparación con los pacientes de otros sectores.

Palabras Clave: *Infecciones fúngicas. Coinfección. Unidad de Cuidados Intensivos. Infección Asociada a la Atención Sanitaria.*

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INTRODUCTION

In December 2019, a viral outbreak began in China, causing a respiratory illness similar to pneumonia. After genomic analysis, the causative agent was identified as a novel coronavirus called SARS-CoV-2. Initially, it caused mild symptoms in healthy people but could become severe in immunocompromised individuals.[1-2] On March 11, 2020, due to the rapid global spread of the respiratory syndrome caused by SARS-CoV-2, the World Health Organization (WHO) declared the Covid-19 pandemic.[3]

During the virus's incubation period, which lasts between two and 14 days, more viral particles are produced, ready to infect other hosts.[4] Although the most common symptoms are similar to those of other viral illnesses (dry cough and fever), they can worsen to the point of requiring hospitalization. This critical manifestation of Covid-19 can be explained by the aggressive inflammatory response caused by the release of pro-inflammatory mediators and the immunosuppression caused by the reduction in CD4+ T and CD8+ T lymphocytes in patients.[5-6] This critical immunological condition, combined with intensive care unit (ICU) admission, increases the risk of fungal coinfections in these patients, especially if they are on mechanical ventilation, using catheters and broad-spectrum antibiotics.[7]

Therefore, fungal coinfections in the context of Covid-19 deserve further study, as these microorganisms generally have the potential to aggravate disease symptoms, complicate prognosis and treatment, and increase mortality rates and length of hospital stay.[5] Candidemia, mucormycosis, and aspergillosis deserve special mention as they are the three most frequently reported secondary infections in Covid-19 patients.[6,8-9] Therefore, studies on this topic are necessary to understand the profile of the most present microorganisms in hospital environments, and to develop strategies and solutions from a public health perspective.

The objective of this study was to evaluate the influence of the Covid-19 pandemic on the distribution of fungal infections in patients admitted to a university hospital in the state of Paraíba from 2020 to 2022.

METHODS

Study location
The study was conducted at a public university hospital in the city of João Pessoa, Paraíba, Brazil.

Study design and period
This is a descriptive, cross-sectional, retrospective study. Data were collected from March 2020 (the beginning of the Covid-19 pandemic) to July 2022 (when the Covid ICU was closed at the hospital).

Data source
Data were collected from all medical records with suspected fungal infections of patients admitted to the ICU (general, neonatal, pediatric, and Covid) and other hospital departments and referred to the Mycology Department of the Clinical Analysis Laboratory Unit. Data collection included the date of sample collection, department of origin, patient sex and age, type of sample collected, result, and microorganism isolated. Medical records without suspected fungal infection were excluded from the study analysis.

Statistical Analysis
Data were tabulated using the *Microsoft Excel 2007®* software to enable descriptive analysis of the fungal infection profile.

Ethical aspects
The study was submitted to the Research Ethics Committee of the Center of Medical Sciences at the Universidade Federal da Paraíba (CAAE 47435121.0.0000.8069), and approved on July 1, 2021, under opinion number 4.820.953, in accordance with recommendations of Resolution 466/2012 of the National Health Council.

RESULTS

In total, data were collected from 456 medical records of patients with suspected fungal infections sent to the Mycology department of the Clinical Analysis Laboratory Unit. Of these, 222 were from female patients and 234 from male patients male, mean age of 41.3 years. Of the 456 medical records, 120 tested positive for some form of mycosis, with some fungus identified (Table 1).

Table 1. Distribution of fungi causing mycoses in patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Fungus	N (%)	Priority level according to the World Health Organization[9]
Aspergillus flavus	2 (1.7)	-
Aspergillus niger	1 (0.8)	-
Candida albicans (or suggestive of *Candida albicans*)	60 (50)	Critical
Candida parapsilosis	26 (21.7)	High
Candida spp. (or suggestive of *Candida* spp.)	8 (6.7)	-
Candida tropicalis	15 (12.5)	High
Cryptococcus neoformans	1 (0.8)	Critical
Unidentified yeast	2 (1.7)	-
Mucor spp.	2 (1.7)	High
Rhizopus spp.	1 (0.8)	High
Trichosporon spp.	1 (0.8)	-
Unspecified zygomycete	1 (0.8)	High

The isolated fungi came from various types of biological samples; the most common was urine, followed by blood samples (Table 2).

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Table 2. Origin of samples positive for mycoses in patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Biological sample	Fungus	N (%)
Liver abscess	*Candida parapsilosis*	1 (0.8)
Unidentified sample	*Candida albicans*	1 (0.8)
Tracheal aspirate	*Aspergillus flavus*	1 (0.8)
	Candida albicans	1 (0.8)
Peripancreatic collection	*Candida* spp.	1 (0.8)
Maxillary sinus crust	Zygomycete	1 (0.8)
Sputum	*Candida albicans*	2 (1.6)
	Candida parapsilosis	1 (0.8)
	Trichosporon spp.	1 (0.8)
Fragment of a facial lesion	*Mucor* spp.	2 (1.6)
Fragment of the maxillary sinus	*Candida parapsilosis*	1 (0.8)
Bronchoalveolar fluid	*Candida albicans*	3 (2.4)
	Candida parapsilosis	3 (2.4)
Tracheal lavage	*Candida albicans*	1 (0.8)
Cerebrospinal fluid	*Cryptococcus neoformans*	1 (0.8)
Ascitic fluid	Suggestive of *Candida* spp.	1 (0.8)
Pleural fluid	*Candida albicans*	1 (0.8)
Nasal mucosa and ethmoid and maxillary secretion	*Aspergillus flavus*	1 (0.8)
Blood	*Candida albicans*	8 (6.6)
	Candida parapsilosis	5 (4.0)
	Candida tropicalis	4 (3.2)
	Unidentified yeast	1 (0.8)
	Aspergillus niger	1 (0.8)
Tracheal secretion	*Candida albicans*	5 (4.0)
	Candida tropicalis	2 (1.6)
Vaginal secretion	*Candida tropicalis*	1 (0.8)
Skin lesion swab	*Candida tropicalis*	1 (0.8)
Necrotic tissue from the nasal cavity	*Rhizopus* spp.	1 (0.8)
Urine	*Candida albicans* (or suggestive of *Candida albicans*)	38 (31.7)
	Candida parapsilosis	17 (14.1)
	Candida spp.	6 (5.0)
	Candida tropicalis	7 (5.8)
	Unidentified yeast	1 (0.8)

Of the 456 medical records analyzed, 229 belonged to patients admitted to the ICU: 17 from the Covid ICU and 212 from the non- Covid ICU (general, neonatal, and pediatric). Among the 212 in the non- Covid ICU, 65 (30.7%) tested positive for some form of mycosis: 57 in the general ICU, five in the neonatal ICU, and three in the pediatric ICU. In the Covid ICU, 14 (82%) of the 17 medical records tested positive for fungal infection (Table 3).

Table 3. Distribution of fungi causing mycoses in intensive care units of patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Sector of origin	Fungus	N (%)
General ICU	*Aspergillus niger*	1 (1.26)
	Candida albicans (or suggestive of *Candida albicans*)	27 (34.18)
	Candida parapsilosis	17 (21.5)
	Candida spp. (or suggestive of *Candida* spp.)	4 (5.1)
	Candida tropicalis	6 (7.6)
	Mucor spp.	2 (2.5)
Covid ICU	*Aspergillus flavus*	1 (1.26)
	Candida albicans	7 (8.9)
	Candida parapsilosis	1 (1.26)
	Candida tropicalis	4 (5.1)
	Unidentified yeast	1 (1.26)
Neonatal ICU	*Candida albicans*	3 (3.8)
	Candida parapsilosis	2 (2.5)
Pediatric ICU	*Candida albicans*	1 (1.26)
	Candida parapsilosis	1 (1.26)
	Candida tropicalis	1 (1.26)

DISCUSSION

Fungal infections are a major public health problem that demands greater attention and resources from health authorities. Although medical advances are being made to treat other diseases, cases of invasive fungal infections are steadily increasing, while access to quality diagnostics and treatment remains severely limited. Individuals with weakened immunity due to pre-existing health problems (autoimmune diseases, cancer, diabetes, among others) and those taking broad-spectrum antibiotics and/or corticosteroids are more prone to infections by pathogenic fungi.[9]

Furthermore, although hospitals are environments dedicated to the treatment and well-being of patients, they tend to be places prone to secondary infections.[10] Nevertheless, the sudden emergence of Covid-19 and its frenetic spread have forced hospitals around the world to adapt to accommodate those affected by the disease. The invasive methods used in the treatment of ICU patients, especially in Covid ICUs, such as intubation,

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catheterization, mechanical ventilation, and the use of multiple antibiotics, combined with prior immunosuppression, make this ward a primary source for approximately 25% of all hospital infections.[11] Therefore, the creation of Covid wards favored the incidence of fungi compared to other wards and increased the morbidity and mortality of hospitalized patients.[12] These findings are corroborated by the data found in this study. A positive result for some mycosis was found in 14 (82%) out of the 17 medical records from the Covid ICU, while only 41 (18%) of the 227 medical records from non-ICU wards and 65 (30.7%) of the 212 medical records from non- Covid ICUs obtained this same result.

The *Candida* genus is certainly the most documented in hospital-acquired infections, accounting for approximately 80% of all mycoses in this setting, and its incidence is 10 to 20 times higher in ICUs than in other areas.[13-14] In this study, almost 91% of reported fungal infections were caused by *Candida* spp. (50% by *C. albicans*, 21.7% by *C. parapsilosis*, 12.5% by *C. tropicalis*, and 6.7% by unidentified species). In the Covid ICU, in particular, this study found that infections caused by *Candida* spp. accounted for 85.7% of mycosis diagnoses. This reinforces the idea that this hospital area, like others, has great potential for the emergence and transmission of fungal coinfections.[12]

As observed in this study, *Candida albicans* is the prominent species among mycoses seen in hospital records during the pandemic period evaluated. It appeared in 50% of diagnoses (n=60), the majority (n=38) of which were from urine samples. This species is in the WHO's critical priority group. Due to its virulence factors, it can cause infections of mucous membranes such as the oropharynx, esophagus and vagina, or invade internal organs and the bloodstream, causing invasive candidiasis, which has a high mortality risk (20% to 50%) and particularly affects immunocompromised individuals.[8-9,15]

Although *Candida albicans* is the most commonly isolated species, non-albicans species have recently emerged, among which *C. parapsilosis* and *C. tropicalis* are the most frequently reported.[16] According to the WHO, both species are in the high-priority group and, like the others, can cause invasive infections with a significant mortality risk.[9] A study in Portugal evaluated the incidence of *Candida* in a cancer hospital over six years, and among 119 isolates, *C. parapsilosis* represented approximately 20% of infections caused by *non-albicans Candida*, followed by *C. tropicalis* with 8.4%.[17] Consistent with this information, in that study, 21.7% of all mycoses were caused by *C. parapsilosis* and 12.5% by *C. tropicalis*.

Furthermore, it is important to highlight that in 6.7% of *Candida* spp. diagnoses in the hospital under study, the species was not identified. This suggests underreporting of other potential species of concern, such as *Candida auris*. This pathogen has caused outbreaks in many countries in recent years and its incidence has increased during the pandemic. In Brazil, there have been three outbreaks of infection by this agent. The first isolated case in an ICU patient occurred in a hospital in Salvador, Bahia, Brazil, and was reported in December 2020.[18] This species is in the WHO's critical priority group because it causes invasive candidiasis with a high mortality rate and is resistant to many antifungals.[9]

Aspergillosis have also been identified in immunocompromised patients and in association with Covid-19.[12,19] *Aspergillus* spp. causes an opportunistic infectious disease that commonly affects hospitalized individuals. Conidia of this fungus can be found on clothing, ventilation systems, and other objects, where they are prone to inhalation by a host. Therefore, patients on mechanical ventilation, especially those already infected with Covid-19, become vulnerable to this microorganism and increase their chances of death.[19] In a study conducted from February to December 2020 in a Brazilian referral hospital, the authors observed eight cases of fungal coinfection in Covid-19 patients, three of which (37.5%) were cases of aspergillosis.[20] In our study, only one patient (7%) in the Covid ICU was diagnosed with pulmonary aspergillosis.

Not unlike this, mucormycosis (or zygomycosis), which can be caused by zygomycetes such as *Mucor* spp. and *Rhizopus* spp., although less frequent, also threatens patients with underlying diseases, those undergoing glucocorticoid treatment and/or invasive medical interventions when associated with Covid-19.[19] In June 2021, India recorded more than 28,000 cases of mucormycosis in the midst of the pandemic, in addition to having confirmed almost half of the total Covid-19 cases.[21] The country also has the largest number of diabetic adults in the world, which is associated with the high incidence of mucormycosis, as this comorbidity is one of the main risk factors.[12,19] According to the Ministry of Health, Brazil recorded 99 cases of mucormycosis in 2021 and 14 cases in 2022, corroborating the idea that based on the latest data available (2021-2022), the incidence of this disease is not high.[22] This information can elucidate the fact that in our study only 0.83% (n=1) of the general diagnoses of fungal infections were caused by *Rhizopus* spp. and an unspecified zygomycete, and approximately 1.7% (n=2) were caused by *Mucor* spp. (from the general ICU), although fungi of the order Mucorales are listed in the WHO high-priority group.[9]

The other fungi found in this study had a very low incidence in the hospital as a whole (0.83% *Trichosporon* spp., 0.83% *Cryptococcus neoformans*; n=1 for both) and no incidence in the ICUs. *Trichosporon* spp. is an opportunistic yeast that can be

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found as a cause of sepsis in neutropenic individuals subject to invasive devices and drug treatments. Therefore, it may contribute to a worse prognosis for patients already suffering from Covid-19.[23] In a study conducted between July and September 2020, the incidence of fungemia caused by a species of *Trichosporon* was reported in a hospital in Salvador, Bahia. Of the 183 patients admitted to the Covid ICU, seven (3.8%) had fungemia caused by *Trichosporon* spp., and 18 (9.8%) by *Candida* spp.[23] In agreement with this study, only one case of *Trichosporon* spp. was found in our study, and the patient did not come from the ICU.

Cryptococcus neoformans is an opportunistic yeast that can cause invasive cryptococcosis when inhaled and disseminated through the bloodstream to internal organs. The high mortality rate of this species, especially in patients with HIV, immunocompromised individuals, with autoimmune diseases and decompensated liver cirrhosis, also places it in the WHO's critical priority group.[9] Co-infection with Covid-19 is scarcely documented in the literature, perhaps due to low incidence or possible underreporting. However, among 716 Covid-19-positive individuals followed in a study, one case was reported in Brazil.[24] Only one case of *C. neoformans* was reported in the present study, but the patient was not in the Covid ICU, indicating a low incidence of this fungus during the Covid-19 pandemic at the hospital under study.

A limitation of this study was the lack of information recorded in some patients' medical records. In addition, because the researchers chose to conduct the study exclusively in critical care settings (ICUs), the sample size was smaller than expected, which constituted another limitation of the study.

Given our findings, the importance of studying fungal infections in hospital settings is clear. Furthermore, our research data, consistent with the literature, also showed that during the pandemic, these fungal infections plagued hospitalized individuals, particularly those with Covid-19, as they were immunosuppressed and/or using invasive devices during ICU treatment. Therefore, we conclude that the profile of hospital-acquired fungal infections was impacted by the pandemic in the public hospital under study, as it resulted in a higher incidence of Covid ICU patients with fungal infections compared to patients in other wards.

TEXTO.

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AUTHORS' CONTRIBUTIONS

Mariana de Assis Valverde contributed to the literature search, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Natan Gomes Emmanuel** contributed to the literature search, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Ana Paloma Tavares** contributed to writing the abstract, interpretation and description of results, review, and statistics. **Wallace Felipe Blohem Pessoa** contributed to project administration, 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

Accidents with biological material among health professionals in Brazil: a cross-sectional study involving medication administration

Acidentes com material biológico entre profissionais de saúde no Brasil: estudo transversal envolvendo administração medicamentosa

Accidentes con material biológico entre profesionales de la salud en Brasil: un estudio transversal sobre administración de medicamentos

Corresponding author:
E-mail: lyrio0687@gmail.com
Address: 584 Pasárgada Street, Itapuã, Salvador,
Bahia, Brazil.

Mariana Perruso Lyrio[1]
João Pedro da Silva Rocha[1]
Caio Pires Silva[1]
Anna Júlia Rocha Azevedo[1]
Gabriel Silva Pinto[1]
Jamile de Miranda Tavares[1]
Caroline Santos Silva[1,2]

[1]Unidompedro Afya University Center, Salvador, Bahia, Brazil.
[2]State University of Feira de Santana, Feira de Santana, Bahia, Brazil.

ABSTRACT

Background and Objectives: Healthcare professionals, particularly nursing technicians, are frequently exposed to occupational risks involving contaminated biological materials, such as blood, increasing their vulnerability to infections like HIV and hepatitis B and C. This study aimed to analyze the association between biological material exposure during medication administration among nursing technicians, compared to other healthcare professionals. **Methods:** A cross-sectional analytical study was conducted using 69.129 work-related accident notifications recorded in the SINAN database in 2022. Sociodemographic and clinical variables were analyzed. The association measure used was the Prevalence Ratio (PR), with 95% Confidence Interval (CI) and $p \leq 0.05$. **Results:** Most affected individuals were aged 26 to 45 years (61.3%) and female (76.9%). Blood was the main biological material involved (74.7%). Nursing technicians showed a 2.54 times higher prevalence of accidents during medication administration compared to other professionals (PR = 2.54; 95% CI: 2.46–2.62; $p < 0.0001$). The Southeast region of Brazil reported the highest number of cases. Although 84.8% were vaccinated against hepatitis B, underreporting remains a concern, with 30.4% of Work Accident Reports (CAT) not issued. **Conclusion:** The high frequency of accidents among nursing technicians highlights the urgent need for public policies focused on prevention, improved reporting practices, and proper use of personal protective equipment (PPE). Underreporting compromises health surveillance and calls for educational and organizational strategies to enhance workplace safety in healthcare settings.

Keywords: *Accidents. Occupational Exposure. Biomaterial. Licensed Practical Nurses.*

RESUMO

Justificativa e Objetivos: Profissionais de saúde, especialmente técnicos de enfermagem, estão expostos a riscos ocupacionais relacionados ao contato com materiais biológicos contaminados, como sangue, elevando o risco de infecções por HIV e hepatites B e C. Este estudo teve como objetivo analisar a associação entre acidentes com material biológico durante a administração de medicamentos entre técnicos de enfermagem, comparando-os a outros profissionais da área da saúde. **Métodos:** Foi realizado um estudo transversal analítico, baseado em 69.129 registros de acidentes de trabalho notificados ao SINAN em 2022. Foram analisadas as variáveis sociodemográficas e clínicas. A medida de associação utilizada foi a Razão de Prevalência (RP), com IC95% e $p \leq 0,05$. **Resultados:** A maioria dos acidentados tinha entre 26 e 45 anos (61,3%) e era do sexo feminino (76,9%). O sangue foi o principal material biológico envolvido (74,7%). Técnicos de enfermagem apresentaram prevalência de acidentes 2,54 vezes maior durante a administração de medicamentos em comparação a outros profissionais (RP = 2,54; IC95%: 2,46–2,62; $p < 0,0001$). A maioria dos casos foi registrada na região Sudeste do Brasil. Apesar de 84,8% estarem vacinados contra hepatite B, observou-se significativa subnotificação (30,4% das CATs ignoradas). **Conclusão:** A elevada frequência de acidentes com técnicos de enfermagem evidencia a necessidade de políticas públicas voltadas à prevenção, qualificação para notificação e uso adequado de EPIs. A subnotificação compromete a vigilância em saúde e exige estratégias educativas e organizacionais para aprimorar a segurança dos profissionais no ambiente assistencial.

Descritores: *Acidentes. Exposição Ocupacional. Material Biológico. Técnicos de Enfermagem.*

RESUMEN

Justificación y Objetivos: Los profesionales de la salud, especialmente los técnicos de enfermería, están frecuentemente expuestos a riesgos ocupacionales relacionados con el contacto con materiales biológicos contaminados, como la sangre, lo que aumenta su vulnerabilidad a infecciones como el VIH y las hepatitis B y C. Este estudio tuvo como objetivo analizar la asociación entre los accidentes con material biológico durante la administración de medicamentos entre técnicos de enfermería, en comparación con otros profesionales de la salud. **Métodos:** Estudio transversal analítico, basado en 69.129 notificaciones de accidentes laborales registradas en el sistema SINAN en 2022. Se analizaron variables sociodemográficas y clínicas. La medida de asociación utilizada fue la Razón de Prevalencia (RP), con IC del 95% y $p \leq 0,05$. **Resultados:** La mayoría de la población que sufrió accidentes tenía entre 26 y 45 años (61,3%) y era de sexo femenino (76,9%). La sangre fue el principal material biológico involucrado (74,7%). Los técnicos de enfermería presentaron una prevalencia de accidentes 2,54 veces mayor durante la administración de medicamentos en comparación con otros profesionales (RP = 2,54; IC95%: 2,46–2,62; $p < 0,0001$). La mayoría de los casos se notificaron en la región Sudeste de Brasil. Aunque el 84,8% estaba vacunado contra la hepatitis B, la subnotificación fue significativa (30,4% de las CAT no emitidas). **Conclusiones:** La alta frecuencia de accidentes entre técnicos de enfermería resalta la necesidad urgente de políticas públicas enfocadas en la prevención, la notificación adecuada y el uso correcto de Equipos de Protección Individual (EPI). La subnotificación compromete la vigilancia en salud y exige estrategias educativas y organizativas para mejorar la seguridad en el entorno asistencial.

Palabras Clave: *Accidentes. Exposición Profesional. Biomaterial. Enfermeros Diplomados.*

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INTRODUCTION

Every day, healthcare professionals face significant risks to their health and well-being due to the very nature of their work. Continuous contact with a variety of patients; in different contexts (home care, outpatient care, or surgery); and daily exposure to biological materials contaminated by microbial agents—including bacteria, viruses, and fungi—or sharp objects subject to contamination can aggravate the risks and, if handled incorrectly, result in infections, allergies, or toxicity to these professionals' bodies.[1]

Among the various categories of healthcare professionals, nursing technicians are the most exposed to risk, since their activities require constant contact with patients in different care settings.[1] Thus, the continuous exercise of healthcare practice, especially by professionals who perform invasive procedures, increases the risks of exposure to potentially contaminated biological materials. Among the infectious agents most frequently associated with these accidents are hepatitis B and C viruses, as well as HIV, whose occupational transmission, although less frequent, still represents a significant concern globally.[2]

Occupational exposure to biological material can occur in several ways, including percutaneous exposure mediated by sharp or piercing instruments such as needles, scalpels, and blades. In addition, there is a risk in circumstances inherent to the work of these healthcare professionals, such as performing laboratory procedures involving punctures, collections, and especially the administration of medications.[3]

Given the scarcity of studies on the subject, this study aims to investigate the association between the occurrence of accidents with contaminated biological materials during the administration of medications among nursing technicians, in comparison with other health professions.

METHODS

An epidemiological, cross-sectional analytical study was conducted using individual data collected from the Notifiable Diseases Information System (SINAN) between January and December 2022. Data extraction and analysis took place in October 2024.

All records of occupational accidents due to exposure to biological material reported in 2022, classified under the ICD-10 code Z20.9, were included, provided that the variable "circumstances of the accident" was filled in as "administration of medication." This variable is part of the standard SINAN notification form and represents, according to the system guidelines, accidents related to the handling of medications during care procedures, such as the preparation and administration of drugs, injections, infusions, and the like. Duplicate records and cases with missing data on the occupation of the accident victim or the circumstances of the accident were excluded.

The independent variable was professional occupation, categorized as nursing technicians and other health professionals. The dependent variable was the circumstances of the accident, dichotomized into "medication administration" and "other." The following descriptive variables were selected: race/color, age, gender, education, geographic distribution, occupation, and circumstances of the accidents. Thus, these were duly verified and associated among nursing technicians in order to understand how these variables were related to the aforementioned events.

The sample for this study included all records of occupational accidents due to exposure to biological material resulting from medication administration among healthcare professionals in Brazil in 2022, totaling 69,129 notifications.

It should be noted that this study is subject to possible methodological biases, among which notification bias and exposure classification bias stand out. Reporting bias occurs due to underreporting of accidents with biological materials in SINAN, since not all professionals formally record events, either due to ignorance of the obligation, fear of reprisals, or excessive work demands. This factor can lead to an underestimation of the actual prevalence of accidents, especially among professional groups with less access or incentive to report. Exposure classification bias may be present in the categorization of professions and in the identification of the exact moment of exposure to biological material. As records are based on self-reported information or information filled out by third parties, there is a risk of inconsistencies in the definition of the circumstances of the accident, such as the administration of medications, which may affect the accuracy of association estimates. Despite these limitations, the use of a national and standardized database helps to minimize these distortions and ensure greater reliability of results.

The descriptive analysis was performed using *Jamovi* software (version 1.6), and the association calculations were conducted using *OpenEpi* (version 3.01), with an estimated Prevalence Ratio (PR), 95% confidence interval, and statistical significance of $p \leq 0.05$.

As this is a public, anonymized database with unrestricted access, there was no need for ethical review, in accordance with Resolutions No. 466/2012, 510/2016, and 580/2018 of the Ministry of Health.

RESULTS

More than 50% of the sample is in the 26 to 45 age group. In older people (66+), this figure is less than 1%. There is a noticeable higher frequency in females

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ACCIDENTS WITH BIOLOGICAL MATERIAL AMONG HEALTH PROFESSIONALS IN BRAZIL: A CROSS-SECTIONAL STUDY INVOLVING MEDICATION ADMINISTRATION

Mariana Lyrio, João Pedro da Silva Rocha, Caio Pires Silva, Anna Júlia Rocha Azevedo, Gabriel Silva Pinto, Jamile de Miranda Tavares, Caroline Santos Silva

(76.9%) compared to males (23.1%). In Brazil, the regions with the highest number of cases were the Southeast (45.3%), Northeast (21.5%), and South (18.5%). A higher incidence was found among white and brown individuals (75%). Only 26.7% of accident victims had completed higher education, and 42.5% had completed secondary education (Table 1).

Table 1. Sociodemographic characteristics of professionals injured by biological material in Brazil in 2022.

Age	N (%)
18 - 25	15386 (22.3)
26 - 35	24219 (35.1)
36 - 45	18132 (26.2)
46 - 55	8102 (13.5)
56-65	2348 (3.4)
66+	348 (0.4)
Total	68535
Sex	
Female	53128 (76.9)
Male	15998 (23.1)
Ignored	3 (0.0)
Total	69129
Region	
North	4071 (5.8)
Northeast	14845 (21.5)
Mid-west	5187 (7.4)
Southeast	31312 (45.3)
South	12835 (18.5)
Total	64197
Race/Color	
White	32893 (47.6)
Brown	25931(37.5)
Indigenous	163 (0.2)
Black	4897 (7.1)
Yellow	540 (0.8)
Ignored	4651 (6.7)
Total	69.075
Education	
Illiterate	53 (0.1)
1st to 4th grade incomplete in elementary school	465 (0.7)
Complete 4th grade of elementary school	376 (0.6)
Incomplete 5th to 8th grade of elementary school	1065 (1.6)
Complete elementary school	1214 (1.8)
Incomplete high school	1631(2.5)
Complete high school	28024 (42.5)
Incomplete higher education	6213 (9.4)
Complete higher education	17610 (26.7)
Not applicable	461 (0.7)
Ignored	8808 (13.4)
Total	65920 (100.0)

Regarding clinical variables, 42.4% of individuals filed a Work Accident Report (WAR), while 21.8% did not file one and 30.4% ignored this information. 84.8% were immunized against Hepatitis B. The main biological material during contamination was blood (74.7%). Regarding the evolution of cases, 37.9% were discharged with a negative source patient and 25.6% were discharged without serological conversion (Table 2).

Table 2. Clinical characteristics of healthcare workers injured by biological material in Brazil in 2022.

WAR issuance	N (%)
Yes	29163 (42.2)
No	15054 (21.8)
Ignored	20985 (30.4)
Does not apply	3885 (5.6)
Total	69087
Hepatitis B immunization	
Vaccinated	56547 (84.8)
Not Vaccinated	3177 (4.8)
Ignored	6951 (10.4)
Total	66675
Biological material	
Blood	50357 (74.7)
Cerebrospinal fluid	442 (0.7)
Blood-tinged fluid	2838 (4.2)
Pleural fluid	129 (0.2)
Serum/plasma	302 (0.4)
Amniotic fluid	104 (0.2)
Ascites fluid	69 (0.1)
Other	8386 (12.4)
Unknown	4744 (7.0)
Total	67371
Evolution	
Discharge with serological conversion	3287 (6.2)
Discharge without serological conversion	13628 (25.6)
Discharge of negative source patient	20163 (37.9)
Abandonment	5617 (10.6)
Death due to accident	58 (0.1)
Death due to other cause	18 (0.0)
Unknown	10414 (19.6)
Total	53185 (100.0)

With the data obtained, it is possible to observe the association between being a nursing technician or other professional and becoming infected during the administration of medication or in other circumstances. In total, we have 69,129 people, of whom 26,652 are nursing technicians, with 8,542 suffering accidents during the administration of medication, while 18,110 suffered accidents on other occasions. Among the 41,109 other professionals, 5,188 suffered accidents with medication and 35,921 suffered accidents in other ways. In total, there were exposures in 13,730 people contaminated when administering medication and 54,031 in other ways. (Table 3).

Table 3. Association between occupation and accident circumstances.

Ocupation	Circunstance				
	Medication	Others	Total	PR (95%CI)	p
Technical	8542	18110	26652	2.54	< 0,00001
Others	5188	35921	41109	(2.462 - 2.619)	

Abbreviation: PR: Prevalence ratio. CI: Confidence interval. P: p-value.

The data analysis obtained an PR of 2.5 and a p-value of 0.0001. This indicates that nursing technicians have a significantly higher prevalence of accidents, facing risks 2.5 times higher than their colleagues in other areas. In addition, the p-value of 0.0001 suggests that this association is statistically significant, showing that the

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higher occurrence of accidents is not a matter of chance. These results highlight the urgent need to develop health and safety policies aimed at preventing accidental injuries and protecting these professionals, contributing to reducing the risk of contamination by biological materials.

DISCUSSION

Accidents involving biological materials, whether contaminated or not, are very common, especially among healthcare professionals who are in constant contact with these types of substances. Given this, in 2022, we had a total of 69,130 cases, a noticeable increase when compared to data from 2014 with 47,292 cases, with nursing technicians being the most affected professionals with 26,652 reports.[3]

After analyzing the data obtained, it was possible to see that most of those involved in accidents with biological materials were white, female workers. Most professionals involved in accidents with biological materials are women, reflecting the female predominance in the healthcare workforce, especially in nursing. This predominance, combined with the work overload resulting from balancing professional life and domestic responsibilities, may increase vulnerability to occupational accidents. In addition, factors such as long working hours, care pressures, and the absence of effective preventive measures contribute to this greater susceptibility among women.[4,5,6]

In this sense, it was also observed that the age group most affected by accidents with biological materials was 26 to 45 years old. The high number of accidents among workers in this age group may also be associated with their limited experience in the field and lack of skill in handling instruments, making it important to spend more time in their work activities and health service routines.[7] Thus, the data found correspond to the literature.

It was also observed that the level of education among injured workers was mainly high school completion. Professionals with lower levels of education are at greater risk of exposure to accidents involving sharp objects. This vulnerability may be associated with less professional experience and a lack of adequate training in safe practices for handling sharp and piercing materials.[8]

After a work accident occurs, it is necessary to fill out the WAR, which is the accident notification form used after exposure to biological material, for example. However, it is not always filled out, leading to underreporting of these incidents. Underreporting may be related to a lack of knowledge about the importance of this record for epidemiological analyses, as well as the excessive bureaucracy involved in reporting an accident.[7] Given this, the data found, with 42.2% of forms issued and 30.4% ignored, correspond to the findings in other literature.

Another important factor to be analyzed is related to the vaccination status against the hepatitis B virus (HBV). In the data found, it was possible to note that 84.8% of workers involved in accidents were vaccinated, which is a large number when compared to those who were not immunized and ignored, totaling 15.2%. However, even though this is a low figure in relation to those who received the vaccine doses, it is a significant figure, mainly because the main accidents involved healthcare professionals, since the vaccine is effective and free, offered by the SUS (Brazilian Unified Health System) in the National Immunization Plan (PNI).[7]

Furthermore, analysis of the data on organic materials most commonly present in accidents revealed a predominance of incidents involving blood, accounting for 50,357 (74.7%) occurrences, as it is handled for various tests. This number may be predominant mainly when associated with the handling of lumen needles, reaffirming data found in other literature. The risk of contamination by diseases such as hepatitis B, hepatitis C, and HIV is considered low, a fact that can be confirmed by the percentage of victims who progressed to discharge without serological conversion (25.6%). However, a considerable number (19.6%) of patients abandoned follow-up. Adherence to clinical follow-up after occupational exposure to biological materials is crucial for the prevention of infections among healthcare professionals. However, studies indicate that the rate of abandonment of post-exposure follow-up can be significant. For example, a survey conducted at a university hospital in Malaysia revealed that 51.4% of healthcare professionals did not complete the recommended follow-up after injuries from sharp objects. These findings underscore the importance of implementing effective strategies, such as regular training, proper use of personal protective equipment (PPE), and provision of accessible information on the safe disposal and handling of materials, to ensure the safety and well-being of these professionals.[9]

It is noted that the most affected region in Brazil was the Southeast. Although legally mandatory, the reporting of occupational accidents is, in practice, subject to underreporting, negatively impacting epidemiological surveillance and the implementation of effective preventive measures. Factors such as the perception of low risk associated with minor injuries, lack of knowledge about the risks involved, and the absence of clear reporting protocols contribute significantly to this underreporting. In addition, work overload and resource shortages in hospital settings can make it difficult to comply with the steps necessary for proper reporting of these incidents. This may have been the case in other regions of Brazil, which reported a

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lower number of cases.[10] However, the Southeast, on the other hand, is also the region with the highest population density in the country, the most developed health network, and a concentration of health professionals and workers in sectors that deal with biological materials, increasing the likelihood of occurrences.

Thus, since the study was conducted using secondary data, it is important to highlight the existence of a possible limitation regarding information classified as "ignored" due to non-completion of the notification form, which may hinder a reliable presentation of the results, as well as the influence of unmeasured factors such as confounding factors such as the workload of nursing technicians compared to other professions. Another inherent limitation of a cross-sectional study is the impossibility of measuring and establishing causality between variables.

Despite the limitations described, the findings of this study offer a relevant contribution to understanding the occupational risks faced by nursing technicians in the administration of medications. The use of a comprehensive national database, such as SINAN, allowed for the analysis of a large number of notifications, providing a comprehensive view of the occurrence of accidents with biological materials in Brazil. In addition, the application of robust statistical measures, such as PR with confidence interval, strengthens the reliability of the results. Thus, this study reinforces the need for policies aimed at the safety of healthcare workers and serves as a basis for future investigations that may explore strategies to mitigate occupational risks in this population.

The findings of this study show a statistically significant association between the occupation of nursing technician and the higher frequency of accidents with biological material during the administration of medications, which demonstrates the occupational vulnerability of this category, which is in a position of greater exposure to biological risks in the healthcare context. The high proportion of accidents involving blood, the predominance of notifications in the Southeast region, and persistent underreporting, even in the face of high vaccination coverage against hepatitis B, indicate persistent failures in the processes of prevention, notification, and surveillance of occupational health.

In this context, there is an urgent need to implement more effective and targeted public policies that promote safe working conditions, ongoing education on biosafety measures, and incentives for the systematic reporting of occupational exposures, in addition to raising awareness about the proper completion of WARs.

It is recommended that future studies be designed to include in-depth contextual and structural factors that contribute to the occurrence and underreporting of these events, including variables such as number of employment relationships, infrastructure, institutional culture, and access to PPE. Longitudinal studies with a qualitative approach can contribute to strengthening protection strategies, intervention planning, and evidence-based policy formulation.

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AUTHORS' CONTRIBUTIONS

Anna Júlia Rocha Azevedo contributed to writing and constructing the article's introduction, searching for existing literature on the topic in databases such as PubMed and the

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ACCIDENTS WITH BIOLOGICAL MATERIAL AMONG HEALTH PROFESSIONALS IN BRAZIL: A CROSS-SECTIONAL STUDY INVOLVING MEDICATION ADMINISTRATION

Mariana Lyrio, João Pedro da Silva Rocha, Caio Pires Silva, Anna Júlia Rocha Azevedo, Gabriel Silva Pinto, Jamile de Miranda Tavares, Caroline Santos Silva

Virtual Health Library, and collaborated with the creation of the slides. **Caio Pires Silva** contributed by cleaning the raw Excel database, leaving only useful variables for the study. He compared data in the discussion, searching for existing literature on the topic in databases such as PubMed and the Virtual Health Library, aiming to identify whether or not it related to the data found in the results, in order to build a coherent discussion that justified the values found in the study. He collaborated on the preparation of the slides for the study presentation and contributed to the introduction. **João Pedro da Silva Rocha** contributed by cleaning the database and uploading it to Jamovi. Processed the data in the program and created the variable tables. Used Excel to sum the data of interest, created the contingency table, and uploaded it to Open Epi. Reviewed the text, making some of the changes suggested by the professor. Helped create the slides. **Jamile de Miranda Tavares** contributed mainly to the introduction and methodological part of the article - allocating the association measures, also contributing to the discussion of the body of the article, revised the text and corrected spelling, semantics, and the part in which the professor guided us. Elaborated with the creation of the slides. **Gabriel Silva Pinto** contributed to the preparation of the introduction, searching for existing literature on the topic in databases such as PubMed and the Virtual Health Library, reviewed the text and corrected spelling and semantic errors in the result and collaborated with the creation of the slides. **Mariana Perruso Lyrio** contributed by cleaning, in Excel, the secondary database collected from Sinan on workplace accidents involving exposure to biological material, leaving only the variables of interest used in the study. He described the data obtained using tables generated by Jamovi, comparing the percentages found among sociodemographic and clinical variables, and the association between occupation and accident circumstances. He helped write the discussion and search for articles to explain the results found in the tables. He reviewed the text and corrected parts that the professor requested during the last meeting before the presentation. He arranged the references for the articles used. He collaborated on the preparation of the slides. **Caroline Santos Silva** contributed as a study advisor, assisting in all stages of the article's development. She reviewed and corrected all sections of the work, ensuring scientific and textual coherence. She formatted the manuscript according to the journal's requirements, guided the development of the discussion and methodology, and suggested adjustments and improvements. Furthermore, she oversaw the search and selection of relevant references, assisted in the interpretation of the results, and guided the final structuring of the article for submission.

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

Smoking cessation program impacts on mortality and hospitalizations for cardiovascular diseases

Impacto do programa de cessação do tabagismo na mortalidade e hospitalizações por doenças cardiovasculares

Impacto del programa de cesación del tabaquismo en la mortalidad y hospitalizaciones por enfermedades cardiovasculares

Corresponding author:
E-mail: 20046340@uepg.br
Address: General Carlos Cavalcanti Avenue, 4748, Uvaranas, Ponta Grossa, Paraná, Brazil.

Emílio Augusto Andrade Borges[1] iD
Erildo Vicente Muller[1] iD
Camila Marinelli Martins[1] iD
Ruann Oswaldo Carvalho da Silva[2] iD

[1]State University of Ponta Grossa, Ponta Grossa, Paraná, Brazil.
[2]Federal University of Paraná, Curitiba, Paraná, Brazil.

ABSTRACT

Background and Objectives: Smoking is an important risk factor for CVD. Tobacco use is associated with health system expenditures and loss of life expectancy and quality of life. Brazil has a tobacco control program and has shown a continuous decline in prevalence. This study verified whether the decrease in smoking prevalence was reflected in mortality and hospitalizations due to CVD, comparing with the same variables for RTD. **Methods:** The period 2006-2023 was divided into six triennia. Data on smoking prevalence, population, and mortality and hospitalizations due to CVD and RTD were extracted from VIGITEL, IBGE, and DATASUS. The Rstudio software, version 4.1.2, was used to perform the linear regression model and the correlation test. **Results:** Prevalence tended to decrease in Brazil and its regions, except for the Midwest. Mortality and hospitalization rates per 100,000 inhabitants showed an upward trend in Brazil. Hospitalizations due to RTD showed a strong downward trend, with only the South showing stability. There was no positive correlation between the prevalence of smoking and the variables mortality rate and hospitalizations per 100,000 due to CVD, while there was a strong positive correlation for hospitalizations due to RTD. **Conclusion:** The participation of other risk factors in mortality and hospitalizations due to CVD should be investigated and awareness campaigns about smoking should be expanded. The tobacco control program is an example of a successful public policy.

Keywords: *Hospitalization. Mortality. Tobacco Use Disorder. Cardiovascular Diseases.*

RESUMO

Justificativa e Objetivos: O tabagismo é um importante fator de risco para doenças cardiovasculares (DCV). O uso do tabaco está relacionado com gastos do sistema de saúde e com a perda da expectativa e qualidade de vida. O Brasil possui um programa de controle do tabagismo e tem apresentado contínua queda da prevalência. Este estudo verificou se houve reflexo da queda da prevalência do tabagismo na mortalidade e hospitalizações por DCV, comparando com as mesmas variáveis para doenças do aparelho respiratório (DAR). **Métodos:** O período de 2006-2023 foi dividido em 6 triênios. Os dados de prevalência do tabagismo, população e mortalidade e hospitalizações por DCV e por DAR foram extraídos do VIGITEL, IBGE e DATASUS. Para realizar o modelo de regressão linear e o teste de correlação foi usado o *software* Rstudio, versão 4.1.2. **Resultados:** A prevalência tendeu a queda no Brasil e suas regiões, com exceção do Centro-Oeste. Os coeficientes de mortalidade e de internamentos hospitalares por 100.000 habitantes apresentaram tendência de alta no Brasil. As hospitalizações por DAR registraram forte tendência de queda, com somente o Sul apresentando estabilidade. Não houve correlação positiva entre prevalência do tabagismo com as variáveis coeficiente de mortalidade e internações hospitalares a cada 100.000 por DCV, enquanto para as hospitalizações por DAR houve forte correlação positiva. **Conclusão:** Deve-se investigar a participação de outros fatores de risco na mortalidade e hospitalizações por DCV e ampliar campanhas de conscientização sobre o tabagismo. O programa de controle do tabagismo é um exemplo de política pública de sucesso.

Descritores: *Hospitalização. Mortalidade. Tabagismo. Doenças Cardiovasculares.*

RESUMEN

Justificación y Objetivos: El tabaquismo es un factor de riesgo importante para las enfermedades cardiovasculares (ECV). El consumo de tabaco está relacionado con gastos del sistema de salud y pérdida de esperanza y calidad de vida. Brasil tiene un programa de control del tabaco y ha experimentado un descenso continuo de su prevalencia. Este estudio verificó si la disminución de la prevalencia del tabaquismo se reflejó en la mortalidad y las hospitalizaciones por ECV, comparándolas con las mismas variables para ER. **Metodos:** El período 2006-2023 se dividió en 6 trienios. Los datos sobre prevalencia de tabaquismo, población y mortalidad y hospitalizaciones por ECV y ER se extrajeron de VIGITEL, IBGE y DATASUS. Para realizar el modelo de regresión lineal y la prueba de correlación se utilizó el *software* RStudio, versión 4.1.2. **Resultados:** La prevalencia tendió a disminuir en Brasil y en sus regiones, con excepción de la región Centro-Oeste. Las tasas de mortalidad y de admisión hospitalaria por cada 100 mil habitantes mostraron una tendencia ascendente en Brasil. Las hospitalizaciones por ER registraron una fuerte tendencia a la baja, mostrando estabilidad solo en la región Sur. No se encontró correlación positiva entre la prevalencia de tabaquismo y las variables tasas de mortalidad y de hospitalización por ECV por cada 100.000 habitantes, mientras que para las hospitalizaciones por ER hubo una fuerte correlación positiva. **Conclusión:** Se debe investigar la participación de otros factores de riesgo en la mortalidad y hospitalizaciones por ECV y ampliar las campañas de concientización sobre el tabaquismo. El programa de control del tabaco es un ejemplo de una política pública exitosa.

Palabras Clave: *Hospitalización. Mortalidad. Tabaquismo. Enfermedades Cardiovasculares.*

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INTRODUCTION

Smoking is recognized as the leading cause of preventable deaths in Brazil and worldwide, constituting a major risk factor for non-communicable chronic diseases (NCDs). In 2021, more than 1.3 billion people were smokers globally, with approximately 80% residing in middle- and low-income countries. From 1990 to 2019, tobacco use was responsible for more than 200 million deaths. Tobacco consumption is strongly associated with the development of cardiovascular diseases (CVDs), respiratory diseases, and various types of cancer.[1-4]

In Brazil, smoking remains a significant public health issue, causing approximately 400 deaths every day. Statistics indicate that smoking is responsible for about 80% of deaths from lung cancer and a substantial proportion of deaths from chronic respiratory diseases such as chronic obstructive pulmonary disease (COPD), in addition to contributing to deaths from heart disease and stroke. In terms of years of life lost, it is estimated that smoking results in the loss of more than 2.6 million years of life annually, either through reduced life expectancy or decreased quality of life. Between 1996 and 2020, smoking accounted for more than 2.3 million deaths among individuals aged 35 years or older, representing approximately 8.5% of total mortality in the country. Around 43% of deaths attributed to tobacco use were due to cardiometabolic causes. Furthermore, COPD remains one of the main causes of death associated with smoking. According to recent data, smoking-related illnesses cost the Brazilian health system more than 23 billion reais annually, of which about 11% are due to diseases resulting from exposure to secondhand smoke. More than 8.7 billion reais are linked to cardiovascular diseases, and almost 6.8 billion to COPD-related conditions.[4-8]

Cardiovascular diseases stand out as the leading cause of death in Brazil, with ischemic heart disease (IHD) and stroke being the primary specific conditions. Approximately 30% of deaths from NCDs in the country are due to cardiovascular causes. Tobacco use, whether through cigarettes or heated products, induces endothelial dysfunction and oxidative stress, promotes the development of atherosclerosis, peripheral arterial disease, and aneurysms, increases blood pressure, activates the sympathetic nervous system, and can lead to atrial fibrillation. These factors culminate in events such as IHD, stroke, venous thromboembolism, and hospitalizations due to heart failure. Regarding respiratory diseases, hospitalizations among smokers frequently occur due to exacerbations of COPD or asthma, pleural effusion, spontaneous pneumothorax, cancer-related complications, and pneumonia. In addition, smoking is associated with conditions such as idiopathic pulmonary fibrosis, emphysema, and tuberculosis.[1,9–13]

In 1989, the National Tobacco Control Program (PNCT) was established, coordinated by the National Cancer Institute (INCA), with the objective of reducing the social acceptance of smoking, preventing initiation, supporting cessation, and protecting the population from exposure to tobacco smoke. Since the implementation of the PNCT, Brazil has recorded a significant decrease in smoking prevalence, which dropped from 34.8% in 1989 to 15.2% in 2006 and further to 9.4% in 2014.[2,14-16]

The justification for the present research lies in the importance of addressing smoking as a public health issue that directly affects mortality and the population's quality of life. This study seeks to contribute to the Sustainable Development Goals (SDGs), particularly SDG 3 (Good Health and Well-being), which aims to ensure healthy lives and promote well-being for all at all ages, and SDG 10 (Reduced Inequalities), which aims to reduce health inequalities related to risk factors such as smoking. Understanding the relationship between smoking prevalence and its health outcomes is essential to improving prevention and control policies and to more effectively directing public health resources and efforts.

In this context, the objective of this study is to assess whether the decline in smoking prevalence has had an impact on mortality and hospitalizations due to cardiovascular diseases (CVDs), comparing these data with the same variables for respiratory diseases (RDs).

METHODS

This study consists of an ecological epidemiological time-series analysis, covering the period from 2006 to 2023, structured into six three-year periods: the first (2006-2008), the second (2009-2011), the third (2012-2014), the fourth (2015-2017), the fifth (2018-2020), and the sixth (2021-2023). The independent variable is the prevalence of smoking, while the dependent variables are the mortality and hospitalization rates related to chronic diseases.

Data on the prevalence of smoking were extracted from the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (VIGITEL), which provides this information annually since 2006, with the exception of 2022. Data on mortality and hospitalizations were obtained from the Mortality Information System (MIS) and the Hospital Information System (HIS), accessed through TABNET of the Department of Informatics of the Unified Health System (SUS) (DATASUS), focusing on ICD-10 codes related to diseases of the circulatory system (ICD I00 to I99) and the respiratory system (ICD J00 to J99). However, mortality data for the year 2023 were not yet available on DATASUS. Population data were obtained from the

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Brazilian Institute of Geography and Statistics (IBGE), based on the 2022 population census. As VIGITEL only covers the adult population (18 years or older) of the capitals and the Federal District (FD), the mortality and hospitalization data were also restricted to the population residing in these locations.

The extracted data were organized in a Google Spreadsheets, where the average prevalence of smoking, as well as the mortality and hospitalization rates for chronic diseases for each three-year period in the different regions and in Brazil, were calculated. To calculate the average prevalence of smoking in each region, the sum of the annual smoking prevalences of the capitals was divided by the total number of capitals in the region. The average was then summed over the years available in the three-year period, and the result was divided by the total number of years with available data. The average prevalence of smoking in Brazil was obtained similarly, by summing the overall prevalences as disclosed by VIGITEL and dividing by the total number of years with available data.

For the averages of mortality and hospitalizations due to chronic diseases in each region, the deaths or hospitalizations that occurred in the capitals were summed, and the total was divided by the total number of years with available data in the three-year period. Then, the mortality and hospitalizations rates per 100,000 inhabitants were calculated, using direct standardization with the total population of Brazil (203,080,756 inhabitants according to the 2022 census) as the standard population. The choice of three-year periods was a strategy to minimize the random variation of the coefficients, given that there were no major changes in mortality rates when analyzing the data year by year.

The statistical analysis was conducted in RStudio (version 4.1.2), where a linear regression model was applied to assess the temporal trends of the study variables. The regression model provided trend coefficients, confidence intervals, p-values, and r². In addition, Pearson's correlation test was performed to verify the relationship between the prevalence of smoking and the mortality and hospitalization rates. The test generated the correlation coefficient, confidence intervals, and p-values, considering that p<0.05 indicates a statistically significant correlation between the variables. Regarding ethical issues, the study respected the ethical guidelines for health research, ensuring data confidentiality, anonymity of individuals, and guaranteeing that the use of information followed the stipulated ethical principles, in accordance with the standards of scientific research in Brazil (single paragraph of article 1 of CNS Resolution No. 510/2016).

RESULTS

For the period between 2006 and 2023, a decrease in the prevalence of smoking was observed in all regions and in Brazil, however, the Central-West region showed a trend towards stability (-0.79%; 95% CI [-1.65% - 0.05%]; p = 0.060). Brazil showed a trend of a 1.29% decrease (95% CI [-1.81% - -0.77%]; p = 0.002) in prevalence every three years. Among the regions, the one with the greatest downward trend was the North, with a trend coefficient of -1.53 (95% CI [-2.57% - -0.48%]; p = 0.015), followed by the South, with a decrease of 1.41% (95% CI [-2.09% - -0.72%]; p=0.004). The Southeast and Northeast regions showed a trend of reduction in prevalence of 1.28% (95% CI [-1.69% - -0.87%]; p<0.001) and -1.23% (95% CI [-2.04% - -0.42%]; p = 0.013) every three years, respectively (Figure 1A).

Regarding the temporal trend of hospitalizations for cardiovascular diseases, hospitalization rates per 100,000 inhabitants increased by 1.74 (95% CI [0.45 - 3.02]; p = 0.019) from one three-year period to another in Brazil. The Northeast Region was the only one that showed an upward trend in hospitalizations, with an increase of 0.79 (95% CI [0.07 - 1.51]; p = 0.037). Regarding the coefficients of the linear regression model for hospitalizations, the North Region showed an increase of 0.46 (95% CI [-0.45 - 1.38]; p = 0.231), the South Region of 0.30 (95% CI [-0.08 - 0.68]; p = 0.095), the Southeast Region of 0.15 (95% CI [-0.74 - 1.06]; p = 0.652) and the Central-West Region of 0.02 (95% CI [-0.46 - 0.50]; p = 0.899) (Figure 1B).

Regarding mortality from cardiovascular disease (CVD) in the period from 2006 to 2023, an increasing trend was observed in almost all regions of Brazil (Figure 1D). The CVD mortality rate increased by 1.05 (95% CI [0.73 - 1.36]; p < 0.001) per 100,000 inhabitants in Brazil as a whole. The only region that showed a divergent trend was the South Region, showing a reduction of 0.04 deaths from CVD every three years (95% CI [-0.12 - 0.03]; p = 0.208), therefore, tending towards stability. The Southeast Region stood out with the highest upward trend in the mortality coefficient, with an increase of 0.38 (95% CI [0.15 - 0.60]; p = 0.009) per 100,000 inhabitants. The Central-West Region registered an increase of 0.17 (95% CI [0.13 - 0.21]; p < 0.001). The Northeast and North regions also showed an increasing trend, with linear regression coefficients of 0.29 (95% CI [0.25 - 0.32]; p < 0.001) and 0.24 (95% CI [0.22 - 0.27]; p < 0.001), respectively.

In the trend of hospitalizations for acute respiratory diseases (ARD) per 100,000 inhabitants, Brazil showed a decrease of 5.23 (95% CI [-7.90 - -2.56]; p = 0.005) every three years (Figure 1C). The Northeast Region recorded the largest decreasing trend, with a variation of

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-2.21 (95% CI [-2.87 - -1.56]; p < 0.001) every three years. The Southeast Region followed with a decrease of 1.10 (95% CI [-1.85 - -0.36]; p = 0.014) in hospitalizations for ARD. The Central-West and North Regions also showed reductions, with trends of -1.02 (95% CI [-1.72 - -0.31]; p = 0.016) and -0.68 (95% CI [-1.21 - -0.15]; p = 0.023), respectively. Stability was observed for the South Region, the decrease in hospitalization rates was -0.20 (95% CI [-0.62 - 0.21]; p = 0.244) every three years.

Finally, the trend of mortality coefficients for ARD during the period from 2006 to 2023 for Brazil showed an increase of 1.05 (95% CI [0.40 - 1.69]; p = 0.010) every three years (Figure 1E). The Southeast Region stood out as the one with the highest increasing trend in deaths from acute respiratory distress syndrome (ARDS), with a coefficient of 0.54 (95% CI [0.18 - 0.89]; p = 0.013). Following this, the Northeast Region registered an increase of 0.28 (95% CI [0.12 - 0.43]; p = 0.007) every three years. For the North Region, the trend was a slight increase with a coefficient of 0.16 (95% CI [0.10 - 0.23]; p = 0.001). Meanwhile, in the Central-West and South regions, the trend was one of stability. The linear regression coefficient was 0.07 (95% CI [-0.02 - 0.16]; p = 0.103) for the Central-West and -0.01 (95% CI [-0.07 - 0.04]; p = 0.556) for the South.
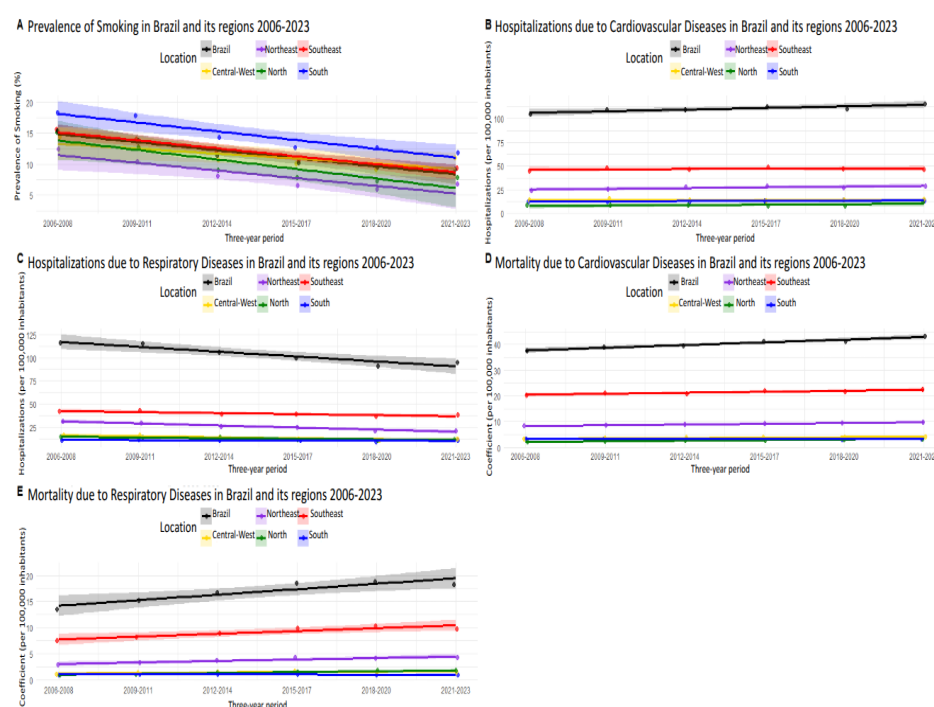
Figure 1. Temporal trends in the prevalence of smoking, hospitalizations, and mortality rates from cardiovascular disease and respiratory diseases.

For the country as a whole, a negative relationship was observed between the prevalence of smoking and hospitalizations for cardiovascular disease (CVD), with a coefficient of -0.84 (95% CI [-0.98 - -0.11]; p = 0.033) (Figure 2a).

Analyzing each Brazilian region, it was observed that in four of the five regions, the prevalence of smoking and hospitalizations for CVD were not correlated. The only region that showed a correlation was the Northeast Region (Figure 2e) with a coefficient of -0.90 (95% CI [-0.98 - -0.33]; p = 0.013) between the prevalence of smoking and hospitalizations for CVD. The correlation values between the prevalence of smoking and hospitalizations for CVD in the six three-year periods from 2006 to 2023 were as follows: for the South Region (Figure 2b), the coefficient was -0.68 (95% CI [-0.96 - 0.29]; p = 0.137); for the Southeast (Figure 2c), Central-West (Figure 2d) and North (Figure 2f) regions, the correlation coefficients were -0.35 (95% CI [-0.90 - 0.64]; p = 0.489), 0.24 (95% CI [-0.70 - 0.88]; p = 0.644) and -0.25 (95% CI [-0.88 - 0.70]; p = 0.628), respectively.
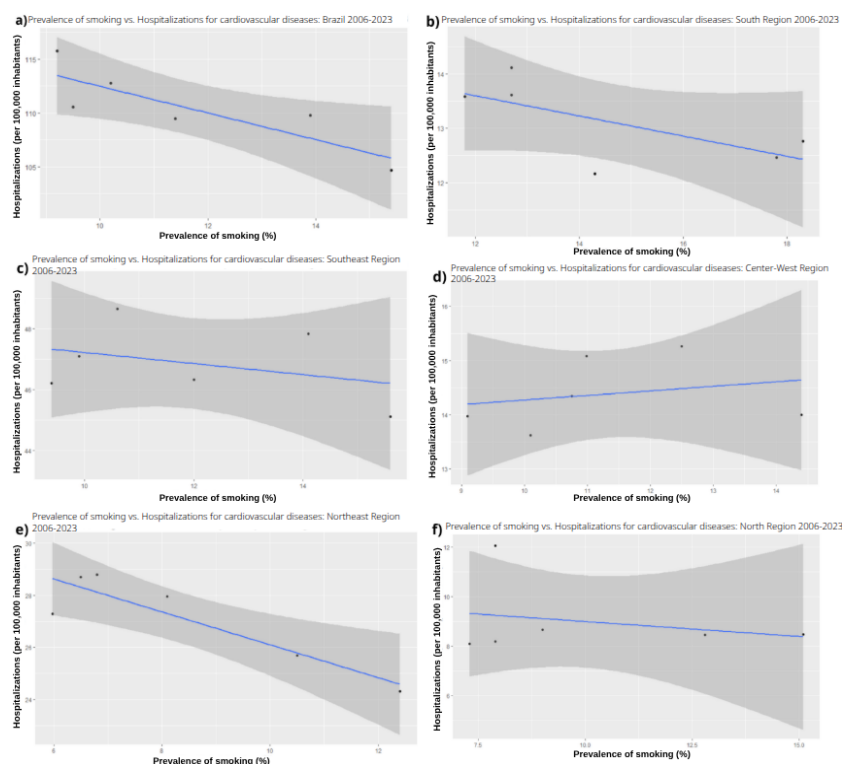
Figure 2. Temporal trends in the prevalence of smoking and hospitalizations for cardiovascular disease (per 100,000 inhabitants). Brazil and regions: 2006-2023.

Regarding the relationship between smoking prevalence and cardiovascular disease (CVD) mortality rate for Brazil and its regions (Figure 3), during the study period, there was a negative correlation (p= 0.008; -0.92 (95% CI [-0.99 - -0.44])) between these variables in the country (Figure 3a). The Southeast (p= 0.013) (Figure 3c), Northeast (p= 0.025) (Figure 3e), and North (p= 0.026) (Figure 3f) regions showed a correlation between smoking and CVD mortality with the following correlation values, respectively: -0.90 (95% CI [-0.98 - -0.35]), -0.86 (95% CI [-0.98 - -0.18]), and -0.86 (95% CI [-0.98 - -0.17]). In the South (p= 0.240) (Figure 3b) and Central-West (p= 0.097) (Figure 3d) regions, smoking prevalence was not related to the CVD mortality rate, with the correlation value for the South Region being 0.56 (95% CI [-0.45 - 0.94]) and for the Central-West Region being -0.73 (95% CI [-0.96 - 0.19]).
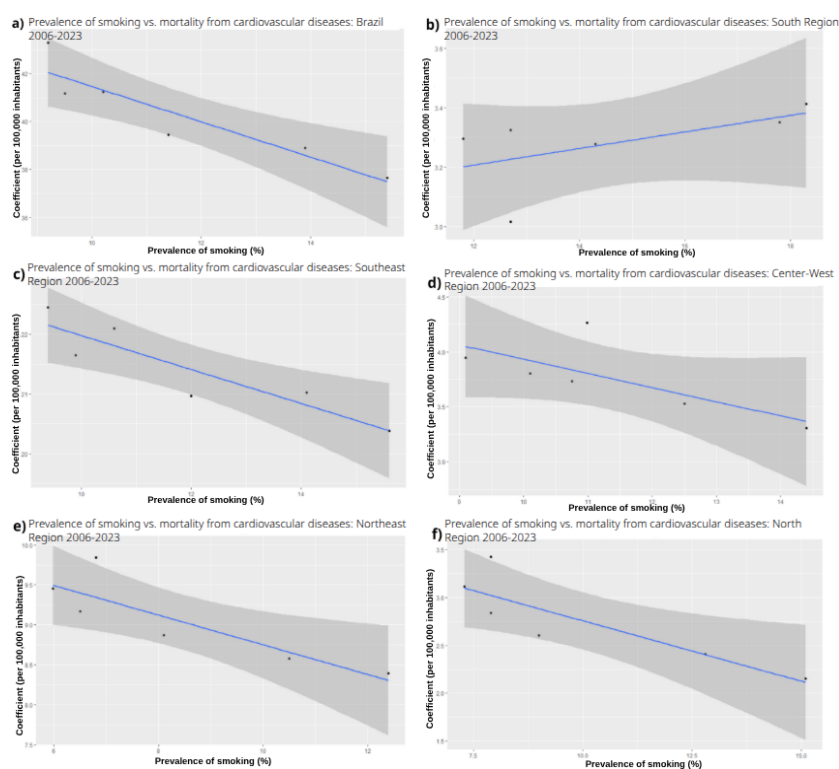
Figure 3. Temporal trend between smoking prevalence and cardiovascular disease mortality rate (per 100,000 inhabitants). Brazil and regions: 2006-2023.

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Analyzing the variables of smoking prevalence and hospitalizations (per 100,000) due to respiratory diseases in three-year periods (Figure 4), Brazil showed a positive correlation (p=0.003) with a correlation value of 0.95 (95% CI [0.62 - 0.99]) between them (Figure 4a). The Brazilian regions followed the country's result; however, the Southern Region (p=0.267; correlation value: 0.54 (95% CI [-0.48 - 0.93])) was an exception (Figure 4b). The regions with a positive correlation between smoking prevalence and hospitalizations due to respiratory diseases presented the following p-values and correlation values: Southeast Region (p=0.005; correlation value: 0.93 (95% CI [0.52 - 0.99])) (Figure 4c); Central-West Region (p=0.018; correlation value: 0.88 (95% CI [0.27 - 0.98])) (Figure 4d); Northeast Region (p=0.005; correlation value: 0.93 (95% CI [0.53 - 0.99])) (Figure 4e); and Northern Region (p=0.046; correlation value: 0.81 (95% CI [0.01 - 0.97])) (Figure 4f).
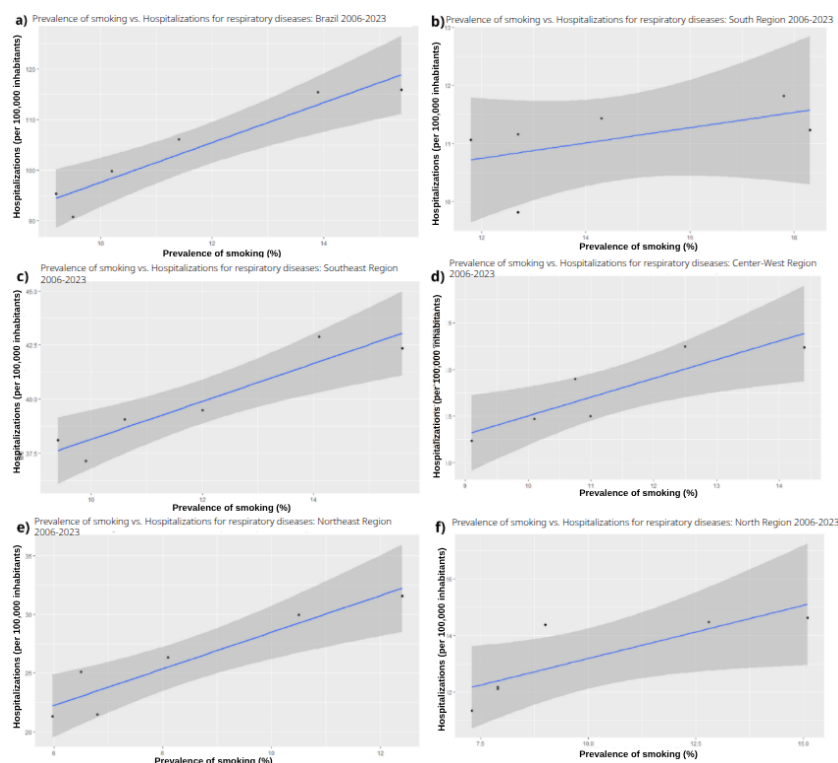
Figure 4. Temporal trend between smoking prevalence and hospitalizations due to respiratory diseases (per 100,000 inhabitants). Brazil and regions: 2006-2023.

Regarding the correlation between the variables of smoking prevalence and mortality rate (per 100,000) from respiratory diseases (Figure 5), a negative correlation was observed at the level of all Brazilian capitals (p-value <0.001; correlation value -0.98 (95% CI [-0.99 - -0.83])) (Figure 5a). Again, the Southern Region diverges from the other regions of the country, showing no correlation (p=0.975) between the variables (correlation value: 0.01 (95% CI [-0.80 - 0.81])) (Figure 5b). The other Brazilian regions follow the trend of Brazil as a whole, presenting the following correlation values between smoking prevalence and deaths per 100,000 inhabitants: Southeast Region (p=0.001; correlation value: -0.96 (95% CI [-0.99 - -0.70])) (Figure 5c); Central-West Region (p=0.014; correlation value: -0.89 (95% CI [-0.98 - -0.32])) (Figure 5d); Northeast Region (p=0.001; correlation value: -0.97 (95% CI [-0.99 - -0.75])) (Figure 5e); and Northern Region (p=0.010; correlation value: -0.91 (95% CI [-0.99 - -0.41])) (Figure 5f).
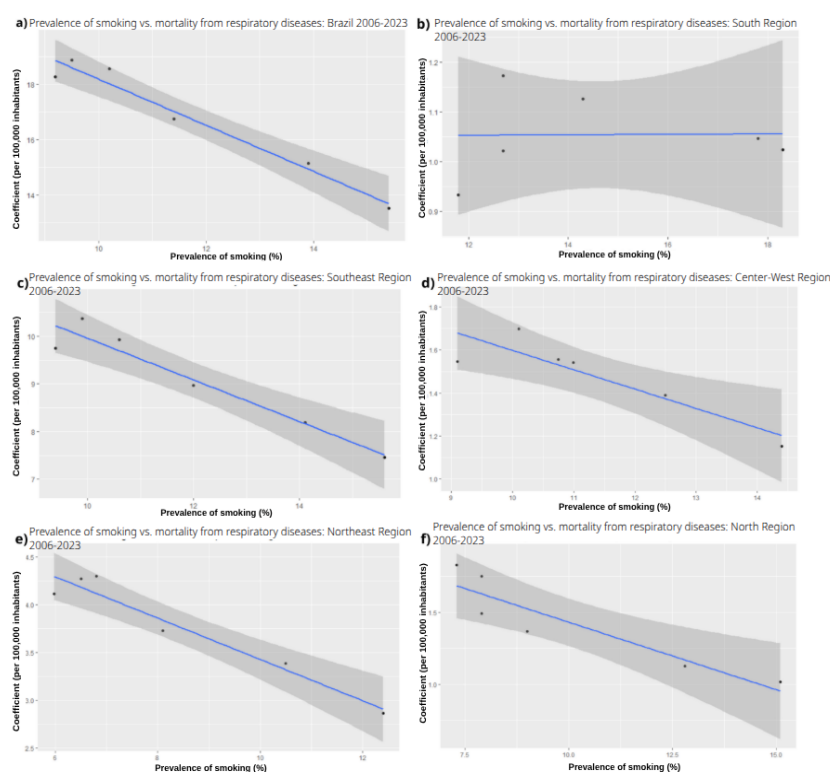
Figure 5. Temporal trend between smoking prevalence and mortality rate from respiratory diseases (per 100,000 inhabitants). Brazil and regions: 2006-2023.

DISCUSSION

The prevalence of smoking in Brazil showed a generalized decline throughout the national territory. However, the regional distribution of this reduction was not uniform. The Southern Region had the highest prevalence of smoking throughout the analyzed period, while the Northeast stood out for having the lowest prevalence in all the three-year periods studied.[17]

The Northern Region, which occupied the third position in terms of prevalence, moved to the fourth position. On the other hand, the Central-West Region, after showing a decrease in smoking rates in the first five three-year periods, experienced an increase in prevalence in the sixth three-year period, exceeding the levels observed in the third three-year period. This increase led the region to show a trend of stability and to rise from the fourth to the second position in the ranking of smoking prevalence.[17]

Brazil has implemented a comprehensive set of strategies for tobacco control, encompassing both legislative measures and sanitary surveillance and treatment actions within the Unified Health System (SUS). In terms of legislation, highlights include the prohibition of advertising and sponsorship by the tobacco industry, the prohibition of tobacco consumption in enclosed public spaces, the requirement of health warnings on tobacco product packaging, and increased taxes on cigarettes, as well as the definition of a minimum price for their sale.[14]

The National Health Surveillance Agency (Anvisa) plays a fundamental role in tobacco control, being responsible for regulating the registration, packaging, and content of tobacco products. Additionally, SUS offers treatment for smoking cessation in Basic Health Units (BHU), where qualified health professionals apply smoking cessation programs.[14,18]

These joint actions aim to reduce the prevalence of smoking in Brazil, minimizing the damage caused by tobacco consumption to individual and collective health. Approximately 80% of smokers want to quit smoking, but only 3% succeed. Due to the chemical dependence on nicotine, several attempts are necessary before cessation. In a study conducted in Curitiba, the majority of participants in the cessation group were female, had completed only elementary school, and had low family income. More than half of those who did not live alone lived with other smokers. The reasons for smoking and the situations that lead to smoking involve anxiety, sadness, post-meal periods or with coffee, and the search for a feeling of pleasure.[18]

People want to quit smoking because they feel it harms their own health and that of their families, in addition to the cost of maintaining the addiction and the example it sets for children. More than 75% of participants in these smoking cessation groups end up using some medication available through the public health system (SUS), 28% abandon the program, and half manage to quit smoking, but with difficulty maintaining abstinence in the following months. Regarding the National Health Surveys (PNS) of 2013 and 2019, passive smoking at home and at work and

exposure to pro-tobacco media decreased, but exposure to anti-tobacco elements, such as warnings and anti-tobacco campaigns, also decreased.[14,18,19]

This study demonstrates that the upward trend in hospitalizations for cardiovascular diseases (CVD) in the country was driven by the Northeast Region, while the other regions remained stable. Thus, there was no impact of the reduction in prevalence on hospitalizations for CVD, as the variables are not related or are negatively related. For comparison purposes, hospitalizations for respiratory diseases (RD) showed a sharp decrease in Brazil, and all regions showed a decrease, although the South tended towards stability.

Regarding mortality from cardiovascular disease, there was also no impact from the decrease in smoking prevalence in this study, as Brazil and almost all regions showed an upward trend in deaths per 100,000 inhabitants or maintained stability. Mortality from respiratory diseases followed the trend of CVD for Brazil.

CVDs do not have tobacco use as the only risk factor; they are also linked to the development and mortality from this group of diseases, including systemic arterial hypertension (SAH), diabetes mellitus, elevated non-HDL cholesterol, obesity, sedentary lifestyle, high alcohol intake, depressive symptoms, air pollution (with a greater effect on strokes), and poor eating habits. CVDs are multifactorial; several situations can lead to pathological changes.[20]

For respiratory diseases, tobacco is directly associated with their etiology. Asthma is related to the exposure of the fetus or newborn to toxic substances in smoke, with non-exposure of the patient to smoke improving disease control. For COPD, the third leading cause of death in the world, quitting smoking is the only intervention that alters the natural history of the disease. In addition to increasing the chance of interstitial lung diseases and lung cancer, smoking also increases the risk of tuberculosis and bacterial pneumonia. Thus, in smoking patients with respiratory diseases, comprehensive clinical approaches and assessments are necessary, as well as encouragement to quit smoking.[12,13]

In conclusion, this study shows a decrease in hospitalizations for respiratory diseases and an increase in mortality rates from these diseases, indicating a higher frequency of fatal outcomes in hospital admissions for respiratory diseases. This study highlights the need for further studies on risk factors and their participation in the burden of CVD in Brazil, as well as investigating the reasons for the stability in smoking rates in the Central-West region. It is necessary to reinforce or expand awareness campaigns about the risks of the habit and about smoking cessation itself. The study demonstrates that, over time, actions in the field of tobacco control are examples of successful public policies, provided they are well coordinated.

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AUTHORS' CONTRIBUTIONS

Emílio Augusto Andrade Borges contributed to the bibliographic research, writing of the abstract, introduction, discussion, interpretation and description of the results, and conclusions. **Erildo Vicente Muller** contributed to the writing of the introduction, methodology, discussion, description of the results, and text revision. **Camila Marinelli Martins** contributed to the statistical analysis, interpretation of the results, and text revision. **Ruann Oswaldo Carvalho da Silva** contributed with the text 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

Evaluation of the clinical and epidemiological profile of patients with paracoccidioidomycosis in a public hospital

Avaliação do perfil clínico e epidemiológico de pacientes com paracoccidioidomicose em um hospital público
Evaluación del perfil clínico y epidemiológico de los pacientes con paracoccidioidomicosis en un hospital público

Corresponding author:
E-mail: joicecarvalho506@gmail.com
Address: Santa Helena Street, 1339, Teresina, Piauí, Brazil.

Mauro Roberto Biá da Silva[1]
Francisca Aline Amaral da Silva[1]
Joice Pereira Carvalho[1]

[1]State University of Piauí, Teresina, Piauí, Brazil.

ABSTRACT

Background and Objectives: The incidence of Paracoccidioidomycosis (PCM) may be underestimated due to the lack of mandatory notification of cases, as systemic mycoses in Brazil are not included in the national list of notifiable diseases. The aim of this study was to evaluate the clinical and epidemiological profile of patients with PCM at a reference center for infectious diseases in Piauí. **Methods:** This is a retrospective, quantitative-descriptive study. It was carried out in a hospital specializing in tropical diseases. A data collection form was used. We included medical records in which the patients had a final diagnosis of PCM, with a hospitalization date between October 2018 and September 2023. Medical records whose final diagnosis was not PCM and that the information was not complete in the medical record were excluded. **Results:** Of the inpatient records checked, 20 were confirmed. Of the patients affected, 100% were male, with the predominant age range between 30 and 60 years (60%), from rural areas, working as farmers (60%). The disease manifested itself in its chronic form (55%), with focal and multifocal lesions being equally prevalent (50%), with an onset time of less than one year (60%), and the presence of secretion (60%). **Conclusion:** The data obtained contributes to a better understanding and perception of the epidemiology of PCM, demonstrating the need to formulate public health policies capable of giving visibility to this neglected disease, which requires strategies for its prevention, diagnosis and treatment.
Keywords: *Paracoccidioidomycosis. Epidemiology. Clinical aspects. Public Hospitals. Retrospective Studies.*

RESUMO

Justificativa e Objetivos: A incidência da Paracoccidioidomicose (PCM) pode estar subestimado em decorrência da ausência de notificação obrigatória dos casos, pois no Brasil micoses sistêmicas não estão inclusas na lista nacional de agravos de notificação compulsória. O objetivo do estudo é avaliar o perfil clínico e epidemiológico de pacientes com PCM em um centro de referência para doenças infecciosas no Piauí. **Métodos:** Trata-se de um estudo retrospectivo e quantitativo-descritivo. Realizado em hospital especializado em doenças tropicais. Foi utilizado como instrumento de coleta de dados um formulário. Foram incluídos os prontuários nos quais os pacientes tiveram diagnóstico final de PCM, com data de internação entre outubro de 2018 e setembro de 2023. Foram excluídos prontuários cujo diagnóstico final não tenham sido de PCM e que as informações não estiveram completas no prontuário. **Resultados:** Dos prontuários verificados de pacientes internados, 20 foram confirmados. Entre os pacientes acometidos 100% eram do sexo masculino, com a faixa etária predominante entre 30 e 60 anos (60%), originário da zona rural, exercendo a atividade laboral de lavradores (60%). A doença se manifestou na sua forma crônica (55%), tendo a extensão da lesão focal e multifocal igualmente prevalente (50%), com o tempo de surgimento menor que um ano (60%), com presença de secreção (60%). **Conclusão:** Os dados obtidos colaboram para uma melhor compreensão e percepção da epidemiologia da PCM demonstrando a necessidade de formulação de políticas de saúde pública capazes de dar visibilidade à doença negligenciada e que requer estratégias de prevenção, diagnóstico e tratamento da PCM.
Descritores: *Paracoccidioidomicose. Epidemiologia. Aspectos clínicos. Hospitais públicos. Estudos Retrospectivos.*

RESUMEN

Justificación y Objetivos: La incidencia de Paracoccidioidomicosis (PCM) puede estar subestimada debido a la falta de notificación obligatoria de los casos, ya que las micosis sistémicas en Brasil no están incluidas en la lista nacional de enfermedades de declaración obligatoria. El objetivo de este estudio fue evaluar el perfil clínico y epidemiológico de los pacientes con PCM en un centro de referencia para enfermedades infecciosas en Piauí. **Métodos:** Se trata de un estudio retrospectivo, cuantitativo-descriptivo. Fue realizado en un hospital especializado en enfermedades tropicales. Se utilizó un formulario de recolección de datos. Se incluyeron historias clínicas en las que los pacientes tenían diagnóstico final de PCM, con fecha de hospitalización entre octubre de 2018 y septiembre de 2023. Se excluyeron las historias clínicas cuyo diagnóstico no fuera PCM y que la información no estuviera completa en la historia clínica. **Resultados:** De las historias clínicas revisadas de pacientes hospitalizados, se confirmaron 20. De los pacientes afectados, el 100% eran varones, con el rango de edad predominante entre 30 y 60 años (60%), procedentes de zonas rurales, que trabajaban como agricultores (60%). La enfermedad se manifestó en su forma crónica (55%), con igual prevalencia de lesiones focales y multifocales (50%), con un tiempo de aparición inferior a un año (60%) y presencia de secreción (60%). **Conclusión:** Los datos obtenidos contribuyen para una mejor comprensión y percepción de la epidemiología de la PCM, demostrando la necesidad de formulación de políticas de salud pública capaces de dar visibilidad a esta enfermedad desatendida, que requiere estrategias para su prevención, diagnóstico y tratamiento.
Palabras Clave: *Paracoccidioidomicosis. Epidemiología. Aspectos clínicos. Hospitales Públicos. Estudios Retrospectivos.*

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Mauro Roberto Biá da Silva, Francisca Aline Amaral da Silva, Joice Pereira Carvalho.

INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic disease resulting from infection caused by a dimorphic fungus that is endemic in the Americas, found from Mexico to Argentina, with the highest incidence in Brazil, Venezuela, and Colombia. *Paracoccidioides brasilienses* prefers moist soil and regions with medium to high rainfall, mild temperatures, and the presence of forests and rivers. Infection by Paracoccidioides sp. is observed in areas of soil management work activities. Humans and nine-banded armadillos (Dasypus novemcinctus) are the main accidental hosts. However, human-to-human transmission has not yet been reported.[1]

Thus, contamination occurs through inhalation of propagules from the mycelial (saprophytic) phase of the pathogen. In the body, the propagules transform into yeast and infection sets in. It is estimated that approximately 10 million people are infected in South America, and up to 2% have developed symptoms of PCM. Most develop the disease years after infection, mainly presenting with pulmonary disease.[2,3]

Given this, PCM manifests as a pneumopathology linked to mucosal and skin lesions, which, when established in the lungs, transforms into a yeast-like form. From the lung parenchyma, it can spread via the bloodstream and lymphatic system to other organs, such as the spleen, liver, bones, and central nervous system. The primary phase of infection usually involves young individuals, as a limited pulmonary disease, which rarely progresses to the acute/subacute stage of the disease, unlike chronic cases, in which individuals have long periods of latency and, during reactivation, pulmonary and/or other organ involvement is observed.[4]

Depending on the incubation period and the characteristics of the infected individuals, PCM usually causes a transient pulmonary infection that can evolve from a subacute to an acute form or, more frequently, can reactivate later as a chronic and insidious disease. In addition, symptoms may manifest later, years or decades later, when the patient may be residing in the city or even in another country outside the endemic region.[6,7]

In the state of Piauí, many families, especially in rural areas, depend on family farming for their livelihood and are therefore constantly exposed to soil contaminated by *Paracoccidioides brasilienses* in its mycelial form and other pathogens. In addition, armadillo hunting is a very common practice in these regions, which makes them susceptible to contracting mycosis and developing the disease. Due to the lack of mandatory reporting of cases, there are no accurate references on the disease, and data collection for epidemiological understanding is carried out in case studies, hospital information, and the Unified Health System (SUS).[6,8]

This study seeks to understand the clinical and epidemiological profile of Paracoccidioidomycosis (PCM) in an endemic region of Piauí, where the disease is underreported and little investigated. The absence of mandatory reporting makes it difficult to obtain accurate data, hindering prevention and treatment strategies. The analysis of cases in a reference center contributes to improve epidemiological surveillance and guide control measures.

METHODS

This is a retrospective, quantitative-descriptive study that aims to examine the characteristics of a group: its distribution by age, gender, origin, educational level, income level, physical health status, and other variables. One of its most significant characteristics is that it allows for a standardized data collection technique.[9]

This study was conducted between September and November 2023 at a hospital specializing in tropical diseases, located in the municipality of Teresina, in the state of Piauí, which provides care to the population through an agreement with the Unified Health System (SUS), where a wide range of infectious and parasitic diseases are treated, including PCM.

Thus, all patients affected by PCM who had been hospitalized in the last 5 years at a referral hospital in the city of Teresina, Piauí, participated in the study. According to information collected at the hospital where the study was conducted, an average of 10 patients are hospitalized annually. Therefore, for this research, all medical records of patients hospitalized with a diagnosis of PCM were used, totaling 20 medical records for data collection. It is worth noting that, since the intention was to work with the total sample, it was unnecessary to perform a sample calculation.

The study included medical records in which patients had a final diagnosis of PCM, without restriction of gender, including young people, adults, and the elderly, with a date of admission from October 2018 onwards, with complete hospitalization information. Medical records in which the information was incomplete were excluded.

A form created by the researchers was used as a data collection tool, which underwent pretesting with three medical records, where it was evaluated and improved. The data obtained were organized in an Excel® spreadsheet and subsequently transferred to a statistical program, which resulted in the construction of graphs and tables. We opted to use the Statistical Package for the Social Sciences (SPSS) version 28, which is available for purchase.

For the descriptive statistical analysis of the data, we used SPSS® version 28 to calculate the absolute and relative frequencies (%) of the categorical variables. Due to the small sample size, no inferential tests were

applied. In parallel, descriptive statistics made it possible to identify relevant clinical and epidemiological patterns of PCM.

To analyze the association between categorical variables, Fisher's exact test was used, considering the small sample size of the study. This test proved to be adequate because it does not require large samples and offers greater statistical precision in the analysis of contingency tables with small frequencies.

The study was submitted to the Research Ethics Committee of the State University of Piauí (REC) and began after approval, under opinion No. 6,190,978 and the Certificate of Ethical Presentation and Appraisal (CAAE): 71167423.4.0000. 5209, approved on July 19, 2023, in accordance with Resolution No. 466, of December 12, 2012, of the National Health Council (CNS).

For data collection, all patients involved in the study were guaranteed anonymity, and for this purpose, their names were not disclosed on the collection forms. We emphasize that, in accordance with CNS Resolution No. 466/2012, the Research Ethics Committee (REC) waived the application of the IC, considering the low risk and the use of anonymized retrospective data. A formal justification was prepared and approved by the REC, guaranteeing the confidentiality and privacy of patients.

RESULTS

A total of 2,488 medical records of patients admitted to the hospital with various diseases were reviewed between October 2018 and September 2023. Among the medical records analyzed, 26 diagnostic hypotheses of PCM were identified. Of these, 20 were confirmed as positive through histopathological examination of sputum. The number of medical records analyzed per year, with suspected and confirmed cases of PCM, is shown below (Figure 1).
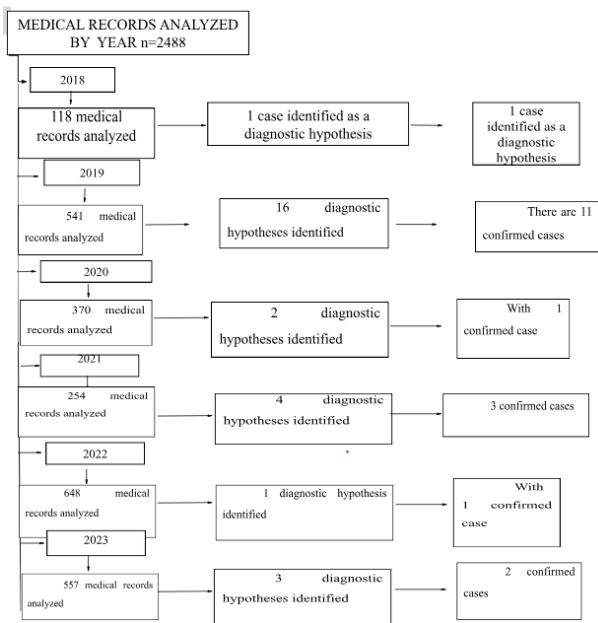

Figure 1. Flowchart showing the distribution of the number of medical records analyzed from 2018 to 2023.

Given the clinical and epidemiological characteristics presented in the study sample, it was evident that males were the only ones affected (100%). The dominant age group was between 30 and 60 years old (60%), and in the sample studied, all cases were male (100%). Regarding the sociodemographic profile, most patients (60%) were between 30 and 60 years old, came from rural areas of the state of Piauí, had incomplete elementary school education, a monthly income of 1 to 2 minimum wages, and worked in agriculture (60%) (Table 1).

Table 1. Sociodemographic characteristics of patients diagnosed with PCM at a public referral hospital in Teresina, Piauí, 2023 (N=20).

Variable	N (%)
Gender	
Male	20 (100)
Female	0
Age at Diagnosis	
Up to 30 years	7 (35)
30 to 60 years old	12 (60)
Over 60 years old	1 (5)
State of Origin	
Maranhão	2 (10)
Pará	1 (5)
Piauí	17 (85)
Residential Area	
Rural	19 (95)
Urban	1 (5)
Education	
No schooling	2 (10)
Incomplete elementary school education	10 (50)
Complete elementary school education	4 (20)
Incomplete high school education	2 (10)
Complete high school education	2 (10)
Month income	
Less than 1 minimum wage	1 (5)
Between 1 and 2 minimum wages	19 (95)
Profission	
Retired	1 (5)
Self-employed	2 (10)
Student	1 (5)
Farmer	12 (60)
Driver	1 (5)
Bricklayer	1 (5)
Fisherman	1 (5)
Rural producer	1 (5)

Analysis of the disease history revealed that paracoccidioidomycosis (PCM) manifested predominantly in the chronic form (55%), with an equal distribution between focal and multifocal lesions (50% each). It was found that the time of onset of symptoms ranged from 3 to 6 months in 60% of cases, accompanied by the presence of secretion in the lesions (60%) and weight loss of up to 15 kg (Table 2).

Table 2. Clinical characteristics of patients diagnosed with PCM at a public referral hospital in Teresina, Piauí, 2023 (N=20).

Variable	N (%)
Clinical Form of PCM	
Acute/Subacute	7 (35.0)
Chronic	11 (55.0)
Not reported	2 (10.0)
Extent of Injury	
Focal	10 (50.0)
Multifocal	10 (50.0)
Time of Lesion Appearance	
Up to 3 months	4 (20.0)
From 3 to 6 months	6 (30.0)
From 6 months to 1 year	2 (10.0)
More than 1 year	1 (5.0)
Not reported	7 (35.0)
Presence of Secretion	
No	8 (40.0)
Yes	12 (60.0)
Weight Loss	
No	2 (10.0)
Yes	18 (90.0)
Weight Reduction	
Up to 15 kilograms	6 (33.4)
From 15 to 30 kilograms	0
Over 30 kilograms	1 (5.5)
Not specified	11 (61.1)

The main regions of the body affected by PCM lesions were identified as the respiratory tract (pharynx, lungs, larynx) as the most affected, followed by the oral cavity (hard palate, soft palate, lips), cervical region, axillary region, testicles, inguinal region, skin, and upper and lower limbs (Figure 2).
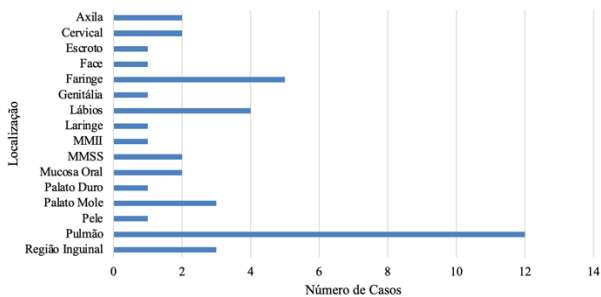
Figure 2. Location of the lesion in patients diagnosed with PCM at a public referral hospital in Teresina, PI, 2023 (N=20).

Regarding the pharmacological treatment of PCM, the antifungal drugs itraconazole and amphotericin B were the main drugs used. Other drugs such as ambroxol, ceftriaxone, sulfamethoxazole+trimethoprim (SMZ+TMP), and azidothymidine (AZT) were used to manage secondary conditions or associated complications (Figure 3).
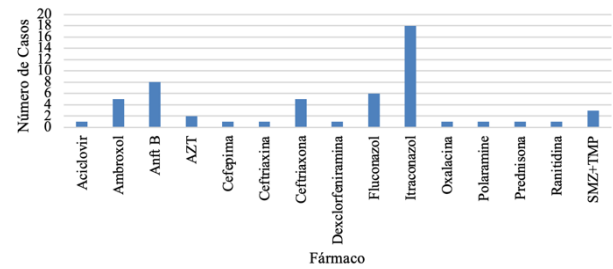

Figure 3. Drugs used in the treatment of patients diagnosed with PCM in a public referral hospital in Teresina, PI, 2023 (N=20).

DISCUSSION

Among the 2,488 medical records analyzed, only 20 cases were confirmed between October 2018 and September 2023. It can be seen that in 2019 there was a significant increase in the number of cases, with a significant decrease the following year, precisely the year the Covid-19 pandemic broke out. It can be assumed that there was underreporting, since PCM, in addition to not being mandatory for reporting, has symptoms similar to other diseases, including the coronavirus.

Furthermore, the study demonstrated that 100% of patients affected by PCM are male. Studies indicate that in the adult population there is a ratio of 5.4 to 10 infected men for every woman. This occurs due to the action of the female hormone estradiol 17-β (hormone that regulates menstruation), which inhibits the transformation of mycelium or conidia into yeast (pathogenic form), preventing the development and progression of the disease, making the disease predominantly male.[4,10]

Concurrently, the age group most affected among the cases investigated is between 30 and 60 years old, since individuals frequently affected by the pathogen are in the most productive phase of their lives because they are exposed to the pathogen in the daily exercise of their work activities.[4]

Furthermore, the results of the study showed that 95% of affected patients are residents of rural areas, while 5% reside in urban areas, and more than half of those residing in rural areas are farmers, since one of the main risk factors for contracting the disease is exposure to soil contaminated by armadillo excrement containing PCM conidia in rural areas, making it an occupational disease for farmers in endemic regions.[7]

In addition, research has shown that the clinical manifestations of the disease present in acute/subacute (juvenile) and chronic forms, with the latter being more prevalent (more than 50% of confirmed cases). Studies show that the juvenile clinical form is prevalent in children and young adults, who have an inadequate Th2 cell response to control fungal infection. The chronic form manifests in 80 to 95% of cases, affecting

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individuals of productive age (after the third decade of life).[11]

Approximately 60% of patients suffering from the chronic form of the disease develop lung lesions. Apparently, this sequela is due to continuous stimulation of fungal antigens and subsequent activation of the immune system and changes in its repair mechanisms. Although long-term antifungal therapy is effective in treating active PCM, it does not seem to affect the development of pulmonary fibrosis.[12]

From a clinical perspective, the research showed that the drugs most commonly used to treat PCM were Itraconazole, Fluconazole, Amphotericin B, and Sulfamethoxazole/Trimethoprim, also known as Cotrimoxazole. According to studies, until the 1940s, there were not enough therapeutic drugs to treat the disease, which is why it was considered fatal. Since then, several therapeutic drugs have been used and have shown promising results. According to clinical research, the drugs currently available are sulfonamides (including cotrimoxazole), amphotericin B deoxycholate, ketoconazole, and triazole derivatives (itraconazole, fluconazole, voriconazole).[13]

Studies have shown that itraconazole is 100 times more active than ketoconazole against PCM, as it is more effective and tolerable, and is considered the drug of choice for controlling patients with lower risk of death and lower recurrence rates. Voriconazole is also a second-generation triazole derivative that has been shown to be as effective as itraconazole, but has been reported to be less safe. Another option is fluconazole, used in cases of elevated liver enzymes, hypersensitivity to sulfonamides or amphotericin B, and neurococcidioidomycosis. Intravenous fluconazole, voriconazole, and itraconazole are available in some countries. In Brazil, itraconazole is used as a long-term therapeutic measure.[13,14]

However, these antifungals have several disadvantages, such as: (i) Azoles have fungistatic, but not fungicidal, effects against *P. brasiliensis* in vivo; (ii) Although azoles are considered safe and effective, treatment is prolonged and its efficacy is variable, ranging from a few months to a year, depending on the patient's condition; (iii) Amphotericin B is highly nephrotoxic.[12]

PCM is a disease that remains neglected by public health, despite being associated with high morbidity and mortality rates. There is still a need for epidemiological studies in areas where the disease is endemic. The above data identified the epidemiological profiles and clinical aspects of populations affected by PCM, which allows health surveillance to create preventive measures aimed primarily at the most vulnerable groups affected by this disease.[8]

Systemic mycoses represent a public health problem in Brazil due to the difficulties in differentiating the symptoms of PCM, as they resemble other pathologies, in addition to the diagnosis and treatment of the disease, which corroborates the high morbidity and mortality rates. The data obtained in this study contribute to a better understanding and perception of the epidemiology of PCM in endemic areas, thus demonstrating the need for public health policies that seek better strategies for the diagnosis and treatment of PCM.

The main limiting factors were the small sample size, which restricts the generalization of the findings. The retrospective nature and dependence on medical records may have led to data loss and underreporting. In addition, the absence of mandatory reporting of PCM in Brazil makes it difficult to estimate the disease more accurately. Despite this, the study contributes to the knowledge of PCM in a little-explored endemic region.

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AUTHORS' CONTRIBUTIONS

Mauro Roberto Biá da Silva research supervisor, contributed to the structuring of the research, made corrections at all stages, structured the methodology, guided the construction of the research form and data collection. **Francisca Aline Amaral da Silva** co-supervisor of the research, supported the supervisor, proofread the text, made corrections at all stages, and corrected the references. **Joice Pereira Carvalho** research assistant, contributed to the writing of the research, construction of the research form, data collection, and interpretation of the collected data.

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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Short Communication

The culture of communication in the antimicrobial program in Brazilian pediatric intensive care

A cultura da comunicação no programa de antimicrobianos em terapia intensiva pediátrica brasileira
La cultura de la comunicación en el programa de antimicrobianos en terapia intensiva pediátrica brasileña

Eliane Carlosso Krummenauer[1] iD
Mariana Portela de Assis[1] iD
Mara Rubia Santos Gonçalves[2] iD
Magda Machado de Miranda Costa[2] iD
Rochele Mosmann Menezes[1] iD
Jane Dagmar Pollo Renner[1] iD
Marcelo Carneiro[1] iD

[1]University of Santa Cruz do Sul, Santa Cruz do Sul, Rio Grande do Sul, Brazil.
[2]National Health Surveillance Agency, Brasília, Federal District, Brazil.

ABSTRACT

Background and Objectives: Antimicrobial Stewardship Programs (ASPs) are essential for optimizing the use of antimicrobials and combating bacterial resistance. This study evaluated the effectiveness of ASPs in Brazilian pediatric intensive care units (PICUs). **Methods:** This multicenter study, conducted in 219 Brazilian hospitals, used a validated form to collect information on antimicrobial use shared with healthcare professionals. The characteristics of the services were analyzed according to their location, level of adherence to ASP actions, and the feedback activities offered to PICU staff. **Results:** The overall implementation level of ASPs in hospitals was considered intermediate, with an average score of 72.46 (±37.60). PICU behavior varied significantly among states. Some states had more survey responses, some had higher hospital adherence, and some excelled in disseminating ASP results. Some institutions were found to have stronger feedback strategies, with most adopting organized institutional actions and approximately half offering personalized actions for prescribers and other professionals. However, several opportunities for improvement were identified. **Conclusion:** The observed imbalance among the analyzed scenarios reveals the urgent need to strengthen the culture of disseminating results, improve the methods used, and increase adherence to ASPs in Brazilian PICUs.
Keywords: *Antimicrobial Stewardship. Intensive Care Units Pediatric. Antibiotic Resistance. Feedback. Efficacy. Surveys and Questionnaires.*

RESUMO

Justificativa e Objetivos: Os Programas de Gerenciamento de Antimicrobianos (PGA) são fundamentais para otimizar o uso de antimicrobianos e combater a resistência bacteriana. Este estudo avaliou a eficácia dos PGA em unidades de terapia intensiva pediátrica (PED-UCI) no Brasil. **Métodos:** Realizado em 219 hospitais brasileiros, este estudo multicêntrico utilizou um formulário validado para coletar informações sobre o uso de antimicrobianos compartilhadas com os profissionais de saúde. As características dos serviços foram analisadas conforme a localização, o nível de adesão às ações do PGA e as atividades de feedback oferecidas aos colaboradores das PED-UCI. **Resultados:** O nível geral de implementação dos PGA nos hospitais foi considerado intermediário, com uma média de 72,46 (±37,60). O comportamento das PED-UCI variou significativamente entre os Estados: alguns apresentaram mais respostas ao inquérito, outros maior adesão dos hospitais, e alguns se destacaram na divulgação dos resultados do PGA. Observou-se que algumas instituições possuíam estratégias de feedback mais robustas, com a maioria adotando ações organizadas de forma institucional e cerca de metade oferecendo ações personalizadas para prescritores e outros profissionais. No entanto, foram identificadas várias oportunidades de melhoria. **Conclusão:** O desequilíbrio observado entre os cenários analisados revela uma necessidade urgente de fortalecer a cultura de divulgação de resultados, aprimorar os métodos utilizados e aumentar a adesão aos PGA nas PED-UCI brasileiras.
Descritores: *Gestão de Antimicrobianos. Unidades de Terapia Intensiva Pediátrica. Resistência a Antibióticos. Retroalimentação. Eficácia. Inquéritos e Questionários.*

RESUMEN

Justificación y Objetivos: Los Programas de Optimización del Uso de Antimicrobianos (PROA) son fundamentales para optimizar el uso de antimicrobianos y combatir la resistencia bacteriana. Este estudio evaluó la eficacia de los PROA en unidades de cuidados intensivos pediátricos (PED-UCI) en Brasil. **Métodos:** Realizado en 219 hospitales brasileños, este estudio multicéntrico utilizó un formulario validado para recopilar información sobre el uso de antimicrobianos compartida con los profesionales de la salud. Las características de los servicios fueron analizadas según la ubicación, el nivel de adhesión a las acciones del PGA y las actividades de retroalimentación ofrecidas a los colaboradores de las PED-UCI. **Resultados:** El nivel general de implementación de los PGA en los hospitales se consideró intermedio, con un promedio de 72,46 (±37,60). El comportamiento de las PED-UCI varió significativamente entre los Estados: algunos presentaron más respuestas a la encuesta, otros una mayor adhesión de los hospitales, y algunos se destacaron en la divulgación de los resultados del PGA. Se observó que algunas instituciones tenían estrategias de retroalimentación más sólidas, con la mayoría adoptando acciones organizadas de manera institucional y alrededor de la mitad ofreciendo acciones personalizadas para prescriptores y otros profesionales. Sin embargo, se identificaron varias oportunidades de mejora. **Conclusión:** El desequilibrio observado entre los escenarios analizados revela una necesidad urgente de fortalecer la cultura de divulgación de resultados, mejorar los métodos utilizados y aumentar la adhesión a los PGA en las PED-UCI brasileñas.
Palabras Clave: *Programas de Optimización del Uso de los Antimicrobianos. Unidades de Cuidados Intensivos Pediátricos. Resistencia a Antibióticos. Retroalimentación. Eficacia. Encuestas y Cuestionarios.*

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INTRODUCTION

Antimicrobial resistance is a growing threat to public health, compromising the effectiveness of infection prevention and treatment. In response, various health organizations, including the World Health Organization, have launched global action plans since 2015 to monitor and prevent infections, identify resistant microorganisms, and manage the use of antimicrobials.[1-2]

Antimicrobial Stewardship Programs (ASPs) are essential initiatives to optimize the use of antimicrobials, protect patients, and combat microbial resistance, especially in pediatric intensive care units (PICUs). According to the Brazilian guideline for implementing ASPs, these programs should include six fundamental components: institutional commitment, which involves management support and the definition of responsibilities; actions to improve the use of antimicrobials, including strategies for optimizing prescriptions; monitoring the use of antimicrobials and microbial resistance, allowing for the analysis of patterns and trends; continuing education and training, ensuring the training of health professionals; integration with the microbiology laboratory, ensuring support for therapeutic decisions based on microbiological data; and measurement of results and feedback of information, promoting continuous communication of data to professionals and managers for strategic adjustments.[3-5]

These programs aim to ensure the appropriate prescription of antibiotics and improve health outcomes, although there are still gaps to be addressed, such as antimicrobial use measures and outcome indicators. Among the essential components of ASPs, measuring results and providing feedback (component 6) play a crucial role in the continuous improvement of prescribing practices and in combating antimicrobial resistance. This component ensures the systematic dissemination of data on antimicrobial use and resistance patterns to professionals and managers, allowing for strategic adjustments and informing clinical decisions. Thus, the ASP should provide regular updates on processes and results, promoting a continuous cycle of evaluation and improvement of care practices.[2-8]

In this context, the "culture of communication" refers to the regularity, systematization, and quality of the dissemination of this information within healthcare institutions. Effective communication not only promotes transparency and alignment among teams, but also influences clinical decision-making and contributes to improving patient safety. Strengthening this process within ASPs can be a determining factor for the success of antimicrobial resistance control strategies.[4]

The objective of this study was to evaluate the regularity of the dissemination of ASP results on antimicrobial use and microbial resistance to professionals and leaders of institutions.

METHODS

A prospective, cross-sectional national survey was conducted. This is an excerpt from the study that evaluated the implementation of the ASP in adult and pediatric intensive care units and general hospitals in Brazil. Participants were recruited through the communication channels of the Brazilian National Health Surveillance Agency (ANVISA), including institutional emails from ANVISA and state health departments, through which they were asked to fill out the form. Participating hospitals voluntarily completed an electronic form (Google Forms®). A total of 662 hospitals with PED-ICUs participated in the study, and 219 (33.08%) had the ASP implemented and comprised the sample of the present study.

The data were collected between October 2022 and January 2023, using a validated instrument for a previous survey and adapted for the PICUs as requested by ANVISA.[9] The data allowed us to evaluate the implementation of the ASP for all components and establish, according to a score, a classification that was considered: inadequate, basic, intermediate, or advanced (each answer had a point value, with some questions allowing multiple answers, requiring all options selected within the same component to be counted).[9]

For the purposes of this study, we chose to extract the data obtained and analyze only the hospitals that had implemented the ASP and investigate the behavior of component 6: dissemination of ASP results regarding the regularity of information on the use of antimicrobials and microbial resistance to antimicrobials to professionals and leaders of the institution.

The statistical analysis included descriptive statistics, with the calculation of absolute and relative frequencies to describe the distribution of the variables investigated. In addition, the classification of the implementation of the ASP in relation to the dissemination of results was categorized into four levels: Inadequate, Basic, Intermediate, and Advanced, as represented in the graphical distribution of the responding hospitals.

To characterize the distribution of states and levels of ASP implementation, a geographical representation was developed, indicating the proportion of hospitals that responded to the survey and their classification in each federal unit. The analysis allowed for the evaluation of the regional distribution of program implementation and the different levels of engagement of hospitals in the monitoring and dissemination of information on antimicrobials.

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS, v. 23, IBM,

Armonk, NY). The variables analyzed were the frequency of disclosure of the antimicrobial susceptibility profile to hospital prescribers, the existence of direct and personalized communication on strategies for improving antimicrobial prescribing, the frequency of disclosure of ASP results to all hospital professionals, the availability and regularity of specific reports on antimicrobial use directed at prescribers, the dissemination of information on microbial resistance and antimicrobial use to relevant hospital sectors, the communication of AMR program objectives, goals, and results to senior management, and the dissemination of this information to all sectors involved in the program. The study was approved on April 5, 2022, by the human research ethics committee of the University of Santa Cruz do Sul with CAAE: 57231722.3.1001.5343, with opinion number: 5.332.386.

This is an observational, cross-sectional, descriptive study with a quantitative approach, carried out from September 20 to October 20, 2023, at the institution's Operating Room (OR). The study was carried out in a teaching hospital, located in the state of Paraná, which has 330 beds, according to the Brazilian National Registry of Health Establishments.

RESULTS

Of the 662 hospitals with PICUs in Brazil, 393 (66.27%) participated in the study. Of these, 219 (33.08%) had the ASP implemented. This also shows the percentage of hospitals with PICUs that responded to the survey by state, as well as the level of adherence to component 6, that is, dissemination of ASP results (Figure 1).
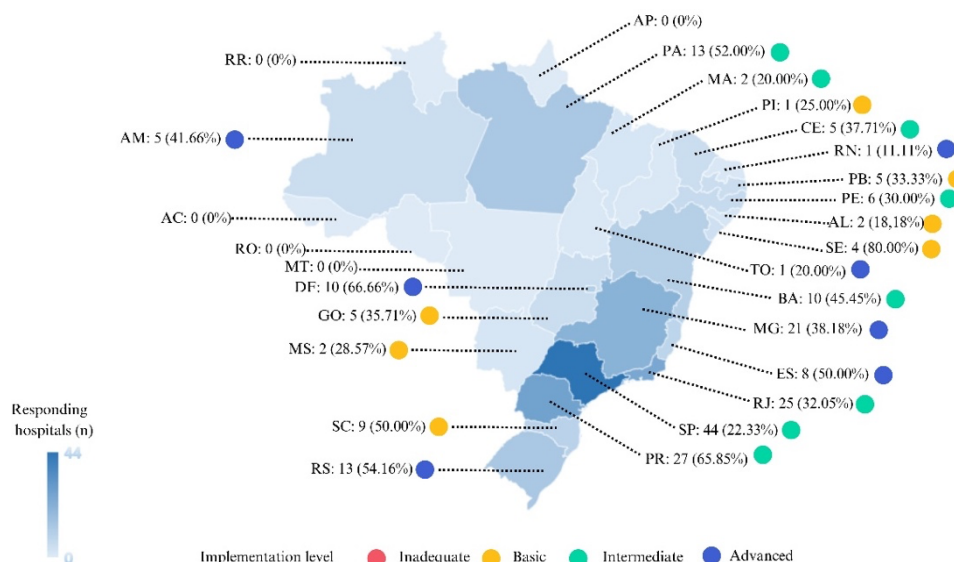

Figure 1. Number (n) of hospitals that responded to the survey on the ASP in PICUs implemented by state, by percentage (%) of respondents and level of adherence to component 6 (dissemination of ASP results).

The results were based on a classification table in a preliminary study. The overall level of implementation of the ASP in Brazil regarding the dissemination of results (component 6) obtained an average of 72.46 (±37.60), that is, an intermediate classification, but with most hospitals at an advanced level (52.06%), followed by intermediate 32 (14.61%). Regarding the participants, the level of implementation of the ASP and the responses to the questions in component 6 were compiled and categorized (Figure 2). The main finding reveals that most participating hospitals had a level of implementation classified as advanced, indicating greater dissemination of information about the ASP within the institutions (Figure 2).
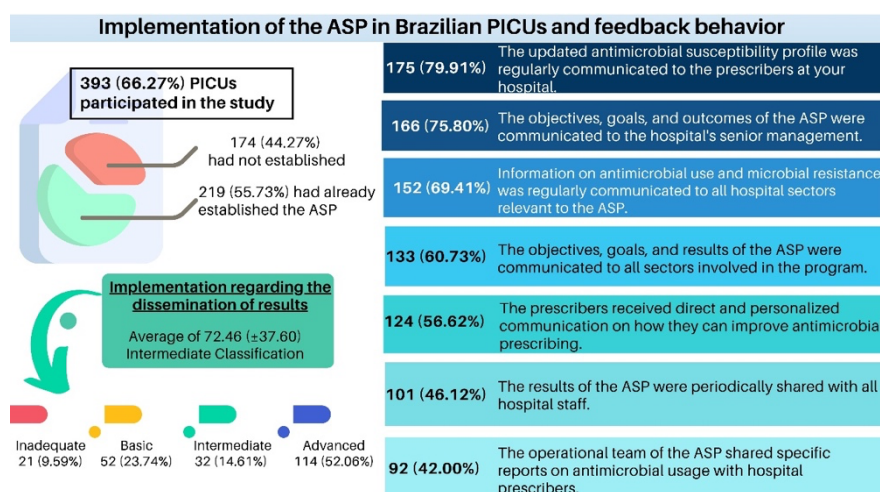
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Figure 2. Implementation of the ASP in PICUs and the level of adherence to component 6 (dissemination of ASP results - regularity of information on the use of antimicrobials and microbial resistance to professionals and leaders of the institution).

DISCUSSION

The behavior observed in the PICUs in this study is variable, with the highest number of respondents from São Paulo, Paraná, and Rio de Janeiro. The highest adherence of hospitals to completing the survey among those that had an ASP was in the states of Sergipe, the Federal District, and Paraná, although with a smaller number of PICUs. Regarding the advanced level of implementation of component 6, Minas Gerais, Rio Grande do Sul, the Federal District, Amazonas, Espírito Santo, Tocantins, and Rio Grande do Norte stood out.

It was found that some feedback strategies are stronger among institutions, with the majority presenting organized, institutional actions and approximately half of the services complying with personalized actions for prescribers and other professionals. This finding reflects the results of a study of ASPs in Latin America, which strongly highlighted the numerous barriers to program development, with particular emphasis on the critical failure of information feedback, revealing a significant obstacle to the effective advancement of these initiatives.[8]

In addition, the study highlighted the need to consider Brazil's continental dimensions and regional diversity, which result in different realities and challenges for the implementation of the ASP. The data corroborate findings from other studies, highlighting the importance of expanding and strengthening the program's reach in all types of establishments.[7-8]

This study showed that the dissemination of ASP results on antimicrobials and microbial resistance is still insufficient and needs improvement. Despite the existence of communication mechanisms, the dissemination of information does not occur systematically and effectively. Therefore, the need to strengthen the culture of dissemination by improving communication and data sharing methods at the local and national levels is reinforced. The findings indicate significant challenges for PICUs in consolidating effective practices, which are essential for team education and the rational use of antimicrobials.

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AUTHORS' CONTRIBUTIONS

Eliane Carlosso Krummenauer contributed to project management, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of figures, conclusion, review, and statistics. **Mariana Portela de Assis** contributed to project management, review, and statistics. **Mara Rubia Santos Gonçalves** contributed to project management, fundraising, review, and statistics. **Magda Machado de Miranda Costa** contributed to project management, fundraising, review, and statistics. **Rochele Mosmann Menezes** contributed to project management, review, and statistics. **Jane Dagmar Pollo Renner** contributed to project management, fundraising, literature review, editing, and statistics. **Marcelo Carneiro** contributed to project management, fundraising, literature review, 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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