

SPATIAL AND TEMPORAL DISTRIBUTION OF SCHISTOSOMIASIS MANSONI IN NORTHEAST BRAZIL FROM 2012 TO 2021

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Highlights: (1) Bahia and Pernambuco recorded a decline in schistosomiasis cases. (2) Significant reduction in cases among individuals with lower education levels. (3) Decreasing trend in schistosomiasis-related deaths.

PRE-PROOF

(as accepted)

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ABSTRACT

The objective of this study is to analyze the spatial and temporal patterns of schistosomiasis in the Northeast region of Brazil between 2012 and 2021. An ecological study was conducted, analyzing variables of schistosomiasis cases reported in the Northeast region of Brazil from 2012 to 2021, as recorded in the Notifiable Diseases Information System (SINAN). A univariate analysis of the cases was expressed in absolute and relative frequencies. The Joinpoint software was used to analyze the temporal trend of mortality. A total of 10,563 cases of schistosomiasis were recorded in Northeast Brazil, with males being the most affected (n=5,779; 54.7%), followed by mixed-race individuals (n=512; 70.3%), those with education levels between 1st and 4th grade of elementary school (n=1,646; 26.7%), and individuals aged 20 to 39 years (n=3,401; 32.2%). The intestinal form was the most prevalent (n=4,625; 75.1%), with a cure outcome in most cases (n=4,775; 82.0%). The state of Bahia recorded the highest number of cases (n=4,866; 42.1%). The study highlights that schistosomiasis remains a prevalent disease in the Northeast region, emphasizing the need for continuous health and environmental policies. **Keywords:** neglected diseases; public health; epidemiological surveillance.

INTRODUCTION

Schistosomiasis *mansoni* is a parasitic disease that affects millions of people worldwide, primarily in tropical and subtropical regions. It is caused by *Schistosoma mansoni*, a trematode flatworm that lives in freshwater. In Brazil, the disease is considered a public health problem, with endemic areas mainly concentrated in the Northeast and Southeast regions of the country. It is estimated that 1.5 million people are infected with the disease in Brazil¹.

Schistosomiasis *mansoni* can cause different clinical manifestations, characterized by acute and chronic forms, with the chronic form being more common. It may present with few symptoms, or patients may be asymptomatic, while in severe cases, death may occur².

There is no specific profile for the occurrence of the disease, as it can affect any human being regardless of gender or age group. However, certain risk factors can increase its transmission, such as contact with contaminated water, living in areas without access to potable water and basic sanitation, and residing in regions where the snail vector is present³.

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In 1975, Brazil established the Special Program for Schistosomiasis Control (PECE) under the Superintendence of Public Health Campaigns (SUCAM). In 1980, it was renamed the Schistosomiasis Control Program (PCE) and is now regulated by the Ministry of Health, with activities carried out under the responsibility of states and municipalities⁴.

Regarding the epidemiological situation of schistosomiasis in Brazil, from 2009 to 2019, 423,117 cases were recorded, with an average prevalence of 4.29%, with the highest number of cases reported in the Southeast and Northeast regions³.

Considering that the Northeast region is an endemic area for schistosomiasis and has significant epidemiological relevance, this study provides an in-depth analysis of metropolitan areas and states in the Northeast through a spatial-temporal approach.

Despite the implementation of the PCE in some areas of the Northeast, which has contributed to reducing severe cases, conducting epidemiological investigations, and providing treatment, challenges remain in eliminating the disease in Brazil. In this context, the present study aims to analyze the spatial and temporal patterns of schistosomiasis mansoni in Northeast Brazil from 2012 to 2021.

MATERIAL AND METHODS

This is an ecological study⁵ involving reported cases of schistosomiasis in the Northeast region of Brazil between 2012 and 2021, considering that this region represents one of the endemic areas for Schistosomiasis mansoni in the country¹. The study period was chosen to obtain robust data, allowing for a comprehensive understanding of the case profile and prevalence of Schistosomiasis mansoni in the region while minimizing the impact of the COVID-19 pandemic and potential underreporting associated with this period. The study region consists of nine states: Maranhão (7,153,262 inhabitants), Piauí (3,289,290 inhabitants), Bahia (14,985,284 inhabitants), Pernambuco (9,674,793 inhabitants), Paraíba (4,059,905 inhabitants), Alagoas (3,365,351 inhabitants), Sergipe (2,338,474 inhabitants), Ceará (9,240,580 inhabitants), and Rio Grande do Norte (3,560,903 inhabitants)⁶.

The data for this study were obtained through secondary data collection conducted from March to May 2023 in the Notifiable Diseases Information System (SINAN), using the TABNET platform from the Department of Informatics of the Unified Health System

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(DATASUS). Demographic data for the northeastern states were also obtained from DATASUS, which provides information collected in the last demographic census (2010) as well as intercensal projections.

The epidemiological profile of the Northeast region of Brazil for the study period was examined using the following variables: Year of positive case; Sex (female and male); Race/ethnicity (unknown; white; Black; Yellow; mixed-race; Indigenous); Education level (unknown; illiterate; incomplete 1st to 4th grade; completed 4th grade; incomplete 5th to 8th grade; completed elementary school; incomplete high school; completed high school; incomplete higher education; completed higher education); Age group (<1 year; 1 to 4 years; 5 to 9 years; 10 to 14 years; 15 to 19 years; 20 to 39 years; 40 to 59 years; 60 to 64 years; 65 to 69 years; 70 to 79 years; 80 years or older); Clinical form (unknown/blank; intestinal; hepato-intestinal; hepatosplenic; acute; other); Case outcome (unknown/blank; cured; not cured; death due to schistosomiasis; death due to other causes).

To analyze mortality trends in the region and in the nine states, the *Joinpoint Regression Program (version 4.6.0.0)* was used. The *Annual Percentage Change (APC)* was calculated with a 95% confidence interval (CI 95%), where a negative APC indicates a declining trend, and a positive APC indicates an increasing trend.

To calculate the annual rate increase and the Average Annual Percentage Change (AAPC), the joinpoint (breakpoint) method was used. This method adjusts time series data with the fewest possible joinpoints (zero, meaning a straight line without breakpoints) and tests whether adding more joinpoints is statistically significant. The significance tests were based on the Monte Carlo permutation method and the logarithmic calculation of the annual percentage change ratio. Each significant point indicating a trend change was included in the final model. To describe the linear trend for each period, the estimated annual percentage change and 95% confidence interval (CI 95%) were calculated for each trend. This resulted in a regression line based on the natural logarithm of the rates, using the calendar year as the regression variable.

Each joinpoint added to the model represents a trend shift, meaning a change in the linear trend, which would introduce a new segment to the time series. The model was adjusted under the assumption that the number of joinpoints could vary from zero to two over the years. The independent variable was defined as the year of case occurrence, while the dependent variable was the rate of confirmed cases per year, calculated directly in the program. The

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confirmed case rate was used as the numerator, and the population for the selected year was used as the denominator, with a coefficient per 100,000 inhabitants.

Data visualizations were created using Python, employing the pandas, matplotlib, geopandas, and numpy libraries. Line charts illustrate the cases per state from 2012 to 2021, including trends and the previously calculated APC for each state, allowing for the visualization of fluctuations and specific trends. The geospatial map highlights the distribution of cases among states, using color intensity to represent the number of cases.

This study was exempt from prior approval by Research Ethics Committees, as it is based on publicly available databases. The dataset does not include any identifiable information such as names or addresses. Although prior approval was not required, the researchers declared their ethical commitment regarding data handling, analysis, and publication, in accordance with Resolution 466/12 of the National Research Council.

RESULTS

The analysis revealed a general downward trend in cases across most states and various sociodemographic groups. It was observed that the reductions were more pronounced in both men and women, with subtle differences between the sexes. The decline in cases was particularly notable among individuals with lower education levels, suggesting that educational interventions may have played a significant role.

Additionally, although most cases progressed to cure, the reduction trend was also observed in schistosomiasis-related deaths, highlighting improvements in treatment and disease management. Geographically, states such as Bahia and Pernambuco, which had the highest number of cases, also showed the greatest reductions, indicating that control efforts may be proving effective in these areas. These trends suggest an overall improvement in schistosomiasis control actions in the Northeast region.

In the univariate analysis of confirmed cases, categorical quantitative variables were distributed according to their absolute and relative frequencies, as shown in Table 1. Simple linear regression analysis was used to estimate trends in time series, identifying whether the trend was increasing, decreasing, or stationary.

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Table 1 - Sociodemographic characterization of confirmed schistosomiasis cases in Northeast Brazil for the period 2012 (N = 10,563).

Variable	n	%	APC* (IC95%)	p-value	Trend
Sex					
Female	4782	45,3	-9,3 (-13,9; -4,4)	0,003	Decreasing
Male	5779	54,7	-8,9 (-12,9; -4,6)	0,002	Decreasing
Race/ethnicity					
White	120	16,7	-8,1 (-12,7; -3,2)	0,006	Decreasing
Preta	48	11,3	-13,6 (-18,6; -8,4)	<0,001	Decreasing
Yellow	6	0,9	-9,4 (-24,6; 4,9)	0,159	Stationary
Mixed-race	512	70,3	-7,5 (-12,3; -2,5)	0,009	Decreasing
Indigenous	2	0,8	-11,8 (-31,0; 12,6)	0,270	Stationary
Education level					
Illiterate	754	12,2	-12,5 (-17,6; -7,1)	0,001	Decreasing
Incomplete 1st to 4th grade of Elementary School	1646	26,7	-11,6 (-17,1; -5,7)	0,002	Decreasing
Complete 4th grade of Elementary School	581	9,4	-12,8 (-20,8; -4,0)	0,011	Decreasing
Incomplete 5th to 8th grade of Elementary School	1084	17,6	-14,3 (-19,7; -8,5)	0,001	Decreasing

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Complete Elementary School	389	6,3	-4,5 (-12,0; 3,5)	0,223	Stationary
Incomplete High School	488	7,9	-11,8 (-17,5; -5,7)	0,003	Decreasing
Complete High School	867	14,1	-7,9 (-12,3; -3,2)	0,005	Decreasing
Incomplete Higher Education	91	1,5	-2,0 (-11,7; 8,7)	0,658	Stationary
Complete Higher Education	263	4,3	12,2 (-4,4; 31,7)	0,160	Stationary
Age					
<1	116	1,1	-8,2 (-16,3; 0,7)	0,066	Stationary
1 to 4	99	0,9	1,1 (-5,6; 8,3)	0,713	Stationary
5 to 9	347	3,3	-12,4 (-15,8; -8,8)	<0,001	Decreasing
10 to 14	584	5,5	-16,4 (-18,5; -14,3)	<0,001	Decreasing
15 to 19	604	5,7	-14,1 (-19,7; -8,2)	0,001	Decreasing
20 to 39	3401	32,2	-12,7 (-17,7; -7,3)	0,001	Decreasing
40 to 59	3328	31,5	-5,8 (-10,6; -0,7)	0,030	Decreasing
60 to 64	641	6,1	-4,5 (-10,7; 2,2)	0,156	Stationary
65 to 69	536	5,1	-2,2 (-8,1; 4,1)	0,439	Stationary
70 to 79	631	6,0	-5,1 (-10,0; 0,0)	0,050	Stationary
80 +	274	2,6	-6,8 (-13,5; 0,5)	0,065	Stationary

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Clinical form

Intestinal	4625	75,1	-13,9 (-19,6; -7,8)	0,001	Decreasing
Hepatointestinal	512	8,3	3,9 (-4,8; 13,3)	0,344	Stationary
Hepatoesplenic	760	12,3	-3,6 (-7,5; 0,5)	0,077	Stationary
Acute	260	4,2	-3,1 (-15,1; 10,6)	0,594	Stationary

Case outcome

Cure	4775	82,0	-11,0 (-16,7; -4,8)	0,004	Decreasing
No cure	270	4,6	-0,5 (-12,9; 13,8)	0,946	Stationary
Death from	531	9,1	4,3 (-1,1; 9,9)	0,103	Stationary
Death from other causes	247	4,2	-11,0 (-18,9; -2,3)	0,020	Decreasing

State

Alagoas	642	6,1	9,3 (-4,4; 25,1)	0,165	Stationary
Bahia	4866	46,1	-13,9 (-18,6; -9,0)	<0,001	Decreasing
Ceará	276	2,6	2,4 (-4,7; 10,0)	0,472	Stationary
Maranhão	289	2,7	-4,5 (-23,9; 19,9)	0,656	Stationary
Paraíba	828	7,8	-9,0 (-24,1; 5,4)	0,178	Stationary
Pernambuco	2385	22,6	-8,1 (-13,2; -2,6)	0,010	Decreasing
Piauí	14	0,1	-5,1 (-20,9; 13,9)	0,494	Stationary
Rio Grande do Norte	249	2,4	0,3 (-9,6; 11,3)	0,947	Stationary

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Sergipe	1014	9,6	-0,3 (-10,3; 10,8)	0,953	Stationary
Northeast	10563	100	-9,0 (-13,3; -4,5)	0,002	Decreasing

*APC: Average annual percentage change.

Legend: ignored/blank cases were excluded. 95% confidence interval.

Source: Authors, 2023.

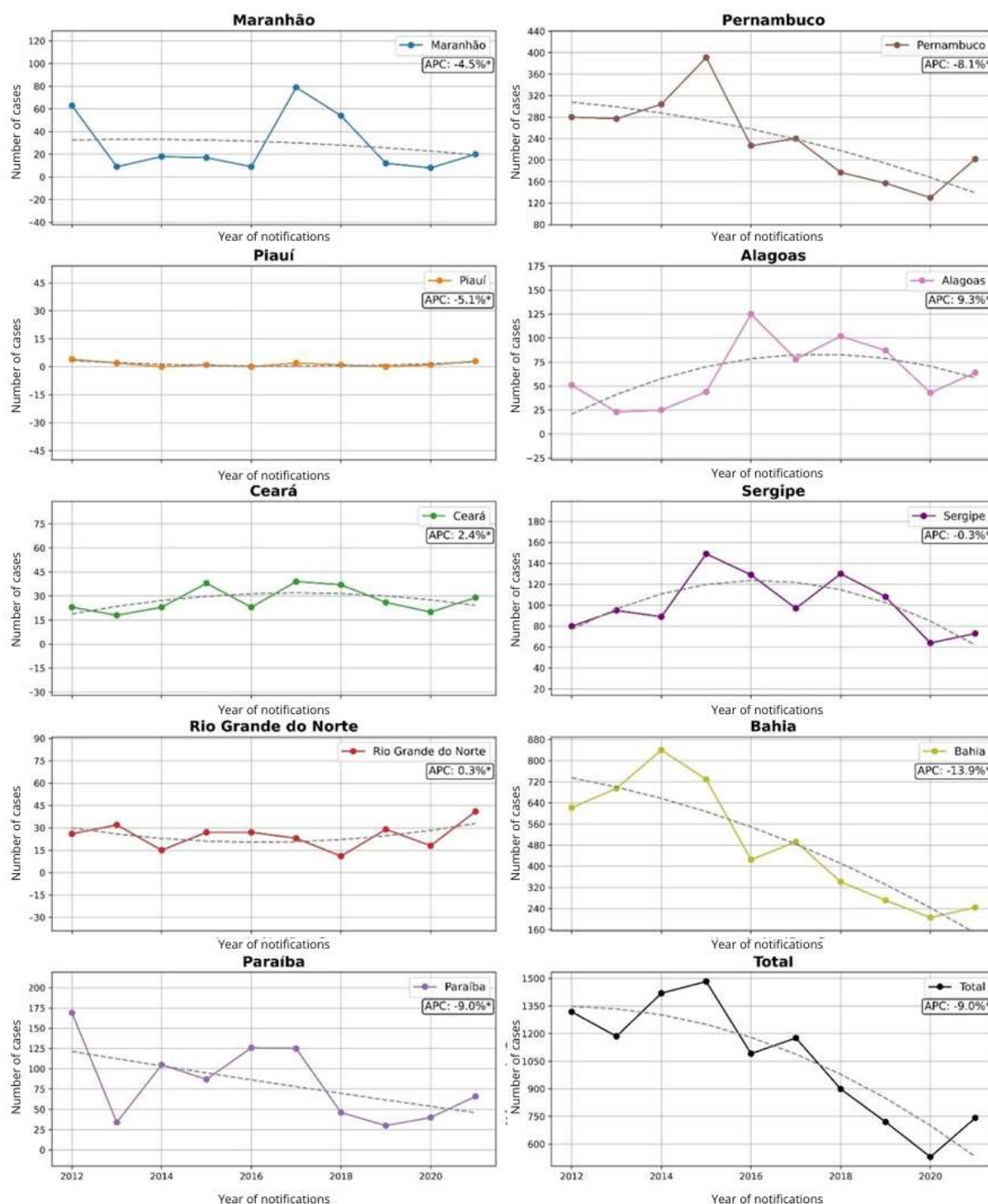
The temporal analysis by joinpoint revealed that in the state of Rio Grande do Norte, there is a single straight line with no inflection points, indicating a linear increasing trend in cases over the years. On the other hand, the graphs for the states of Alagoas and Ceará show the appearance of two lines and one inflection point, indicating an increase in the trend. All other states exhibited a decrease in confirmed cases (Figure 1). In time series analysis, the random variation of the measure is caused by noise, which appears as roughness in the lines of time series graphs⁷.

A detailed analysis of the data further indicated that Bahia and Pernambuco, states that together represent a significant portion of schistosomiasis cases in the region, showed statistically significant reductions in the incidence of the disease. In Bahia, which accounted for 46.1% of the cases, a mean annual reduction of 13.9% was observed ($p < 0.001$), while in Pernambuco, with 22.6% of the cases, the reduction was 8.1% ($p = 0.010$). These data underscore the effectiveness of the control and prevention measures implemented in these states, suggesting that the specific strategies adopted may have significantly contributed to the reduction of cases.

Additionally, the analysis by education level showed that individuals with lower educational levels, such as those with incomplete 5th to 8th grade of elementary school, experienced a sharp decrease of 14.3% annually ($p = 0.001$), indicating the importance of educational campaigns and awareness efforts in mitigating the disease. These findings highlight the need to continue and intensify efforts in public health policies aimed at these regions and demographic groups.

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Figure 1 - Temporal trend of confirmed schistosomiasis cases in the Northeast of Brazil from 2012 to 2021.



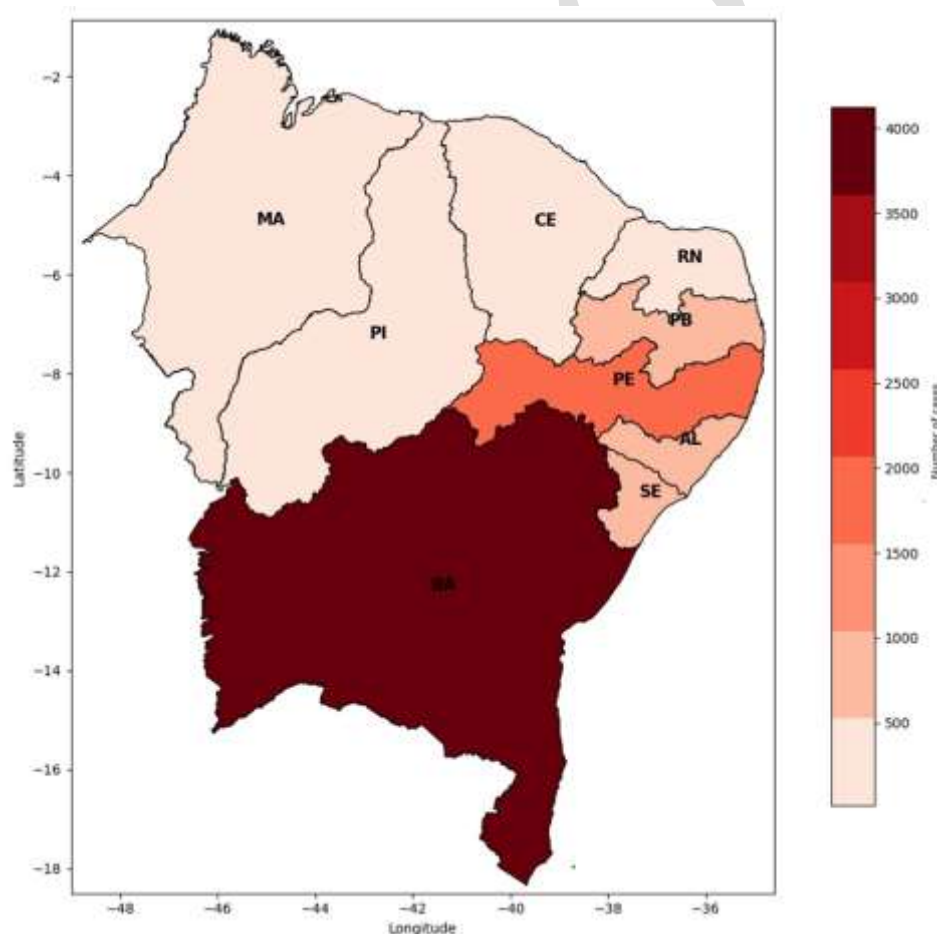
Indicates that the Annual Percentage Variation (APC) is significantly different from zero to the alpha value of 0.05.
Statistical Analysis performed in Joinpoint software. The gray dotted curve represents the trend between 2012 - 2021

Source: Authors, 2023.

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In Figure 2, the areas of highest concentration of schistosomiasis cases are observed. The areas in darker red shades indicate regions with high rates, surrounded by municipalities with similarly high rates, demonstrating a High/High spatial pattern, predominantly in the states of Bahia, Pernambuco, Sergipe, and Paraíba. The areas in lighter red shades represent municipalities with low rates, surrounded by municipalities with similarly low rates (Low/Low), located in the northern and western regions of Maranhão, the coastline of Ceará, Rio Grande do Norte, Pernambuco, and some regions of Alagoas, with no predominant colors in Piauí. The states are categorized into eight color bands, showing the variation in the number of cases across different regions.

Figure 2 - Concentration of confirmed schistosomiasis cases in the Northeast of Brazil from 2012 to 2021.



Source: Authors, 2023.

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DISCUSSION

The results of this study demonstrate that there is a trend of decline in schistosomiasis in the Northeast, which may coexist as public health policies on sanitation, water, and nutrition are being implemented. However, there are still regions with a considerable number of cases. Schistosomiasis can affect individuals of any gender³, and in this study, little difference was observed between the percentages found in men and women, although men are more affected. According to Resendes and colleagues⁸, both men and women have common water usage habits, which can affect both genders.

However, the higher percentage in men is related to difficulties in accessing healthcare services and gender issues, as men seek preventive actions less frequently compared to women⁹⁻¹⁰.

Regarding race, a significant portion of individuals self-identified as mixed-race. The Northeast has the largest proportion of mixed-race population in the country (59.8%), with the states of Alagoas, Maranhão (both with 66.9%), and Piauí (64.3%) having the largest mixed-race populations in Brazil¹¹.

Regarding age groups, there was a predominance of individuals aged 20 to 39, followed by 40 to 59 years. In other words, the majority of the notifications occurred in the economically active age group. This corroborates the findings of Barreto and Lobo¹², who analyzed the distribution of schistosomiasis cases in the Northeast (2010-2017) and found that the age group with the highest incidence of schistosomiasis was 20-39 years (34.68%), followed by 40-59 years (28.89%). This is justified by the fact that these individuals are more likely to be exposed to contamination through work in farming and fishing, in addition to contamination via water used for domestic and leisure purposes.

The results of this study align with international findings, such as the research conducted in Tanzania, which indicates higher disease prevalence in children up to 15 years old and a variation in infection intensity between different geographical areas. In the Northeast of Brazil, the age group of 10 to 14 years showed a significant reduction in the incidence of the disease, in line with the trend observed in the study. These parallels suggest that, both in Brazil and in

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other affected regions, factors such as age and geographical location influence the transmission dynamics of the disease¹³.

Most individuals in this study had incomplete schooling, between the 1st and 4th grades of elementary school. Education is a significant factor that affects an individual's health, influencing access to information and the adoption of preventive practices. For individuals with lower schooling levels, the data highlights the importance of educational campaigns and targeted interventions, emphasizing that improvements in education can contribute to better public health outcomes¹⁴.

Factors such as social class, age group, and education can influence knowledge of a particular disease and health care practices¹⁵. In Zambia, Africa, it was observed that the incidence and prevalence of the disease in the country are influenced by demographic, socioeconomic, and environmental factors¹⁶.

The study results indicated that more than half of the cases were diagnosed with the intestinal clinical form. The lack of basic sanitation found in most metropolitan and rural areas of the Northeast, as well as exposure to river bathing, may explain this. This result was also found by Rodrigues and Pereira¹⁷, who conducted a study in western Bahia, describing that the prevalent clinical form was intestinal, associated with age group. They justified this by stating that adolescents and adults bathe more in rivers, while elderly individuals typically have the hepatoesplenic form, which is the most severe form of the disease due to prolonged exposure to contamination.

Regarding the evolution of the disease, most cases resulted in cure, but there were also cases of death³. When undiagnosed and untreated, the disease can lead to death. For individuals who develop the hepatoesplenic form, the outcome may be death, as this form is the most severe due to the high parasitic load¹⁷.

In Brazil, the Southeast and Northeast are the regions with the highest number of schistosomiasis cases. In the Northeastern states of Bahia, Alagoas, Pernambuco, Sergipe, Paraíba, and Rio Grande do Norte, the disease transmission is endemic, while in Maranhão, Ceará, and Piauí, transmission is focal, data also confirmed by the temporal analysis of this study³.

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It is worth noting that schistosomiasis is present in 19 Brazilian states, with the eight Northeastern states on this list. Reviewing the historical landmark of schistosomiasis in Brazil, the point of origin was the ports of Recife and Salvador, where schistosomiasis was introduced through the transatlantic slave trade from the West African coast. From there, the disease expanded across northeastern Brazil due to migration movements toward areas with poor sanitation conditions¹⁸.

In a study in Ethiopia, a country with sanitation issues similar to those in northeastern Brazil, it was reported that to reduce *S. mansoni* infestation, large-scale treatment of at-risk population groups is needed, as it is considered a public health problem. Access to education on hygiene and potable water can help significantly reduce schistosomiasis cases, in addition to controlling snails through improvements in basic sanitation¹⁹.

Over the 10 years analyzed in this study, it is evident that the region is experiencing a decline in cases, though some states still show significant numbers of confirmed cases. According to the Ministry of Health²⁰, the state of Pernambuco ranks second in Brazil for schistosomiasis cases, being endemic in 102 of the 185 municipalities, especially in the Zona da Mata and coastal areas, according to the latest epidemiological report published by the National Health Surveillance System. An observational study in the state on the epidemiological evaluation of schistosomiasis concluded that poor socioeconomic and sanitary conditions favor the occurrence of the disease²¹.

In Ceará, schistosomiasis is endemic and concentrated in the metropolitan basin, the main consumer of water in the state. The introduction of the disease in Brazil occurred during the colonial period, brought by African slaves, and the local poor sanitation conditions perpetuated transmission. The persistence of the disease in the region highlights the need for improvements in sanitation, access to clean water, and health education, in addition to focusing control and surveillance efforts in high-prevalence areas to reduce the disease burden²².

In Rio Grande do Norte, 249 schistosomiasis cases were reported between 2012 and 2021. According to Barbosa et al.²³, it can be said that the prevalence of intestinal helminthiasis is lower in the areas studied in Rio Grande do Norte due to its location in the state's dry zone,

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while certain areas in Pernambuco and Alagoas are located in the forested or coastal forest zones of these states.

In Maranhão, the profile of reported cases followed a similar pattern to Ceará, with 289 confirmed cases during the study period; however, symptoms of the disease have been present since before 1975. Studies show that several neighborhoods in the state have transmission hotspots, and other regions are still maintaining the disease prevalence²⁴.

Regarding Mendes²⁴ study on schistosomiasis in Maranhão, it is mentioned that factors such as water supply, inadequate sanitation, and waste collection have weak correlation with the appearance of the disease. However, it is important to note that in various parts of the study, the reduction in schistosomiasis cases due to improved sanitation conditions is mentioned. Therefore, there is an apparent contradiction in this observation, suggesting the need for a more detailed and comprehensive analysis of the determinants of schistosomiasis in Maranhão's specific context.

The state of Paraíba showed a large number of cases, but a decrease over the years is evident. This fact may be related to the effective actions of the PCE in the state, observed from the decrease in the number of cases there²⁵.

Among the Northeastern states, Sergipe was one that showed a casuistic trend (n=1014). It is the smallest state in Brazil, and according to data from the Epidemiological Surveillance of the State Health Department (SES) of Sergipe in 2017, of the 75 municipalities, 51 are considered endemic²⁶. The epidemiological scenario shows that there has been a reduction in adherence to the PCE in Sergipe municipalities, which contributes to the increase in cases since adherence to the program favors early diagnosis and prevents worsening of the clinical condition²⁷.

Similarly, Alagoas also showed a significant number of cases, with the highest percentage in 2021. The disease in Alagoas spread to urban and coastal areas, and factors such as sanitation, education, health, and vector control need improvements for disease control in the state²⁸.

Piauí had the lowest number of cases among the Northeastern states. This state is not considered endemic, with its transmission being focal. The highest occurrence of cases is in the

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municipality of Picos²⁹. According to the IBGE's⁶ 2010 census, only 40.2% of households in Picos had adequate sanitation. This is concerning from an epidemiological perspective because poor socio-environmental conditions can contribute to the spread of schistosomiasis³⁰.

The results identified priority areas for investments in basic sanitation and access to potable water. The importance of educational programs for awareness and prevention of the disease is highlighted, emphasizing the need to strengthen epidemiological surveillance systems. By directing resources and efforts to the most affected areas and populations, schistosomiasis incidence can be reduced, improving the health and quality of life of the affected communities.

It is believed that the number of cases is higher than observed in all states because the study had limitations in some states due to possible underreporting in secondary data from SINAN. Additionally, there is a possibility of errors in completing notification forms by professionals and updating data in the systems. To overcome these limitations, continuous action by health surveillance centers and the implementation of epidemiology offices with support to municipalities in health and the environment is suggested.

CONCLUSION

The results of this study provide contributions to the formulation of public health and environmental policies. A downward trend in the incidence of the disease was observed in several states of the region, especially in Bahia and Pernambuco. Furthermore, an unequal distribution of the disease was identified, with areas of concentration and higher risk, such as the metropolitan basin of Ceará. These results highlight the importance of targeted preventive strategies to protect the most vulnerable groups, such as children and individuals with low education. It is expected that these findings will guide health managers and professionals in implementing effective measures to control and prevent schistosomiasis in Northeastern Brazil, contributing to better public health and reducing the disease's impact in the region.

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