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ORIGINAL ARTICLE

EVALUATION OF THE SCHISTOSOMIASIS CONTROL PROGRAM (PCE) IN AN ENDEMIC AREA, NORTHEASTERN BRAZIL: A POPULATION-BASED AND 10-YEAR TIME SERIES STUDY

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ABSTRACT

Schistosomiasis is an endemic disease in Brazil and the State with the highest positive rate in the country is Sergipe. Herein, we assessed data from the Brazilian Schistosomiasis Control Program (PCE) in the State of Sergipe between the period 2008 and 2017. We evaluated data about schistosomiasis and snails of the genus *Biomphalaria*. We used the log-linear regression model (joinpoint) to assess temporal trends and the Kernel estimator for spatial statistics analysis. According to the PCE, Sergipe has 51 endemic municipalities for schistosomiasis. Nevertheless, information about the disease and that collected by the PCE has not been recorded regularly in all endemic municipalities. Additionally, only nine municipalities (17.6%) carried out the malacological survey. The average of positive rate from schistosomiasis in Sergipe was 8.4%. However, our data suggest that it may be underestimated. The spatial analysis maps (Kernel maps) showed areas of high transmission of the disease in municipalities close to the São Francisco River and in the metropolitan region of the State. Altogether, our findings suggest that schistosomiasis has been underreported and it is still a serious public health concern in Sergipe. In addition, there are significant failures in the conduction of PCE's activities by the municipalities.

KEY WORDS: Schistosomiasis; Epidemiological monitoring; Spatial analysis; Brazil.

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INTRODUCTION

Intestinal schistosomiasis is a serious and chronic parasitic disease, caused by trematode worms of the species *Schistosoma mansoni*, and present mainly in low-income countries from Africa and Latin America (WHO, 2017). Brazil is the country with the highest prevalence rate for the disease in the Americas and most of cases and deaths have occurred in the Northeast and Southeast regions (Paz et al., 2021; Santos et al., 2017; Tibiriçá et al., 2011).

Considering the high prevalence and mortality rates of the disease in the country, the Special Schistosomiasis Control Program (PECE) was created in 1975. This program aimed mass diagnosis and treatment in endemic areas and malacological surveys (do Amaral et al., 2006; Costa et al., 2017). The PECE was replaced by the Schistosomiasis Control Program (PCE) in 1996. After that, the activities were decentralized, and the municipalities were responsible for conducting the program. Furthermore, PCE resources, which were initially managed by the Federal government, were also redistributed for the cities to manage them (Costa et al., 2017; Favre et al., 2001).

Notably, there was a decrease in the number of patients with severe forms of the disease (hepatosplenic) and in the mortality rates from schistosomiasis in the country after implementation of the PCE. Regardless of that, the disease is still endemic in many States, mainly in the Northeastern Brazil (Paz et al., 2020; WHO, 2017). In addition, the program funds are limited which can affect the PCE's activities (Brasil, 2014; Favre et al., 2001). Currently, the main actions conducted by the PCE are parasitological surveys, mass treatment, environmental sanitation measures, and health education. Moreover, the data collected by the program are tabulated by technicians from the Municipal Health Departments in the PCE Information System (SISPCE). All data is of public domain and available on the Brazilian Ministry of Health´s website (Brasil, 2014, 2020; Costa et al., 2017).

Studies using Geographic Information Systems (GIS) are important to describe a region. Tropical infectious diseases are geographically influenced, so the location characteristics might be used in a combat plan. (Barbosa et al., 2017). The Kernel Density Estimator is an important tool that can be used in the region spatial analysis. The Kernel shows in a gradient of color intensity a relation with infection rates, the number of cases showing the areas of greatest intensity, called hotspot (Araújo et al., 2007). Studies using GIS were carried out in endemic locations, allowing the identification of risk areas, prevalence of human cases, vector reproduction areas and other related factors, whether in small cities or in States. These studies allow a better visualization of epidemiological data and they help to identify areas that should have treatment and prevention of schistosomiasis prioritized (Barbosa et al., 2012; Santos et al., 2017, 2016a).

Sergipe is the State with the highest prevalence rate and the fourth in deaths percentage rate from *S. mansoni* infection in Brazil. More importantly, Sergipe showed an increase in time-trend on the mortality rate due to schistosomiasis between the years of 1997 and 2017 (Paz et al., 2020). Furthermore, PCE data indicates that 51 from the 75 municipalities in Sergipe are endemic for schistosomiasis (Brasil, 2011). However, previous assessments of our research group identified the lack of data on the SISPCE database in Sergipe (Santos et al., 2016b). Considering this, we aimed herein to assess the PCE data in the endemic municipalities of the State of Sergipe between the period from 2008 to 2017, using a temporal and spatial modeling.

MATERIAL AND METHODS

Design and study area

We carried out an ecological, population-based, and 10-year time series study with data on schistosomiasis from the State of Sergipe. 75 municipalities in the State were analyzed. Herein, we used spatial and temporal analysis techniques to assess parasitological and malacological data available in the SISPCE website.

The State of Sergipe is located in the coastal strip of the Northeastern Brazil, with the São Francisco River running along its border with the State of Alagoas (Figure 1). The State can be geographically divided into metropolitan area and inland municipalities (the metropolitan area includes the capital, Aracaju, and four other municipalities). In addition, the State occupies an area of 21,910 km², has an estimated population of 2,318,822 million inhabitants, and the human development index (HDI) is low (0.665) (IBGE, 2020).

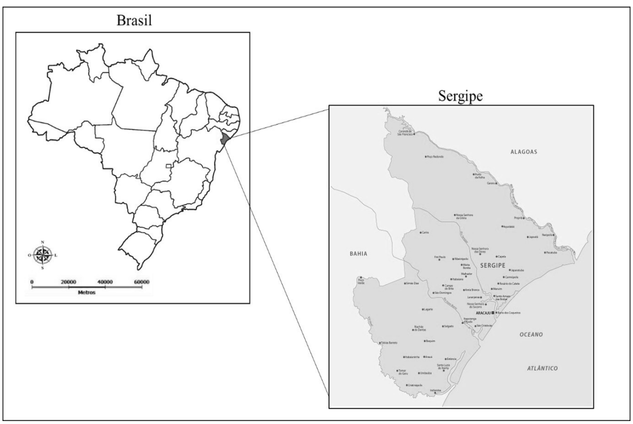

Figure 1. Map of the State of Sergipe, with the São Francisco River on its border with the State of Alagoas on the North side.

Data source and analysis

First, we collected epidemiological data on schistosomiasis provided by the Brazilian Ministry of Health, such as the number of Municipalities evaluated by the PCE, assessed population, number of Kato-Katz tests performed, and positive tests for *S. mansoni*. These parasitological data are recorded according to the results of the Kato-Katz method (Brasil, 2020). In addition, we extracted data on malacological surveys, such as number of snails collected and analyzed, number of species of the genus *Biomphalaria*, and number of positive specimens for *S. mansoni*. Descriptive data were tabulated and analyzed in Microsoft Excel software 2017 version. Subsequently, we calculate the percentage of evaluated municipalities by the PCE and the schistosomiasis' positivity rate for each year of the study, considering the positive cases of *S. mansoni* in relation to the examined population. Lastly, for spatial analysis, the digital cartographic mesh of the State of Sergipe, in shapefile format, was obtained from the Geographical Projection System in latitude/longitude (Geodesic Reference System, 2000), available on the IBGE´s (Brazilian Statistics Institute) website (IBGE, 2020).

Time trend analysis

We assessed the time trend of the data using the segmented log-linear regression model, through the Joinpoint Regression Program 4.7.0.0 version. Initially, we performed the Monte Carlo permutation test to select the best model for inflection points, applying 9999 permutations and considering the highest coefficient of determination of residuals (R2). Afterwards, the annual percentage changes (APC) and their respective confidence intervals (95% CI) were calculated. Herewith, a positive and significant APC (p-value <0.05) indicates increasing trend. Alternatively, a negative and significant APC indicates decreasing trend. Non-significant APC (p-value ≥ 0.05) indicates stable trend regardless of APC values.

Spatial analysis

We carried out the spatial statistics analysis on the positivity rate from schistosomiasis in the municipalities from Sergipe, trough the Kernel estimator per centroid and using TerraView software 4.2.2 version. Hereupon, we mapped the hot areas (or hotspots) in the State, which represent the areas with the highest positivity rates for schistosomiasis. Importantly, this Kernel analysis, through statistical data smoothing techniques, indicates points of concentration of cases in a spatial distribution and in a continuous surface from point data (Cromley & McLafferty, 2012).

Ethical considerations

This study used public-domain aggregate secondary data and followed the ethical precepts of research involving human beings established by the Resolution 466/2012 of the National Health Council (CNS) and the Declaration of Helsinki. This study was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE: 92576818.0.0000.5546).

RESULTS

Descriptive and temporal trend analysis of the epidemiological characteristics of schistosomiasis in the State are presented in Table 1. Interestingly, we observed that not all 51 municipalities, which are endemic for the disease, carried out PCE activities during the study period (37 in 2008 and 26 in 2017; average = 34.7). Additionally, there was an expressive reduction in the percentage of municipalities performing PCE activities (72.6% in 2008 to 51.0% in 2017). We observed a decreasing time trend in the assessed population (APC = -7.8; p-value = 0.01), in the number of Kato-Katz tests performed (APC = -8.3; p-value = 0.002), and in the number of positive tests (APC = -12.1; p-value = 0.0001). Otherwise, there was a stability in the positivity rate for schistosomiasis (average = 8.4%; APC = -2.2; p-value = 0.15) in these 10 years of activities of the PCE in Sergipe.

Similarly, we observed that there are failures in the records of snails of the genus *Biomphalaria* in the municipalities evaluated by the PCE in Sergipe. Surprisingly, there are only data available between 2008 and 2014. Furthermore, only nine municipalities (17.6%) provided information on captured snails in 2014. The municipality of Lagarto was the only one that had data available through all years, until 2014. Concerning this, most species were *B. glabrata* (n = 20,106), but specimens of *B. straminea* (n = 149) were also identified (Table 2). As important, we identified 514 (2.5%) specimens positive for *S. mansoni*.

Lastly, to identify areas of higher occurrence of schistosomiasis cases, we assessed the spatial distribution of them in the municipalities of Sergipe for each year of the study (Figure 2). We identified high-risk areas of schistosomiasis cases (the hotspots in orange and red) in the South-central, Northern coast (near the São Francisco River) and the metropolitan area. Additionally, we observed a significant reduction in both high and low-risk areas (in green) for schistosomiasis over the years of the study. Importantly, the absence of data in the municipalities of the hinterland is due to the absence of PCE actions in these municipalities.

Table 1. Time trend analysis and epidemiological indicators of the Schistosomiasis Control Program (PCE) in endemic municipalities (n = 51) for schistosomiasis in the State of Sergipe, Northeastern Brazil, between the years of 2008 and 2017. Time trend analysis were performed by the joinpoint regression model.

Epidemiological indicators	Study period														
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total	Average	APC	95% CI	p-value
Municipalities evaluated by the PCE (n)	37	38	34	42	39	33	29	36	33	26	-	34.7	-	-	-
Percentage of evaluated municipalities (%)	72.6	74.5	66.7	82.4	76.5	64.7	56.9	70.6	64.7	51.0	-	68.0	-2.6	-5.5 to 0.3	0.056
Assessed population (n)	107,110	115,657	143,841	99,331	105,648	89,827	60,628	89,256	40,160	54,577	906,035	-	-7.8	-13.3 to -2.0	0.01
Kato-Katz tests (n)	81,543	84,052	98,473	72,644	71,585	62,542	43,494	61,485	30,494	39,776	646,088	-	-8.3	-12.7 to -3.6	0.002
Positive tests for *S. mansoni* (n)	8,528	7,529	8,055	6,705	5,437	5,081	2,790	4,580	3,020	2,816	54,541	-	-12.1	-8.1 to -6.7	0.0001
Positive rate for *S. mansoni* (%)	10.5	9.0	8.2	9.2	7.6	8.1	6.4	7.4	9.9	7.1	-	8.4	-2.2	-5.6 to 1.2	0.15

Table 2. Snails of the genus *Biomphalaria* collected in municipalities from the State of Sergipe, and registered by the PCE, and positive rate of infection by *Schistosoma mansoni*, between the period of 2008 and 2014.

Species of the genus *Biomphalaria*	Collected (n)	Positive for *S. mansoni* (n)	Positive rate (%)
B. glabrata	20,106	513	2.6
B. straminea	149	1	0.7
Total	20,255	514	2.5

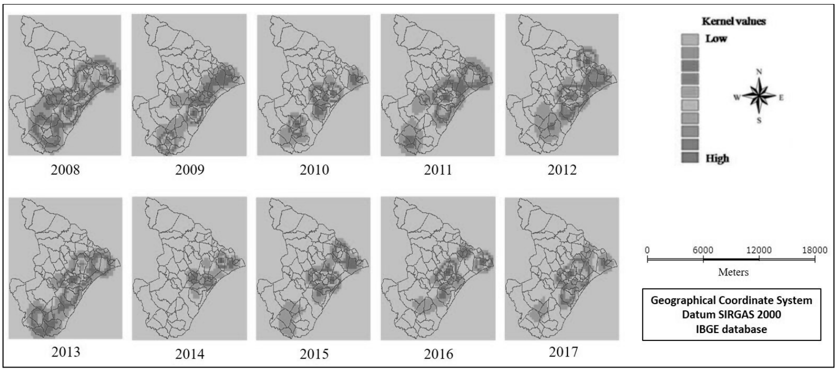

Figure 2. Kernel spatial analysis maps on the positive rate of schistosomiasis in the municipalities of the State of Sergipe between the period of 2008 and 2017.

DISCUSSION

Schistosomiasis is the second most impacting parasitic disease in the world (behind only malaria) and still represents a serious public health concern, especially in developing countries, such as Brazil (Paz et al., 2021; Tibiriçá et al., 2011). Despite being preventable and treatable, schistosomiasis affects almost 240 million people worldwide and more than 700 million are living in endemic areas (WHO, 2017). Herein, we demonstrated some failures in the PCE activities in several endemic municipalities of Sergipe. Regardless of the decreasing time trend observed in the number of positive tests, the positive rate was stable between 2008 and 2017, and the number of schistosomiasis cases may be underestimated in Sergipe. Considering this, investments and improvements in the PCE are necessary for the effective control of the disease in endemic municipalities of the State.

Importantly, the SISPCE should contain complete information on all 51 endemic municipalities for schistosomiasis in Sergipe and regularly updated this information annually. Nonetheless, we observed herein that there is a lack of data in most of endemic municipalities and a reduction in the number of municipalities carrying out the activities of the PCE, as observed in another study (Cruz et al., 2020). Considering this, we suggest that the real situation of schistosomiasis in the State of Sergipe is even worse. Likewise, under reporting the data considerably limits the accomplishment of epidemiological surveys with the data provided by SISPCE (Farias et al., 2011; Santos et al., 2016b). Remarkable, Sergipe is the State with the highest prevalence rate from schistosomiasis in Brazil (Rollemberg et al., 2011; Santos et al., 2016b). Despite this severe epidemiological situation, our results demonstrate that most of the endemic municipalities in Sergipe do not satisfactorily comply with the standards recommended by the Brazilian Ministry of Health in order to carry out the PCE activities (Quinino et al., 2009).

Furthermore, the proper handling of malacological surveys is necessary to identify and assess *S. mansoni* transmission foci (Araújo et al., 2007; Costa et al., 2017; Favre et al., 2001). However, we consider that the lack of data on *Biomphalaria* snails is one of the most serious problems of the PCE in Sergipe. Herein, we noted that most endemic municipalities do not conduct malacological surveys on a regular basis. More importantly, there is no data on *Biomphalaria* sp. in any municipality of Sergipe in the last years of this time series (from 2015 to 2017). On the other hand, time trend analysis showed stability in the percentage of positive cases for schistosomiasis in Sergipe between 2008 and 2017. As a result, the lack of data on foci of *Biomphalaria* sp. in the State with the highest prevalence rate from schistosomiasis can considerably compromise the identification and monitoring of areas at risk of transmission and the disease control (Barbosa et al., 2000; Zanardi et al., 2019).

Notably, studies using spatial analysis techniques are required to map and comprehend the spatial dynamics of the schistosomiasis (Barbosa et al., 2012, 2017; Paz et al., 2020; Santos et al., 2016b, 2017). Additionally, they allow us to identify high-risk clusters of the schistosomiasis and, therefore, they can assist health managers in investing and directing emergency actions to control the disease. Using Kernel estimator, we identified the most affected areas by *S. mansoni* in Sergipe and they included municipalities in the North of the State (near the São Francisco River) and those in the metropolitan area. Importantly, some municipalities close to the São Francisco River have large irrigation areas for rice cultivation. These areas have *S. mansoni* transmission foci and significantly increase the risk of infection, mainly among farmers (Rollemberg et al., 2015). Concerning the hotspots in the metropolitan area, we must consider that those municipalities are in the coastal strip and have many rivers and lakes. These environmental characteristics along with the lack of basic sanitation, especially in the poorest neighborhoods and slums, maintain the disease transmission cycle (Sokolow et al., 2016).

Conversely, the spatial analysis maps also showed a reduction in high-risk areas (hotspots) for schistosomiasis in Sergipe over these 10 years. Additionally, there is a lack of data in about half of the endemic municipalities in 2017 and absence of the PCE activities in 32% (24/75) of the municipalities, all from the interior of the State. Importantly, PCE is not usually performed in non-endemic areas (Katz, 2018). Notwithstanding, regardless of these cities are not considered endemic for schistosomiasis, the absence of data may be masking and underestimating the real prevalence of the disease in inland municipalities.

Interestingly, time trend analysis showed decreasing trends in the number of positive tests for *S. mansoni*. Likewise, there was a reduction in the assessed population, in the number of Kato-Katz tests performed, and in the number of endemic municipalities carrying out PCE actions. Considering this, and that the positive rate showed a stable trend in the study period, we can attest that there was no effective reduction in schistosomiasis in the State and that the disease control target established by the Word Health Organization (WHO) for 2030 is far from being reached in the State (Kura et al., 2021).

Our study has some limitations that needs to be mentioned. As this is an ecological study and using secondary data from the SISPCE, there may be under information reporting collected and notified by the PCE. As a result, this can affect data analysis and, consequently, the actual status of the disease in the State. Despite this, our findings are alarming and corroborate the under cases reporting of schistosomiasis and the failures of the PCE in monitoring and controlling the disease in Sergipe.

Taken together, our data demonstrate that there are important failures in the activities of the PCE in endemic municipalities of Sergipe. Remarkable, there was a reduction in the number of endemic municipalities performing the program's activities and most of them do not contain malacological information. Furthermore, regardless the number of positive tests decrease , the positive rate presented a stable trend. Herewith, we consider that there is under schistosomiasis cases reporting in Sergipe and the disease situation in the State may be even more concerning. Therefore, it is necessary to reassess and restructure the actions of PCE in the State. In addition, more investments are required to train technicians for collecting data, performing parasitological tests and comprehensive treatment of positive ones. Despite this, it is mandatory to reinforce that schistosomiasis is a neglected tropical disease, and that its occurrence is strongly associated with poverty, deficiencies in sewage system and in the access to safe drinking-water. Considering this, we emphasize that the control of the schistosomiasis does not depend exclusively on the actions of the PCE. The implementation of public policies to improve socioeconomic determinants and health conditions are essential to interrupt the transmission of *S. mansoni* and, consequently, reduce the disease transmission cycle.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest to disclose.

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