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Major Article

Spatial analysis for the identification of risk areas for schistosomiasis mansoni in the State of Sergipe, Brazil, 2005-2014

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Abstract

Introduction: Schistosomiasis is a parasitic infectious disease with a worldwide prevalence. The objective of this work is to identify risk areas for schistosomiasis mansoni transmission in the State of Sergipe, Brazil, during the period from 2005 to 2014. **Methods:** We conducted an epidemiological study with secondary data from the Information System Control Program of Schistosomiasis [*Sistema de Informação do Programa de Controle da Esquistossomose* (SISPCE)]. Temporal trends were analyzed to obtain the annual percentage change (APC) in the rates of annual prevalence. In addition to the description of general indicators of the disease, the spatial analysis was descriptive, by means of the estimator of intensity kernel, and showed spatial dependence by indicators of global Moran (I) and Local Index of Spatial Association (LISA). Thematic maps of spatial distribution were made, identifying priority intervention areas in need of healthcare. **Results:** There were 78,663 cases of schistosomiasis, with an average of 8.7% positivity recorded; 79.8% of the cases were treated, and Sergipe showed a decreasing positive trend (APC: -2.78). There was the presence of spatial autocorrelation and a significant global Moran index (I = 0.19; p-value = 0.03). We identified clusters of high-risk areas, mainly located in the northeast and southcentral of the state, which each had equally high infection rates. **Conclusions:** There was a decreasing positive trend of schistosomiasis in Sergipe. Spatial analysis identified the geographic distribution of risk and allowed the definition of priority areas for the maintenance and intensification of control interventions.

Keywords: Schistosomiasis. Epidemiology. Geographical information system. Spatial analysis.

INTRODUCTION

Schistosomiasis is a parasitic infectious disease that has a worldwide prevalence(1) (2). It is an acute and chronic parasitic disease caused by trematode worms of the genus *Schistosoma*, and disease transmission has been reported in 78 countries of Latin America, Africa and Asia. In 2012, at least 249 million people needed preventive treatment for schistosomiasis, and 42.1 million people were reported to have been treated(3).

Brazil is the country that is most affected in the Americas(4), with 42.9 million people exposed to the risk of infection and about 6.8 million infected individuals(5) (6). In view of its potential for expansion, it is considered to be one of the most serious public health problems(7). In Brazil, the disease occurs in all regions, with areas of concentration in the Northeast and in the State of Minas Gerais(4). According to the Schistosomiasis Control Program [*Programa de Controle da Esquistossomose* (PCE)] data, there were 7.1 million exams of feces in 1,060 endemic municipalities - with a positivity for *Schistosoma mansoni* of 5.4% - performed in the period from 2008 to 2012(8). In Northeastern Brazil, the planorbidae *Biomphalaria glabrata* and *Biomphalaria straminea* are the two intermediate hosts most important in disease transmission(9).

In Brazil, schistosomiasis is more intensely distributed on a continuous and contiguous strip of land, over almost the entire coastline, following the trajectory of important hydrographic

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basins[7]. In these endemic schistosomiasis areas, in addition to monitoring, the control of these conditions involves reducing the occurrence of severe forms and deaths, reducing the prevalence of the infection (to levels lower than 5%), and indicating measures to reduce the expansion of the endemic areas[10] [11].

In Sergipe, schistosomiasis transmission occurs mainly in two regions: the Atlantic Forest and the coast. The annual average of hospital admissions for schistosomiasis from 2005 to 2010 was 17 admissions, with a reduction in this rate from 1.58 per 100,000 inhabitants in 2005 to 0.44 per 100,000 inhabitants in 2010. The average number of deaths in the same period was 17, and the mortality rate per 100 thousand inhabitants remained at 0.86 during this time interval[12].

Considering the lack of more recent local studies, it would be salutary for health professionals and managers to have access to accurate information from health analyses of the magnitude and significance of schistosomiasis through the construction of epidemiological scenarios, thereby facilitating the planning and implementation of interventions consistent with local health conditions. Thus, the objective of this study is to identify the risk areas for schistosomiasis mansoni in the State of Sergipe, Brazil, during the period from 2005 to 2014.

METHODS

This is a chronological and epidemiological study based on secondary data reported in the Schistosomiasis Control Program Information System [*Sistema de Informação do Programa de Controle da Esquistossomose* (SISPCE)] from the Secretariat of Health of Sergipe *[Secretaria de Estado da Saúde de Sergipe* (SES-SE)][13]. It examined the historical series (2005 to 2014) of the prevalence in endemic municipalities[12] in the State of Sergipe.

Sergipe is located on the coast of Northeastern Brazil; its capital city of Aracaju is composed of 75 municipalities. It has a population of 2,068,017 inhabitants and an area of 21,910,354km², equivalent to 0.26% of the national territory[14].

The epidemiological data obtained correspond to the following variables: performed total exams, percentage of positivity for *Schistosoma mansoni* eggs, pending treatment refusal and/or absence, and the number of subjects treated from 2005 to 2014 in the municipalities of the State of Sergipe. The laboratory technique recommended by the Ministry of Health was the parasitological examination according to the Kato-Katz method[15].

Epidemiological indicators were calculated (the percentage of positivity of the studied population), and the coverage indicators of the program were determined (the proportion of the population examined by the studied population, the proportion of municipalities studied per endemic municipalities, refusal of pending treatment and/or lack of treatment, and the coverage of treatment).

The *JoinPoint Regression* Program[16] was used to calculate the temporal trends of the annual prevalence of schistosomiasis for a consecutive series of ten years. The annual percentage variation **as** annual percentage change **(**APC), with a confidence interval (CI) of 95%, was calculated by means of Poisson regression. The significance tests used were based on the method of permutation of Monte Carlo[17]. The significance level adopted was 5%.

Thematic maps were constructed for the prevalence of schistosomiasis in the municipalities for the period examined. The prevalence in each municipal period was stratified into three levels: low - less than 5% prevalence; average - prevalence between 5 to 19.9%; and high - prevalence equal or greater to 20%[10]. The kernel intensity estimator was also used by smoothing the statistically generated surface density for the visual detection of *hot spots*, indicating agglomeration in a spatial distribution and a continuous surface from point data[18] [19].

The autocorrelation between the rates of prevalence of the disease was used to investigate if the spatial distribution of the endemic regions occurs randomly or follows some pattern of occurrence in the space. A spatial proximity matrix was rendered - obtained by the criterion of contiguity - while adopting a level of significance of 5%, and the total index of Moran (I) was calculated[20].

The Moran mirroring diagram was used to indicate the critical areas of transition, in order to compare the value of each municipality with the neighboring municipalities and check the spatial dependence, as well as to identify the spatial patterns through the Local Moran Index[20] [Local Index of Spatial Association (LISA)]. Spatial quadrants were generated: Q1(high/high) and Q2 (low/low), i.e., municipalities with similar values to those of its neighbors, indicating positive spatial association points characterizing the spatial aggregates; Q3(high/low) and Q4 (low/high) indicating negative points of spatial association where municipalities have distinct values from their neighbors, thus characterizing discrepant observations, represented visibly by BoxMap[21].

Local Index of Spatial Association has detected regions with significant local spatial correlation ($p<0.05\%$). Local indicators have produced a specific value for each area, correlating to the identification of clusters visualized by the LisaMap. The last stage of the analysis merged the areas that have positive spatial correlation (identified by BoxMap) with statistically significant spaces above 95% (identified by LisaMap) generating the MoranMap, which is useful for the identification of clusters and of identifying priority areas. Moran maps were constructed for the spatial representation, whereas the municipalities with statistically significant differences ($p<0.05$)[21].

The cartographic base of the State of Sergipe was provided by *Instituto Brasileiro de Geografia e Estatística* [(IBGE) Digital Urban Charter of the State of Sergipe][14]. The cartographic projection corresponded to the Universal Transverse Mercator system, using the model of the Earth Horizontal Datum, South American Datum (SAD) 1969 and zone 24S. The descriptive data were tabulated and analyzed by GraphPad Prism version 5.01. TerraView 4.2.2 was used for spatial analysis[22].

Ethical considerations

For conducting this study, authorization was previously requested from the Coordination of epidemiological surveillance of the State of Sergipe. The research project that included this study was submitted for approval to the Research Ethics Committee at the *Universidade Federal de Sergipe* (Number 23373713.1.0000.5546 - report 453303/2013).

RESULTS

The available results (**Table 1**) indicate that the record of the data in the SISPCE in Sergipe revealed a sharp fall in analyzing the operational indicators. Its computerization was started in 1995 and has been deployed today in all the municipalities that are endemic. A total of 896,373 schistosomiasis tests were carried out in the municipalities of the endemic areas of Sergipe, between 2005 and 2014. Of these exams, 78,663 (8.8%) were positive for *S. mansoni* eggs. The highest prevalence of the disease occurred in the year 2008 (10.4%) and the lowest (6.4%) in 2014.

Also in **Table 1**, there was a reduction of 59.3% in the amount of schistosomiasis examinations in the state, ranging from 106,904 in 2005 to 43,494 in 2014. In that same period, there was also a variation in the number of municipalities that had provided data for the SISPCE: average 38.8 ± 5.9 [standard deviation (SD)]. The greatest number of municipalities providing records was 48 in 2007, corresponding to 94.1% of the total of municipalities; the lowest record of municipalities providing data was 29, corresponding to 56.8% and, consequently, a reduction of the studied population. The lowest record of outstanding treatments by absence (281) was observed in 2014, and the highest record was 3,493 medical cases pending issues, which occurred in 2006. Regarding the treatment coverage of parasitism of the cases, there was fluctuation between the years analyzed, with the years 2008 to 2012 showing that the treatment coverage was lower than recommended by the PCE Ministry of Health. Sergipe presented a coverage of treatment of 79.8% between the years 2005 to 2014.

Taking into account the results of the Poisson regressions, the State of Sergipe presented a decreasing tendency of positivity for schistosomiasis which was statistically significant (APC= -2.78; CI = -5.8 to 0.3; p<0.0005), throughout the historic series analyzed. In **Figure 1** punctual schistosomiasis prevalence rates can be viewed as well as the annual trends estimated by *Joinpoint* for the State of Sergipe from 2005 to 2014.

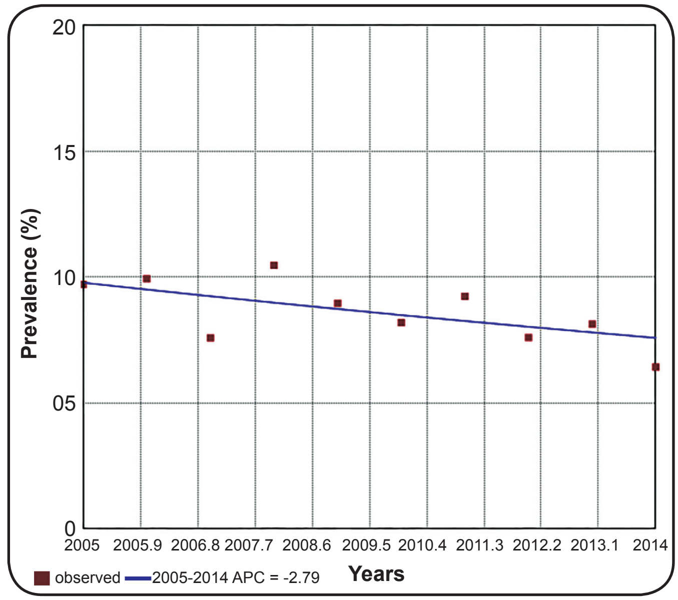

FIGURE 1. Trend chart (%) prevalence of infection by *Schistosoma mansoni* in State of Sergipe, 2005 to 2014. APC: annual percentage change.

The distribution and spatial analysis of the rates of prevalence of schistosomiasis, according to the data of the SISPCE, between the years 2005 to 2014 in the municipalities of Sergipe. The geographical distribution of the endemic regions reached approximately 68% of the state's municipalities. In the spatial distribution of municipalities by schistosomiasis prevalence rates **(Figure 2A)**, the proportion of municipalities with a prevalence above 20% was significantly greater in the east zone of the State of Sergipe than in the Agreste (p<0.05); 19 (38%) of endemic municipalities presented a high prevalence (above 20%), 23 (46%) presented an average prevalence (5 to 20%) and the lowest prevalence (below 5%) was observed in 8 (16%) municipalities. Municipalities not assessed due to

TABLE 1

Operational Indicators of the Schistosomiasis Control Program, State of Sergipe, Brazil, 2005 to 2014.

	Years										
Indicators	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**Total**
Municipalities studied	42	46	48	37	38	34	42	39	33	29	-
Endemic municipalities	51	51	51	51	51	51	51	51	51	51	-
Population studied	132,883	183,184	169,306	107,110	115,657	143,841	99,331	105,648	89,827	60,628	1,207,415
Examinations carried out	106,904	141,090	134,046	81,543	84,052	98,473	72,644	71,585	62,542	43,494	896,373
Positive exams	10,372	14000	10,166	8,528	7,529	8,055	6,705	5,437	5,081	2,790	78,663
Prevalence (%)*	9.7	9.9	7.5	10.4	8.9	8.1	9.2	7.6	8.1	6.4	8.7
Proportion of studied/endemic municipalities (%)	82.3	90.2	94.1	72.5	74.5	66.6	82.3	76.4	64.7	56.8	-
Pending due to refusal	0	0	0	0	0	0	0	0	0	0	0
Pending due to absence	2,874	3,493	2,393	1,480	1,434	1,774	1,151	1,486	636	281	17,002

*Number of positive people for *Schistosoma mansoni*/number of people examined X 100.

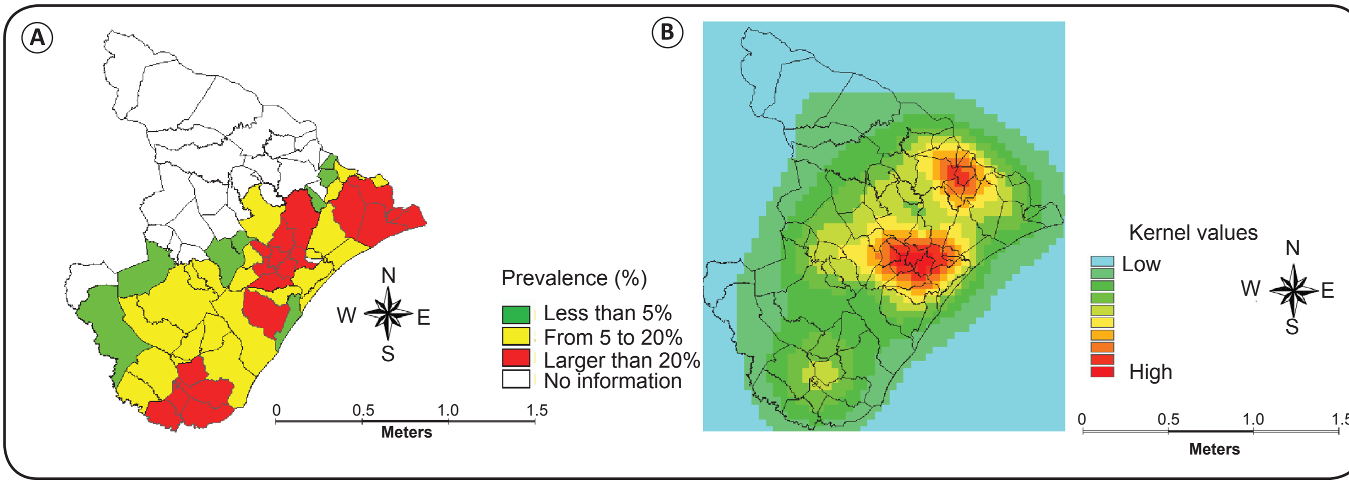

FIGURE 2. (A) Spatial distribution of the prevalence of infection by *Schistosoma mansoni* in State of Sergipe, Brazil, 2005 to 2014. **(B)** Map of the Kernel analysis on the population density of the infection by *Schistosoma mansoni*, Sergipe, Brazil, 2005 to 2014.

lack of information are shown in white areas on the maps. The municipalities with the highest prevalence of the disease were Santa Rosa de Lima (34.6%), São Cristóvão (32.2%) and Ilha das Flores (29.2%). The kernel density estimator, through interpolation (**Figure 2B**), showed a high density (hot spot) of the highest rates of occurrence of schistosomiasis cases (point intensity) located near the Northeastern region (Cedro de São João, Malhada dos Bois, São Francisco, Telha, Aquidabã and Propriá), the central region (Santo Amaro das Brotas, Maruim, Malhador, Santa Rosa de Lima, Divina Pastora, Nossa Senhora do Socorro, Rosario do Catete and Laranjeiras) and less intensity in the southern region of the state (Arauá, Itabaianinha, Umbaúba, Cristinápolis, Indiaroba and Santa Luzia do Itanhy). It is noteworthy that the municipality of General Maynard, despite being located in areas of high schistosomiasis prevalence, had no reported cases in the SISPCE **(Figure 2** and **Figure 3).**

It was observed that the presence of spatial autocorrelation for the whole period examined, because the total Moran index was significant for this distribution (r= 0.19; p value=0.03), indicated the existence of *clusters* (**Figure 3A**). Moran's global index for each year was calculated, showing significance also in every year analyzed, as shown in **Table 2.** The positive value of Moran infers that neighboring municipalities have similar schistosomiasis prevalence rates. Thus, municipalities with high coefficients are close to others with the same profile, and those with low values are located in the vicinity of other municipalities with the same characteristics.

The BoxMap in **Figure 3B** shows areas classified according to their position in the Moran mirroring diagram. It was observed that groups with high schistosomiasis prevalence rates and neighbors with similar values (high-high) were concentrated mainly in the east (Neópolis, Pacatuba, Ilha das Flores e Brejo Grande), the Center (Laranjeiras, Maruim, Rosario do Catete, Siriri, Divina Pastora and Riachuelo) and the South (Umbaúba, Cristinápolis, Indiaroba and Santa Luzia do Itanhy). Moreover, clusters with low rates and neighbors with similar values (low-low) are located

TABLE 2

Moran Global index (I) the prevalence rates of schistosomiasis mansoni per year, State of Sergipe, Brazil, 2005-2014.

Year	Moran Global Index value (I)	p-value
2005	0.39	0.01
2006	0.36	0.01
2007	0.38	0.01
2008	0.22	0.01
2009	0.08	0.01
2010	0.06	0.03
2011	0.31	0.01
2012	0.04	0.02
2013	0.09	0.01
2014	0.06	0.01
Period total	**0.19**	**0.03**

in the southwest region (Lagarto, Riachão do Dantas, Tobias Barreto, Boquim, Salgado, Simão Dias, São Domingos and Brejo Grande), the northeast (Cedro de São João, São Francisco, Propriá and Telha) and east (Barra dos Coqueiros, Santo Amaro, Pirambu and Japaratuba). There were areas still displaying characteristics which would classify them as being in epidemiological transition, such as containing municipalities with opposite prevalence rates, represented by high and low prevalence in the south, east and northeast. Municipalities were also observed with low rates among the cities with high rates dispersed throughout the state.

The LisaMap (**Figure 3C**) shows clusters of municipalities that differ from the others, with statistically significant local spatial dependence (with the 5% level). These are: Umbaúba, Itabaiana, Brejo Grande, Pacatuba, São Francisco, Cedro de São João, Nossa Senhora das Dores, Riachuelo and Divina Pastora.

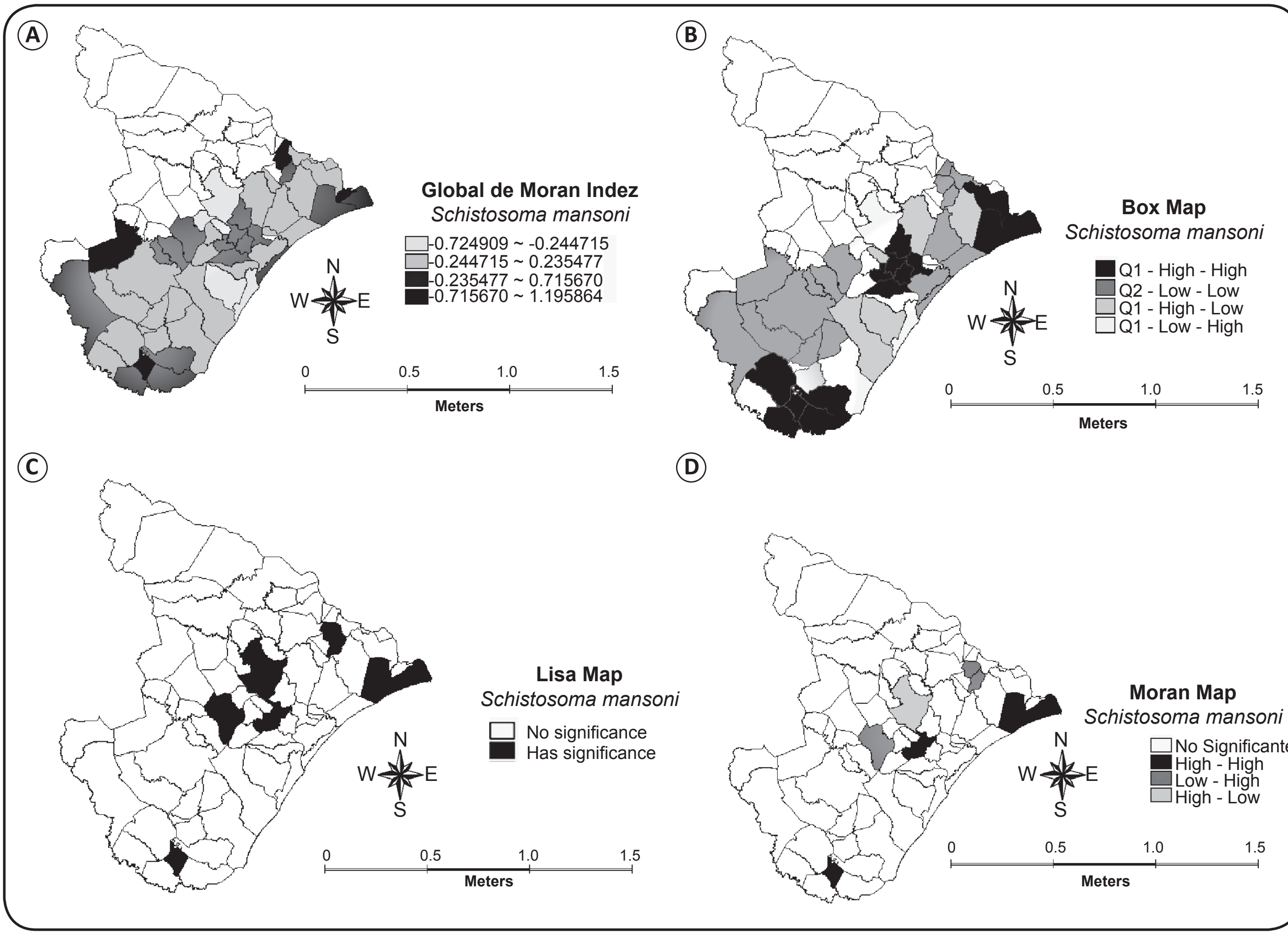

FIGURE 3. Spatial analysis of the prevalence of infection by *Schistosoma mansoni*, 2005 a 2014, State of Sergipe, Brasil. **(A)** Spatial distribution of Global Moran Index value; **(B)** BoxMap; **(C)** LisaMap; **(D)** MoranMap.

The results obtained by MoranMap (**Figure 3D**) verify clusters considered high-risk areas for schistosomiasis due to the grouping of municipalities with equally high rates among themselves (high-high) -- these municipalities were Umbaúba, Brejo Grande, Pacatuba, Divina Pastora and Riachuelo. Other clusters with low prevalence rates (low-low) are concentrated in the state, represented by the municipalities Cedro de São João, São Francisco and Itabaiana. The city of Nossa Senhora das Dores was considered transitional because it contained contrary rates (high-low), i.e., high values surrounded by areas showing low rates.

DISCUSSION

The State of Sergipe has an average positive rate for schistosomiasis of 8.7% in the historical series analyzed - higher than the national average (5.9%) for the same analyzed period (8) - with a decreasing trend in prevalence, but registering many municipalities with a prevalence of 20%, especially in the East Sergipana zone, which is concerning. Despite the study's limitations with the use of secondary data from census surveys conducted by SISPCE[23] [24], the available information may portray the endemicity of the disease in the State of Sergipe and allow the formulation of more effective control strategies[11]. It is worth mentioning that the study period (2005-2014) corresponded to the post-decentralization stage of PCE, when the disease control measures were the responsibility of the municipalities, and each went on to perform the activities according to their criteria and conditions[25] [26].

The geographic distribution of the epidemic reaches 68% of the state's counties[25], with the highest prevalence rates (over 20%) mainly concentrated in the eastern and coastal areas of the state. Ministry of Health data indicate that in northeast Brazil (which contains Sergipe), with the highest reported cases of schistosomiasis and one of the highest mean prevalence rates, this endemic disease is a major cause of mortality from communicable disease[27].

The data available in *Departamento de Informática do Sistema Único de Saúde* (DATASUS) indicate that the registry in SISPCE from Sergipe showed a sharp overall decline from 2005 to 2014, coinciding with the implementation of decentralization actions and coupled with the municipalization of carrying out the census and schistosomiasis surveys[24]. Consequently, in 2014 only 56.86% of the endemic municipalities were registered in the system, presenting an unsatisfactory coverage of the municipalities. Although the routine program activities will be implemented, municipalities have difficulties in exercising them due to the reduced operational framework that is needed to control other endemic diseases, in addition to municipalities performing such activities with their own criteria according to the availability of equipment, which has also been cited in other studies[11] [24] [26].

The data show much lower prevalence rates compared to those found in the 70's, when the activity of the PCE was started in the Northeast, but with a practically stable percentage for the endemic regions between the monitoring stage[11] [24] to values less than 5% as recommended by the World Health Organization (WHO)[28]. This reduction of the disease in the state is evident when comparing the results of this study with others conducted in Sergipe[29] and is similar to results in other states[25] [30] [31]. The northeast is an important ecological reserve of the intermediate hosts of *S. mansoni* and the State of Sergipe is historically endemic[29]. The disease positive analysis in Brazil, held by the Ministry of Health on the historical series from 1990 to 2010, showed the reduction scenario, with average positivity of 8% and a decrease trend of 0.25% per annum[27].

It should be noted that there was a significant reduction in the quantitative and population examinations in those municipalities of Sergipe, which may influence this reduction in positivity, a situation which has also observed in other studies[32] [33]. Even when analyzing the operational indicators, the state has not reached the treatment goal of diagnosed cases[13], in which the number of disputes by absence remained high during the period. This may reflect deficiencies in the planning of actions and services in the treatment phase, such as the patient's search for compatible schedules with their routine, or lack of access to services and integration with primary care teams. Such indicators are important in the planning of control measures and monitoring and can provide evidence of failures in the adopted model[33]. This fact also reflects the difficulty of the state to develop specific, harmonized and integrated actions of health care policies although they are linked to the Family Health Strategy *[Estratégia Saúde da Família* (ESF)].

The favorable environmental conditions, presence of intermediate hosts and socioeconomic conditions, such as widespread poverty, difficult access to medical care, and low levels of hygiene and sanitation, enable the survival of these parasites and the maintenance of the transmission cycle in the state[28] [32] [34]. In this study, it can be noted that the distribution of prevalence of schistosomiasis rates in Sergipe was not random; existing patterns of grouping municipalities present similarities between them according to the Moran Global Index. Clusters with high rates of densities in the north and center, as well as a lower density in the southern region, were evident. For a better understanding of this scenario, there is a need for fundamentally larger studies with consideration of other variables related to socioeconomic conditions and infrastructure, and variables related to environmental and behavioral aspects, as such those which influence the infection process.

In addition, the change in climate and ecological factors can influence the population dynamics of the transmitter snails; this requires a malacological survey in catch basins to detect breeding patterns of epidemiological importance. It is worth mentioning that the non-occurrence of schistosomiasis in towns like General Maynard, located in high-density areas cases, may be related to the underreporting of cases and/or not providing data to SISPCE.

Over the past few years, the country has achieved a considerable increase in the urbanization rate and, as a result, changes in the demographic and epidemiological patterns. Although there have been significant improvements, such as a reduction in mortality from infectious diseases and increased life expectancy[35], the persistence of diseases associated with poor living conditions still constitutes a historical challenge, requiring monitoring models that involve social contexts[36]. In this regard, the cities of Aracaju, Nossa Senhora de Socorro, São Cristóvão, Propriá, Barra dos Coqueiros, Estância, Carmópolis, Itabaiana and Laranjeiras, that have the highest Human Development Index [*Índice de Desenvolvimento Humano* (IDH)][14] of the state, still present constant cases of schistosomiasis concentration in urban areas characterized by socioeconomic disparities. This resurgence is related to deficiencies in the sanitation infrastructure in poor peri-urban areas of cities. Disease transmission control goes beyond the capacity of health professionals, and mass treatment should be done with government actions that combine installation of water and sewage in houses, changes in the environment, health education, combating snails, in addition to the diagnosis and treatment of infected persons[37].

The existence of spatial autocorrelation of schistosomiasis prevalence rates shows that nearby areas tend to have similar rates, favoring the formation of clusters. The agglomeration of cases is not only due to the choice of bringing people but is mainly the product of a series of urban and political factors that favor spatial segregation[38]. In addition, areas classified as epidemiological transition areas were checked[20] because there are neighboring areas with opposite prevalence (i.e., some high and other low prevalence rates of schistosomiasis). In these areas, the actions to control the infection should be intensified to reduce the number of cases and the spread of disease.

This study demonstrates the need to define integrated schistosomiasis control strategies. The endemic control programs, even instrumented with effective technologies, have not achieved efficiency in their actions because they are making use of a centralized logic that is interventionist, medicalized and standardized for all endemic areas[30]. As much as there are limitations and challenges, SISPCE is a breakthrough in the monitoring and surveillance of schistosomiasis, requiring continuity of action by the municipalities and the use of spatial analysis of cases of schistosomiasis to estimate the risk of disease transmission, set priorities and deepen the analysis of the environment, parasitic infections and the definition of preventive measures.

Despite the limitations that include the use of secondary data and its inherent problems mainly related to possible underreporting of cases, we observed a downward trend in the positivity of schistosomiasis in Sergipe in recent years. Schistosomiasis mansoni shows a pattern of heterogeneous spatial distribution, evidenced by the delimitation of clusters in the northeastern, central and southern regions of the state. The spatial analysis of methodological techniques used were effective in the delimitation of risk areas for schistosomiasis in the state which deserve to be incorporated into endemic disease control activities, as well as useful in defining priority areas for intensifying investments and control activities.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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