Urban schistosomiasis: An ecological study describing a new challenge to the control of this neglected tropical disease

Elainne Christine de Souza Gomes,[a,*] Iris Edna Pereira da Silva,[a] Wheverton Ricardo Correia do Nascimento,[a,b]
Rodrigo Moraes Loyo,[a] Ana Lúcia Coutinho Domingues,[c] and Constança Simões Barbosa,[a]

[a]Schistosomiasis Reference Laboratory, Department of Parasitology, Aggeu Magalhães Institute, Fiocruz - Ministry of Health, Recife, PE, Brazil.
[b]Department of Tropical Medicine, Federal University of Pernambuco, Recife, PE, Brazil.
[c]Center of Medical Science, Clinical Hospital, Federal University of Pernambuco, Recife, PE, Brazil.

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Summary

Background Social and environmental vulnerabilities contribute to the persistence and increase of Schistosomiasis, which has been a public health problem in Brazil and worldwide. In this study, we aimed to monitor the entry, installation, and maintenance of schistosomiasis transmission in an urban area on the Brazilian coast over two decades (2000–2010/2010–2020).

Methods This population-based cross-sectional study was conducted in Porto de Galinhas, state of Pernambuco, Brazil, to investigate the dynamics of schistosomiasis transmission in the urban area. Through 3 malacological and parasitological surveys and using geoprocessing technologies, schistosomiasis transmission foci (STF), as well as cases of the disease were identified and quantified. Statistical and geoprocessing tools were used to analyse the data.

Findings Overall, the number of STF decreased from 15 (2000) to 11 (2010) and then to 9 (2020). Although the infection ratio of snails in 2000 has decreased from 16·1% to 5·8% in 2010, we observed an increase to 7·2% in 2020. Additionally, 6,499 individuals were analysed (2012 in 2000; 2459 in 2010, and 2028 in 2020) and the prevalence of human infection has decreased over years, from 32·5% (2000), 16·6% (2010) to 8·8% (2020). The disorderly urbanization process was directly related to the spatial distribution of STF and schistosomiasis cases, causing a new scenario where people became infected by walking on unpaved and flooded streets.

Interpretation Although we observed a decreasing in schistosomiasis cases and STF, this NTD became a health problem related to urbanization in the study area. The challenge to overcome this new sort of transmission will require a greater understanding of the disorderly migration, spatial occupation, and degradation of the environment.

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Keywords: Urban schistosomiasis; Transmission; Neglected tropical disease; Schistosoma mansoni; Biomphalaria grabrata; Urbanization; Brazil

Introduction

Schistosomiasis is one of the oldest human parasitic infections and has evolved together with humanity over the centuries.[1] The most ancient register of this disease dates back to 5800–4000 years before Christ (BC) on a human skeleton discovered in Syria, where a schistosome egg with a terminal spine was found, which could be from *Schistosoma haematobium* or *S. intercalatum.*[2] Despite this record in Syria, it is believed that the 'cradle' of schistosomiasis remains the region of the great African lakes, an area in which both the definitive and the intermediary hosts are in a permanent state of evolution.[3] From Africa, this illness has spread around the world and today affects 78 countries worldwide.[4] It is estimated that 250 million people are infected[5] and

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*Corresponding author.
E-mail address: elainne.gomes@fiocruz.br
(E.C.d.S. Gomes).

Research in context

Evidence before this study

To investigate the urban transmission of schistosomiasis, we searched PubMed for relevant articles published in English between February and April, 2021, using the search terms "Schistosomiasis" or "Schistosoma" together with "urbanization" or "Urban transmission" or "Georreferenced." This search identified 179 articles. Out of these, studies that did not carry out selection of participants by population-based surveys and did not present schistosomiasis urban transmission were excluded.

Added value of this study

The first initiative to reduce schistosomiasis in Brazil was the Special Schistosomiasis Control Program (PECE), implemented in 1975. It was a Public Health strategy to control the endemic disease across the country. The first strategy adopted was to carry out coproscopic and malacological surveys to define the epidemiological profile of the disease. Then, strategies based on periodic mass drug administration (MDA) of the population, control of the vector mollusc through the application of molluscicide in water collections and basic sanitation in specific locations were also adopted. Finally, epidemiological surveillance and treatment of new cases in endemic areas were established. There was a significant reduction in the prevalence of schistosomiasis in most endemic municipalities. However, it was not enough to eradicate the disease in the entire national territory. The Schistosomiasis Reference Laboratory has been conducting research in Epidemiology, Malacology, Clinical aspects, and Schistosomiasis Control. During the 60s and 80s, the disease was considered one of the biggest rural diseases in Pernambuco, one of the most endemic states located in Northeast of Brazil. In the 90s, the Laboratory started to investigate the effects of disorderly migration to coastal areas on the spread of the disease to urban and under development areas. The changes in the epidemiological profile of the disease were described in the following decades in Pernambuco, Brazil. Our study shows the introduction of schistosomiasis (2000) in a coastal area whose main economic source is based on tourism; and the chronification process of the disease characterized by reduced prevalence and parasitic burden that maintain the cycle of transmission of the disease without causing alerts to the health system. Through a detailed analysis of data collected over two decades investigating the urban transmission of schistosomiasis, this study aims to provide information that can be used worldwide to face this new challenge in schistosomiasis control.

Implications of all the available evidence

This spatial and temporal analysis shows the progress in the control of schistosomiasis in 2000–2020. Although the prevalence of schistosomiasis has decreased 50% in each decade of this century (2000-2010/2010-2020), the social impacts generated by unemployment and poverty led thousands of infected individuals to move to areas where the vectors lived. Although the MDA has been recommended as the main approach for schistosomiasis disease control, further implementation should be done in environmental modification and interventions in behaviours of migrants to reduce local and worldwide disease prevalence. Schistosomiasis is a disease related to quality-of-life housing and sanitary environmental adequacy. It is not feasible to eliminate disease through control programs based only on MDA without investments in poverty reduction by increasing population incomes and by promoting better urban infrastructure, including housing conditions and assured access to quality water.

approximately 700 million people are at risk of infection.[6]

It is known that wars, international trade, spontaneous and forced migrations are the main reasons for the dissemination of schistosomiasis. The last one is appointed as the way schistosomiasis was introduced in Brazil, by the slave trade from Africa from the sixteenth century until 1888, with its abolition.[7] Although African slaves were probably infected with more than one species of *Schistosoma*, only *S. mansoni* managed establish a full cycle in the country, due to the presence of vector snails commonly implicated in the transmission in Brazil (*Biomphalaria glabrata, B. straminea, and B. tenagophila*).[8,9] Upon arrival in Brazil, the disease was established in coastal areas of the country, especially in the Northeast and in some Southeast states and, according to the last national epidemiological survey, it is estimated that 1.5 million people would be infected in the country.[10] This number represents a significant decrease in the prevalence of this disease and is the result of several strategies implemented by the Schistosomiasis Control Program in Brazil since the mid-eighties.[10,11]

The strategies used by this program included Massive Drug Administration (MDA) of the population, vector-borne control by applying molluscicide in natural and artificial breeding sites, controlling the severity of morbidity by surgical methods, and involving primary care in early diagnosis and treatment.[11,12] All these interventions also reduced the number of severe morbidity and mortality.[10,13] However, it seems that it was not enough to control the disease, since it expanded to new non-endemic and urban areas all over the country by the migratory flux of people from endemic rural areas.[14–18] As a result, people started to get infected in urban spaces, walking through temporary snail breeding sites on flooded streets.[19–22] rather than the classic transmission observed in rural areas, when people got infected through contact with parasite-harboring snails in natural water sources during labor and leisure activities (fishing, farming, swimming).[15]

The role of urbanization on neglected tropical diseases (NTD) is a subject that has raised attention in the past decade, because it is the first time in human history that more people live in urban areas than in rural ones (56 and 44%, respectively), and, by 2050, this number is expected to reach 66% of the world population.[23] Urbanization is usually associated with economic progress and better social and health conditions; however, for developing countries, such progress does not come together with better living conditions.[24] The negative effect of rapid urbanization is the disorderly occupation of land; environmental degradation; low-quality housing; and absence of water, sanitation, and hygiene (WASH).[22–25] Schistosomiasis, one of the main water-associated vector-borne diseases, has adapted easily to urban environments, and is frequently reported worldwide.[26–32]

In Brazil, since the nineties, there are many reports of the urban occurrence of schistosomiasis.[12,16,18,33] The migration of infected people from rural to urban areas, looking for better jobs and life conditions at the coast, is the main reason for the expansion of this disease to new areas, especially on the coast of Pernambuco state (Northeast of Brazil), where the first records for urban schistosomiasis transmission were registered in the country.[19,33,34] Disease transmission was established when infected people set new housing on the coast, where vector snails were already present or were introduced to this new areas though sands drained from rivers of endemic areas that were destined for civil construction during urbanistic development in these coastal region.[20,33]

The touristic beach area of Porto de Galinhas, located on the coast of Pernambuco, represents the described scenario for schistosomiasis transmission. In 2000, this location recorded the biggest epidemic of acute schistosomiasis cases caused by *S. mansoni* ever registered in the literature worldwide (410 cases = 62% of all cases registered in 2000), after a flood that left the locality underwater for days.[20] After that, the disease remained established in the area and, in 2010, it was considered endemic.[35] It is important to register that the vector snails implicated on transmission (*B. glabrata*) were not the ones present on the river that cross the location (*B. straminea*).[20,36]

Despite the frequent register of urban schistosomiasis and its clear relationship with mobility of the population from the rural to the urban area, and the environmental degradation from disordenated construction on the outskirts of the cities without proper urban and sanitary conditions, there is a lack of studies presenting a deep analysis of this new challenge to control schistosomiasis in growing urban spaces. This article aims to present the results of two decades of monitoring the entry, installation, and maintenance of schistosomiasis transmission in an urban area on the coast of Brazil, and to provide some perspective to overcome the huge challenge of controlling it.

Methods

Study area

This study was conducted in the locality of Porto de Galinhas, in the municipality of Ipojuca, on the southern coast of the state of Pernambuco, Brazil, approximately 60 km from the state capital. The study area was composed of the neighborhoods of Merepe III, Salinas, Socó, and Pantanal (Figure 1). The other three neighborhoods (Merepe I, II, and Vila de Porto) of this location were excluded from the study because they comprise hotel areas and vacation homes with high infrastructure and low population density. Since 2000, this locality has been monitored by our research group and three malacological and parasitological surveys were conducted during the last two decades (2000–2010/2010–2020) using the same methodology. It is important to mention that this research was also based on an empirical approach by data gathered upon observation, experience with similar events, and researchers' expertise.

Similarly to most coastal urban in Northeast Brazil, the snail ecology in the study area, is characterized by focal and artificial breeding sites, influenced by the rainfall regime and precarious sanitation situations, with open sewers, which facilitates its displacement to other spots within the same area. The population of the study area is unknown once it is a touristic and vacation area that has a huge influx of people, however, unpublished data from local authorities estimated a population variation of 6–8 thousand inhabitants. And from our own experience, during the last parasitological surveys (2010 and 2020), 5706 and 6100 individuals were, respectively, registered to participate in the surveys.

Study's design, data gathering and analysis

This research is an observational, population-based, cross-sectional study. For a better understanding of the methodology adopted, this section was divided into methods of mapping, malacological and parasitological surveys, and spatial data analysis.

Locality mapping

The locality was georeferenced by the global positioning system (GPS) technology, using a GPS receiver with a minimum accuracy of 10 m, configured in the Universal Transverse Mercator (UTM) projection Datum SIRGAS 2000. The location was mapped on the ground by walking, and the unit of mapping was the block. Subsequently, using the TrackMaker Pro software, GPS data was transferred; processed to correct and adjust the blocks, streets, and access roads; and saved in shape files. All foci of schistosomiasis transmission (snail infected by *S. mansoni* releasing cercariae) and the residences with confirmed schistosomiasis cases were georeferenced. From these data, it was possible to perform all spatial analyses using the ArcGis 10 software.

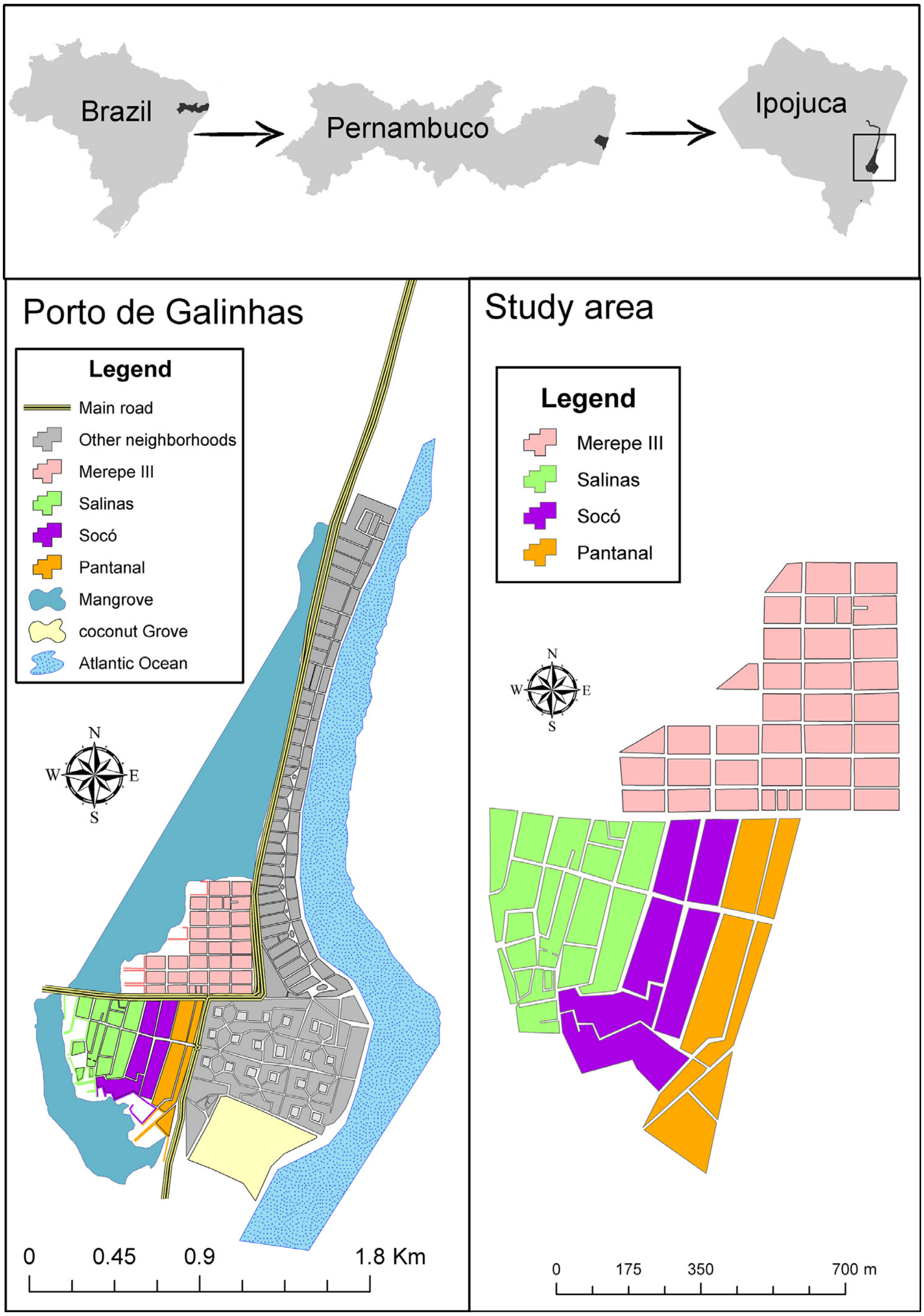


Figure 1. Study area location. Maps of Porto de Galinhas, Ipojuca, Pernambuco state, Brazil. The figure represents the study area. On top one can see the maps of Brazil, Pernambuco, and Ipojuca. The map of Porto de Galinhas shows all neighborhoods of the locality and the ones included in this study (Merepe III, Salinas, Socó, and Pantanal), as well as the main geographical features present.

Malacological survey

During locality mapping all snail breeding sites found in the study area were identified based on the external morphology of the snail shells.[37] This identification was performed immediately after rainy season when all breeding sites are active (snails in water collection). Subsequently, during one year, each breeding site was visited once a month to collected snails. To standardize collection efforts snails were collected by one collector for a period of 15 min, using scoops and tweezers, and were properly packed into moistened ventilated plastic pots and labelled to be transported to the Schistosomiasis Reference laboratory at Aggeu Magalhães Institute – Fiocruz to be examined. The collection period of 15 min was standardized in our laboratory when snail breeding sites are artificial and shallow, adapted from previous method to estimate snail density.[38] To confirm schistosomiasis infection and identify Schistosomiasis Transmission Foci (STF), snails were exposed to artificial light to release cercariae.[39] Negative snails by this technique were reexamined 15 days later, and those that remained negative were squashed on glass plates measuring 15 × 9 cm and individually examined for sporocysts (larval stages) of *S. mansoni*.[40] Snail density per breeding site was determined according to the total number of snails collected in each breeding or collection station per month. Natural infection rate or infectivity rate (IR) was calculated based on the proportion of positive molluscs for *S. mansoni* relative to the total number of molluscs examined. Annual infection rates were calculated for each transmission focus to estimate the potential of disease transmission. Although preliminary studies demonstrated only the presence of *B. glabrata* in the study area.[20,22,36] from all snails collected every month, a random sample of 5% of the snails was removed for dissection of the genital apparatus and taxonomic confirmation of the species.[37]

Parasitological survey

A parasitological census survey was conducted by coproscopic tests on the population living in Porto de Galinhas in the years 2000, 2010, and 2020. All the surveys started at the end of the raining season, after the population was exposed to STF. Although all population was invited to participate in all the surveys, the sample size estimation for the parasitological surveys considering the largest population and prevalence ever recorded for the study period (6100 individuals / 32·5% prevalence), and, taking as parameters the acceptable margin of error of 5%, design effect of 1.0, clusters of 1.0 and a 99% confidence level, indicated a total sampling of 531 individuals, proving that all surveys exceeded the minimum sampling. This sample calculation was performed in the software Epi Info 7.2 (DCD, Atlanta, EUA) through StatCalc - Sample Size and Power. In each parasitological survey the population percentage that joined the research was above 35%.

All population of the study area were invited and voluntarily registered to take part in the survey. Participants did not receive any compensation for participating in the surveys. After signing the consent form provided by the Ethics Committee of the Aggeu Magalhães Institute – which approved this study (ID number: CAAE 02075118.0.0000.5190), – individuals who agreed to participate in this research received a plastic container to collect a stool sample, identified by name. Samples were collected and referred to the laboratory to be examined using the Kato-Katz method (2 slides for each faecal sample), which identifies schistosomiasis cases by finding parasite eggs.[41] This method also allows parasite load quantification (number of eggs per gram (EPG) of stool). Cases were classified by the intensity of infection, using the World Health Organization (WHO) standards: 0-99 EPG (light infection), 100-399 EPG (moderate infection), and > 400 EPG (heavy infection).[42] The prevalence of schistosomiasis in Porto de Galinhas was calculated by the ratio of the total number of positive individuals per total number of examined individuals multiplied by 100. Following the guidelines from the Brazilian Ministry of Health, the prevalence was classified as low (<5%), medium (5-25%), and high (>25%).[9] Prevalence was further evaluated considering various demographic parameters, including sex, age-range and socioeconomic index of the municipality. Sex and age range were related to prevalence of schistosomiasis in all surveys, as well as some socio-economic indices of the municipality.

Spatial analysis

Thematic maps were created to demonstrate the spatial distribution of STF, schistosomiasis cases, and prevalence by blocks. Kernel density estimation (KDE) was used to calculate the density of malacological and parasitological features within a neighborhood (snail's density and infection rate by STF; cases density by residence) and to create maps identifying hotspots within the study area. These hotspots represent the high-risk areas for schistosomiasis to occur. The parameters used to do the kernel analysis were: method data classification 'Natural breaks (Jenks),' with nine classes; and bandwidth method, defined using an adaptive radius for case data and with 100 m influence radius for malacological analyses, with the area unit defined in m^2. All spatial analyses were performed using the ArcGis 10 software.

We used three satellite images to show the environmental changes over the years (2006–2020). There is no high-resolution satellite image for the year 2000 available. The closest image is from 2006. The images referring to August 2006 and June 2010 were obtained by panchromatic and multispectral sensors on board of the QuickBird satellite, with a spatial resolution of 0·6 and 0·5, respectively. The image from September 2020 was obtained with a multispectral sensor on board of the GeoEye 1 satellite, with a spatial resolution of 0·5. The images were taken from an open-source database under Creative Commons Attribution License (CC BY U.S. Geological Survey Department of the Interior/USGS). The images were used for illustrative purposes only.

Statistical analysis

The non-parametric Kruskal-Wallis with Dunn's test was used to verify the difference in snail infection rates

(IR) over the years. Those results were presented with median and interquartile ranges. To evaluate the human parasitological prevalence and differences over the years, univariate comparisons (2010 vs. 2000 and 2020 vs. 2010) with the chi-squared test and as post hoc analysis the Fisher's exact test were used. The Kruskal-Wallis with Dunn's test was used to verify the significant difference between parasite load over the years. Additionally, the Cochrane-Mantel-Haenszel test was used to assess the effect of time on the prevalence while adjusting for sex or neighborhood. The statistical tests were performed using the software GraphPad Prism and R Studio. The statistical significance was considered when *p*-value <0.05.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of this report. All the authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The impact of urbanization on the environment of Porto de Galinhas can be seen by satellite images that register the intense and disorderly occupation of the urban space and natural areas represented by the mangrove biome that surrounds the village (Figure 2). The images show the transformation of the environment over fourteen years, where one can observe the agglomeration of residences and the limits of blocks, streets, and roads, replacing green areas, which have practically disappeared. This figure also shows the design of the blocks and their restructuring over time. The number of blocks increased 30·2% in two decades, from 53 (2000), 62 (2010), to 69 (2020).

Since the first outbreak of schistosomiasis cases in Porto de Galinhas, the number of STF decreased from 15 in 2000 to 11 in 2010 then to 9 in 2020 (Figure 3). According to the result of the three malacological surveys, *B. glabrata* was the only species found in the location. The year 2000 registered the highest IR of the snails: 16·1% were infected by *S. mansoni*. In 2010, the density of snails was the highest noted (4,707), but, at the same time, this year presents the lowest IR (5·8%). In 2020, the lowest number of snails (1607) was recorded; however, IR started to increase again (7·2%). Despite all this variation, only the increasing of density and the decreasing of IR between 2000 and 2010 presented statistical significance (Figure 3). It is important to notice in Figure 3 that the STF distribution started more widespread out in the study area in 2000, however has been concentrated in Salinas over the years. One can also observe that, in 2000, the highest IR were registered in Pantanal (P 15) and Socó (P 14), with 32·4% and 31·0%, respectively (Figure 3A). Since 2010, Salinas has shown the most important STF, registering an IR of 49·0% (P 05) and of 30·8% (P 06) (Figure 3B/3C).

The spatial analysis of malacological data presented in Figure 4 identified the risk areas for schistosomiasis transmission based on density and IR of snails by each STF. Kernel analysis of snail density identified a hotspot in Merepe III in 2000 (Figure 4A), followed by a transition of risk from Merepe III to Salinas (Figure 4B) in 2010 and the setting of risk in Salinas in 2020 (Figure 4C). Nevertheless, when data were analysed by IR of each STF, we found that, in 2000, risk of transmission was present all over the study area, with two important hotspots in Pantanal and Socó (Figure 4D). Differently from risk maps of snail density, no risk transition area was observed and Salinas became the riskiest area for schistosomiasis transmission since 2010 (Figure 4E/F).

The parasitological survey conducted in 2000, 2010, and 2020 sampled a total of 2,012, 2,459, and 2028 individuals, respectively, totalling 6,499 participants. This population represents, on average, 50% of the study area residents. Table 1 shows the epidemiological detailed information related to the surveys. It is important to note that, in general, the number of cases and prevalence have decreased over the years. In particular, the prevalence has reduced by 50% at each decade, from 32·5 (2000) to 16·6 (2010), to 8·8 (2020). In contrast, the median parasite load decreased from 2000 to 2010, but increased from 2010 to 2020. Despite the general reduction of these health indices, the highest prevalence has moved from Pantanal and Socó to Salinas. In addition, Salinas represented the neighborhood where people had the lowest parasite load infection in 2000, but in the following years it was the only area in which parasite load kept increasing (Table 1), becoming the most important epidemiological neighborhood for schistosomiasis transmission over the years.

The association of epidemiological and demographic data demonstrated that male and female were equally sampled in all parasitological surveys, but male presented a higher number of cases, prevalence, and parasitological load. Despite the decrease in the number of cases and prevalence over the years in both sexes, following the general trend of this study, male and female presented a decreasing trend on parasitological load between 2000 and 2010 and an increasing of it between 2010 and 2020. The prevalence of cases by age also presented a downward trend in univariate comparisons (2010 vs. 2000 and 2020 vs. 2010), being teenagers and young adults (11—40 years old) the most affected by the disease. Additionally, for prevalence, there is a statistically significant association between age group and year of survey when adjusted by neighborhood (Cochran-Mantel-Haenszel $M^2 = 159.3$, df = 6, p-value < 0.001), and in a post-hoc analysis, the four

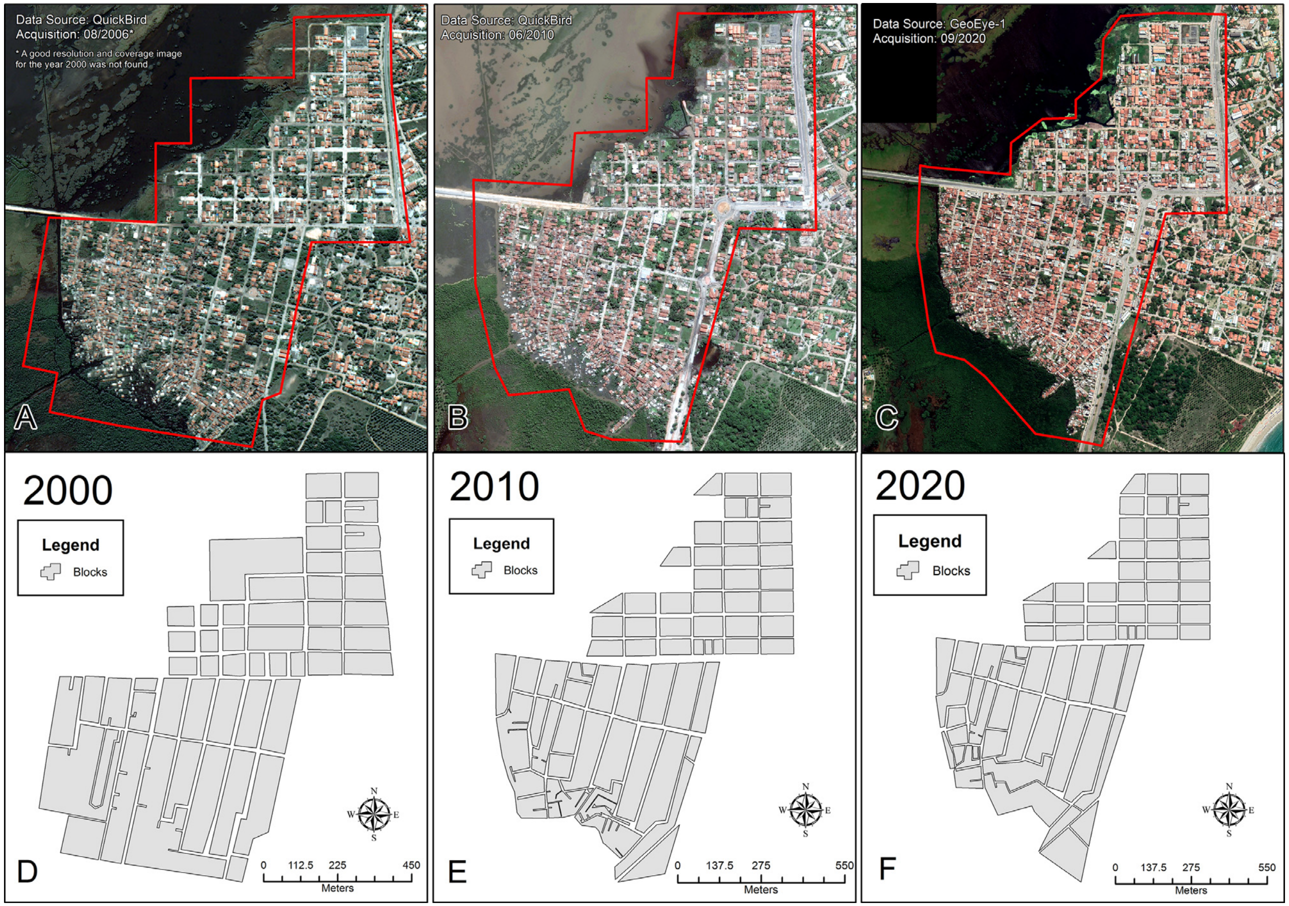
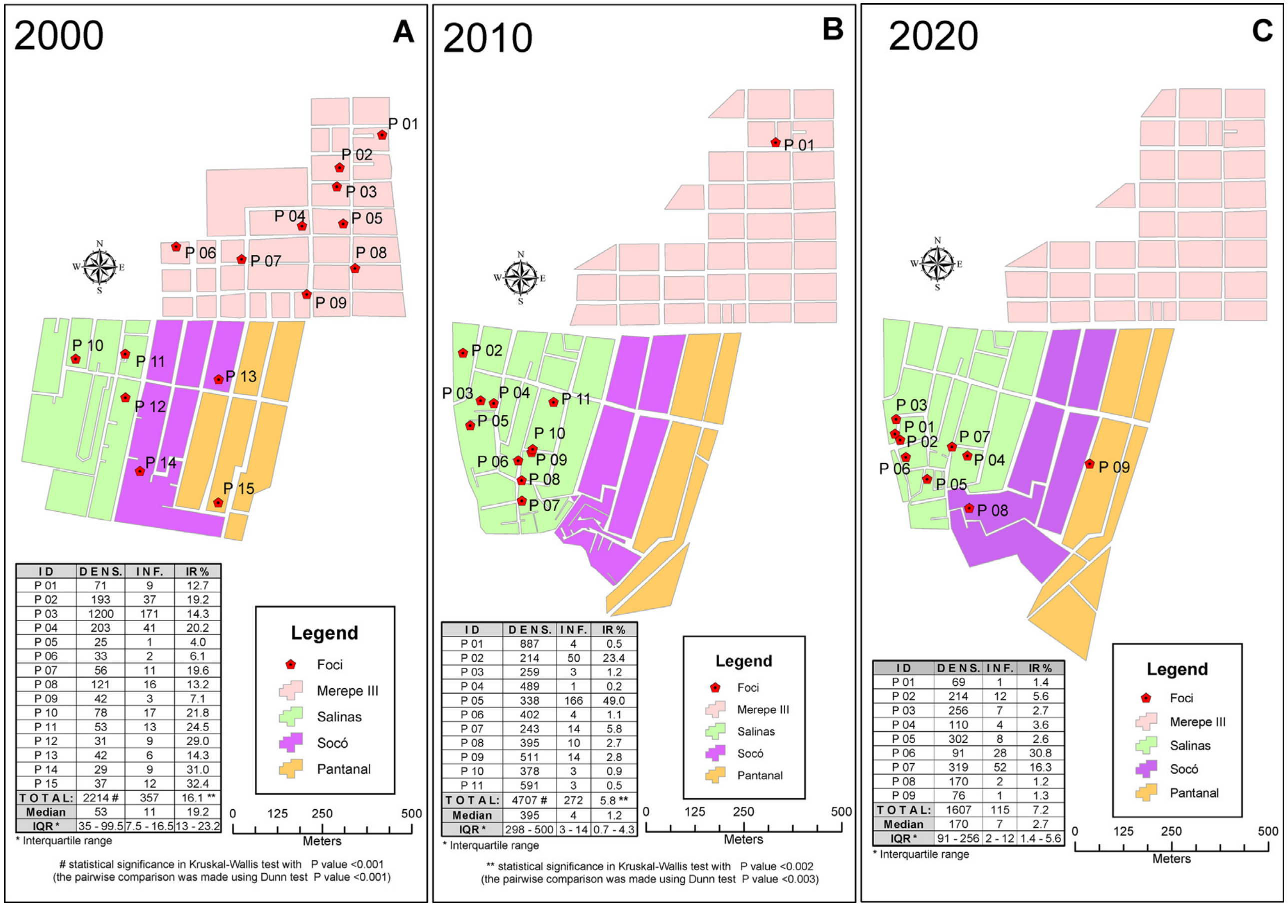


Figure 2. Representation of environmental change and design of blocks in Porto de Galinhas/Brazil, during the past two decades (2000−2010/2010−2020). In the satellite images A, B, and C, we have the study area delimited by the red polygon; one can observe the area of urbanization with largest agglomerations over the years 2006, 2010, and 2020, respectively in A, B, and C. Figure D, E, and F represent the sketch of the blocks in the study area and their changes over 2000, 2010, and 2020, respectively.



ID	DENS.	INF.	IR %
P 01	71	9	12.7
P 02	193	37	19.2
P 03	1200	171	14.3
P 04	203	41	20.2
P 05	25	1	4.0
P 06	33	2	6.1
P 07	56	11	19.6
P 08	121	16	13.2
P 09	42	3	7.1
P 10	78	17	21.8
P 11	53	13	24.5
P 12	31	9	29.0
P 13	42	6	14.3
P 14	29	9	31.0
P 15	37	12	32.4
TOTAL:	2214 #	357	16.1 **
Median	53	11	19.2
IQR *	35 - 99.5	7.5 - 16.5	13 - 23.2

* Interquartile range

\# statistical significance in Kruskal-Wallis test with P value <0.001 (the pairwise comparison was made using Dunn test P value <0.001)

ID	DENS.	INF.	IR %
P 01	887	4	0.5
P 02	214	50	23.4
P 03	259	3	1.2
P 04	489	1	0.2
P 05	338	166	49.0
P 06	402	4	1.1
P 07	243	14	5.8
P 08	395	10	2.7
P 09	511	14	2.8
P 10	378	3	0.9
P 11	591	3	0.5
TOTAL:	4707 #	272	5.8 **
Median	395	4	1.2
IQR *	298 - 500	3 - 14	0.7 - 4.3

* Interquartile range

** statistical significance in Kruskal-Wallis test with P value <0.002 (the pairwise comparison was made using Dunn test P value <0.003)

ID	DENS.	INF.	IR %
P 01	69	1	1.4
P 02	214	12	5.6
P 03	256	7	2.7
P 04	110	4	3.6
P 05	302	8	2.6
P 06	91	28	30.8
P 07	319	52	16.3
P 08	170	2	1.2
P 09	76	1	1.3
TOTAL:	1607	115	7.2
Median	170	7	2.7
IQR *	91 - 256	2 - 12	1.4 - 5.6

* Interquartile range

Figure 3. Spatial distribution of schistosomiasis transmission foci in Porto de Galinhas/Brazil, during the past two decades (2000−2010/2010−2020). The figure represents the spatial distribution of schistosomiasis transmission foci (by *Biomphalaria glabrata* snails) across the neighborhoods (Merepe III, Salinas, Socó, and Pantanal) in the study area over the years 2000 (A), 2010 (B), and 2020 (C). The lower left part of each map has a table with information on the number of snails collected (DENS.), number of infected snails (INF.), and the percentage of snail infected by *S. mansoni*/Infection Rate (IR%) for each collection site (ID).

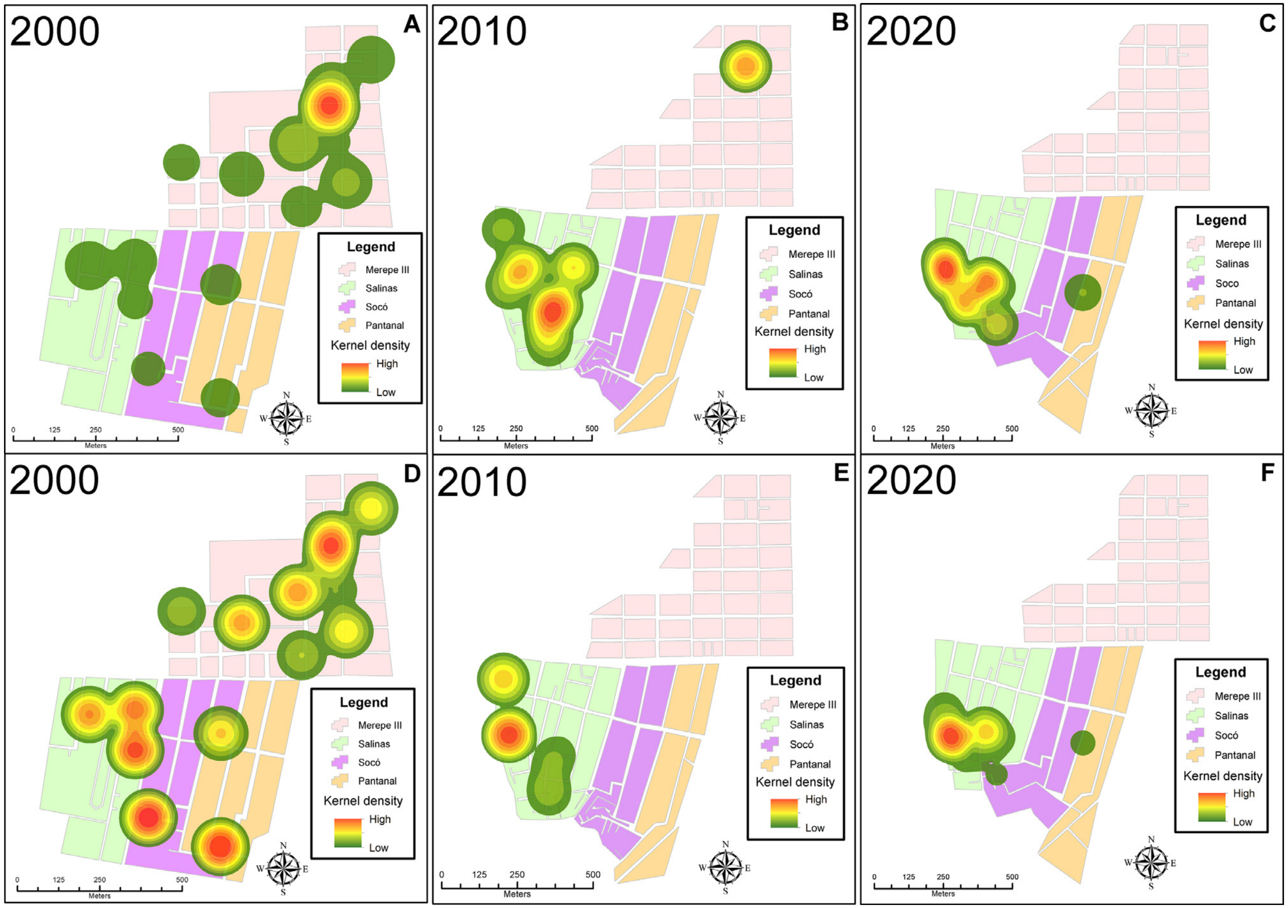


Figure 4. Kernel maps of snail density and infection rate per schistosomiasis transmission focus in Porto de Galinhas/Brazil, during the past two decades (2000−2010/2010−2020). Figure A, B, and C demonstrate the kernel density estimation based on the number of snails collected per collection point over the years 2000, 2010, and 2020, respectively. In D, E, and F, one can observe the same estimator based now on the infection rate of snails collected at each point by the same timeline.

	Sampled (n)			Schistosomiasis cases (n)			Prevalence% (CI95%)				Parasite loadMedian (IRQ) #			
	2000	**2010**	**2020**	**2000**	**2010**	**2020**	**2000**	**2010**[d]	**2020**[e]	***P* value**	**2000**	**2010**	**2020**	***P* value**
Neighborhood														
Merepe III	292	315	198	86	14	12	29·5 (24.5–34.9)	**4·4 (2.6–7.3)**	**6·1 (3.4–10.3)**	**<0.001**	60 (24–168)	48 (24–156)	36 (24–117)	0.260
Salinas	771	1263	984	169	259	109	21·9 (19.1–25.0)	20·5 (18.3–22.8)	**11·1 (9.2–13.2)**	**<0.001**	36 (24–108)	60 (24–156)	72 (24–264) [f,g]	**<0.001**
Socó	462	590	583	157	96	54	34.0 (29.8–38.4)	**16·3 (13.5–19.5)**	**9·1 (7.1–11.9)**	**<0.001**	60 (24–132)	36 (12–96) [f]	72 (30–234)[g]	**0.001**
Pantanal	487	291	263	241	40	5	49·5 (45.0–53.9	**13·7 (10.2–18.2)**	**1·9 (0.7–4.5)**	**<0.001**	96 (36–192)	36 (12–81) [f]	24 (24–24) [f]	**<0.001**
Total	**2012**	**2459**	**2028**	**653**	**409**	**179**	32·5 (30.4–34.5)	**16·6 (15.2–18.1)**	**8·8 (7.6–10.1)**	**<0.001**	60 (24–156)	36 (12–132) [f]	72 (24–192) [g]	**<0.001**
Sex														
Male	981	1169	933	370	239	114	37·7 (34.7–40.8)	**20·4 (18.2–22.8)**	**12·2 (10.2–14.4)**	**<0.001**	72 (36–180)	60 (24–180)	96 (24–252) [g]	**0.032**
Female	1031	1290	1095	283	170	65	27·4 (24.8–30.2)	**13·1 (11.4–15.1)**	**5·9 (4.6–7.5)**	**<0.001**	60 (24–132)	36 (12–96) [f]	60 (24–132) [g]	**<0.001**
Total	**2012**	**2459**	**2028**	**653**	**409**	**179**	32·5 (30.4–34.5)	**16·6 (15.2–18.1)**	**8·8 (7.6–10.1)**	**<0.001**	60 (24–156)	36 (12–132) [f]	72 (24–192) [g]	**<0.001**
Age														
0–10	540	558	410	91	44	15	16·8 (13.9–20.2)	**7·9 (5.9–10.4)**	**3·6 (2.1–6.0)**	**<0.001**	60 (24–144)	36 (12–174)	120 (60–648) [g]	**0.019**
11–20	464	415	269	220	86	39	47·4 (42.9–52.0)	**20·7 (17.1–24.9)**	**14·5 (10.7–19.2)**	**<0.001**	72 (36–168)	54 (24–198)	108 (48–228)	0.176
21–30	347	469	265	137	110	31	39·4 (34.5–44.7)	**23·4 (19.8–27.5)**	**11·7 (8.3–16.1)**	**<0.001**	64 (24–168)	48 (24–183)	72 (24–288)	0.436
31–40	296	382	378	113	79	47	38·2 (32.8–43.8)	**20·6 (16.9–25.0)**	**12·4 (9.4–16.1)**	**<0.001**	60 (24–156)	36 (12–108)	60 (24–144)	0.418
41–50	146	299	312	45	40	25	30·8 (23.9–38.7)	**13·4 (9.9–17.7)**	**8·0 (5.4–11.6)**	**<0.001**	60 (24–126)	60 (24–108)	60 (24–174)	0.753
51–60	98	178	218	25	25	11	25·5 (17.9–35.0)	14·0 (9.6–20.0)	**5·0 (2.7–8.9)**	**<0.001**	60 (42–150)	24 (12–54) [f]	36 (24–120)	**0.005**
>61	99	146	163	22	18	10	22·2 (15.1–31.4)	12·3 (7.8–18.7)	**6·1 (3.2–11.0)**	**<0.001**	54 (21–192)	30 (12–63)	24 (24–24)	0.349
Total	**1990**[a]	**2447**[a]	**2015**[a]	**653**	**402**	**178**	32·5 (30.4–34.5)	**16·4 (15.0–17.9)**	**8·8 (7.6–10.1)**	**<0.001**	60 (24–156)	36 (12–132) [f]	72 (24–192) [g]	**<0.001**
Socio-economic indices of the municipality (Ipojuca)*														
Estimated population	59.230	80.637	97.669		-			-						-
HDI[b]	0,457	0,619	-		-			-						-
Schooling 6 to 14 years	79,73%	97,30%	97,30%		-			-						-
GDP[c] *per capita* (R$)	23.281,76	112.791,21	122.169,48		-			-						-
GDP[c] (R$)	1.380.166,30	9.095.144,70	11.570.549,17		-			-						-

Table 1: **Epidemiological, demographic and social-economic index registered in Porto de Galinhas and its municipality in the last two decades (2000–2010/2010–2020).**

**Demographic information to demonstrate population growth over the years and economic development in the region. Source: IBGE – Brazilian Institute of Geography and Statistics (https://cidades.ibge.gov.br/brasil/pe/ipojuca/panorama).*

 # Interquartile Rager

[a] *Missing date related to age from 47 individuals during the three parasitological surveys.*

[b] *Human Development Index*

[c] *Gross Domestic Product*

[d] *The 2010 prevalence and 95%CI values in bold showed significant difference in relation to the year 2000 in the Chi-square test.*

[e] *The 2020 prevalence and 95%CI values in bold showed significant difference in relation to the year 2000 in the Chi-square test.*

[f] *Significant difference in relation to the year 2000 in Kruskal-wallis test (the pairwise comparison was made using Dunn test).*

[g] *Significant difference in relation to the year 2010 in Kruskal-wallis test (the pairwise comparison was made using Dunn test).*

neighborhood showed a significant association between age group and year of survey related to the prevalence reduction ($p < 0.001$). Nevertheless, there is no association between age group and year of survey when adjusted for sex (Cochran-Mantel-Haenszel $M^2 = 3.9823$, df = 2, p-value = 0.136). The maintenance of infection intensity over the years demonstrates the chronicity of the disease in the study area. Although the relationship between socio-economical indices of the municipality of the studied area and the occurrence of schistosomiasis have not been the aim of this study, it is important to notice an increase in those indices (Table 1).

A better understanding of epidemiological scenarios of schistosomiasis cases can be achieved by the spatial distribution of the cases in each studied year, since one can observe the transition of case occurrence in between the neighborhoods. Figure 5A shows that cases in 2000 occur all over the area, but, since 2010, they start to be concentrated in Salinas and Socó, rarely occurring in Merepe III (Figura 5B/C). However, it is when we run kernel analysis that the real risk areas for schistosomiasis occurrence become clear. Initially, the risk areas were concentrated in Pantanal and Socó in 2000, expanding to Salinas in 2010, and setting in this neighborhood nowadays (2020) (Figure 5D/E/F).

The same pattern of risk is observed when the population is considered to calculate the prevalence of schistosomiasis by block. In 2000, a high prevalence (> 25%) was observed all over the study area, being the most frequent registered by block, followed by medium prevalence, as it can be seen in Figure 6A. In 2010, we observed the inverse, with medium prevalence found in almost all blocks, except for four blocks located in Salinas (Figure 6B). In 2020, all three prevalence classifications are registered in Porto de Galinhas, and although Salinas continues to concentrate the largest number of blocks with high prevalence, it was the first time that low prevalence was registered in the blocks of this locality (Figure 6C).

Discussion

In this retrospective study, we try to demonstrate the impact of urbanization over schistosomiasis transmission in an area undergoing urban expansion. The whole natural history of this infectious disease in the study area represents the results of human activities on the environment, causing deep changes in ecosystems, which favored the emergence of the disease. In this population-based, cross-sectional study, we described the complete process of introduction and maintenance of the transmission in an urban area in an increasing process of expansion and modification, as it can be seen in the presented satellite images. After 20 years of monitoring, some important remarks may help to better understand the expansion of schistosomiasis to urban areas and the dynamics of urban transmission that have been observed worldwide and has become a challenge to control programs.

The natural mangrove biome, characteristic of beach areas on the Brazilian coast, was the area mostly affected by disorderly urbanization.[22] This biome is essential for the flow of oceanic waters during the regime of the seas.[43] Once this area was one of the most occupied, where precarious houses were built, water runoff during high seas was affected, facilitating the occurrence of floods during rainy periods.[19,22,25,44] These floods help to increase STF in number and extension, further exposing the population to the risk of infection, as reported in previous studies.[36,44,45] This scenario presented in Porto de Galinhas can be reproduced anywhere as a consequence of the rapid global urbanization, causing poverty and unhealthy living conditions.

As expected, the only snail vector found in the study area was *B. glabrata*. The spatial uniform distribution of STF in 2000 can be explained by the huge flood that left the location under water for weeks. After rainwater runoff, the STF were established as artificial snail breeding sites on the unpaved streets of all neighborhoods. With the advancement of the urbanization process, the neighborhood of Merepe III, which had the highest number of STF (60%) in 2000, underwent a process of urban improvements, with partial sanitation and paving of the streets, which explains the drastic reduction in the number of STF in 2010 and its absence in 2020. Such a change was expected to take place, since the paving and planned engineering for environment modification hinder the occurrence of artificial snail breeding sites; moreover, sanitation is the main strategy to reduce and eliminate environment contamination with sewage, the main source of snail infection.[22,31,44–47]

The opposite changes occurred in the neighborhood of Salinas, represented by a disorderly agglomeration of unstructured housing lacking basic sanitation. The consequence was the concentration of most STF in this neighbourhood since 2010, as this area had all the elements to maintain STF: snail breeding sites contaminated with sewage from residences of infected people.[22,35,44] Beside, Salinas is the region most affected by floods during the rainy period, suffering the effects of overflow of mangrove waters occupied by the residences. The elevation of the main road that separates Salinas from Merepe III helps to accumulate water on the streets of Salinas, and the absence of paving facilities the maintenance of snail breeding sites.[22,48] The kernel risk maps related to the malacological survey clearly shows the transition of risk areas from Merepe to Salinas, identified by the hotspots. These hotspots usually identify the most epidemiologically important STF, which is directly related to the higher chances of transmission and occurrence of cases.

The distribution of schistosomiasis cases across the years follows the same pattern of STF, and IR hotspots

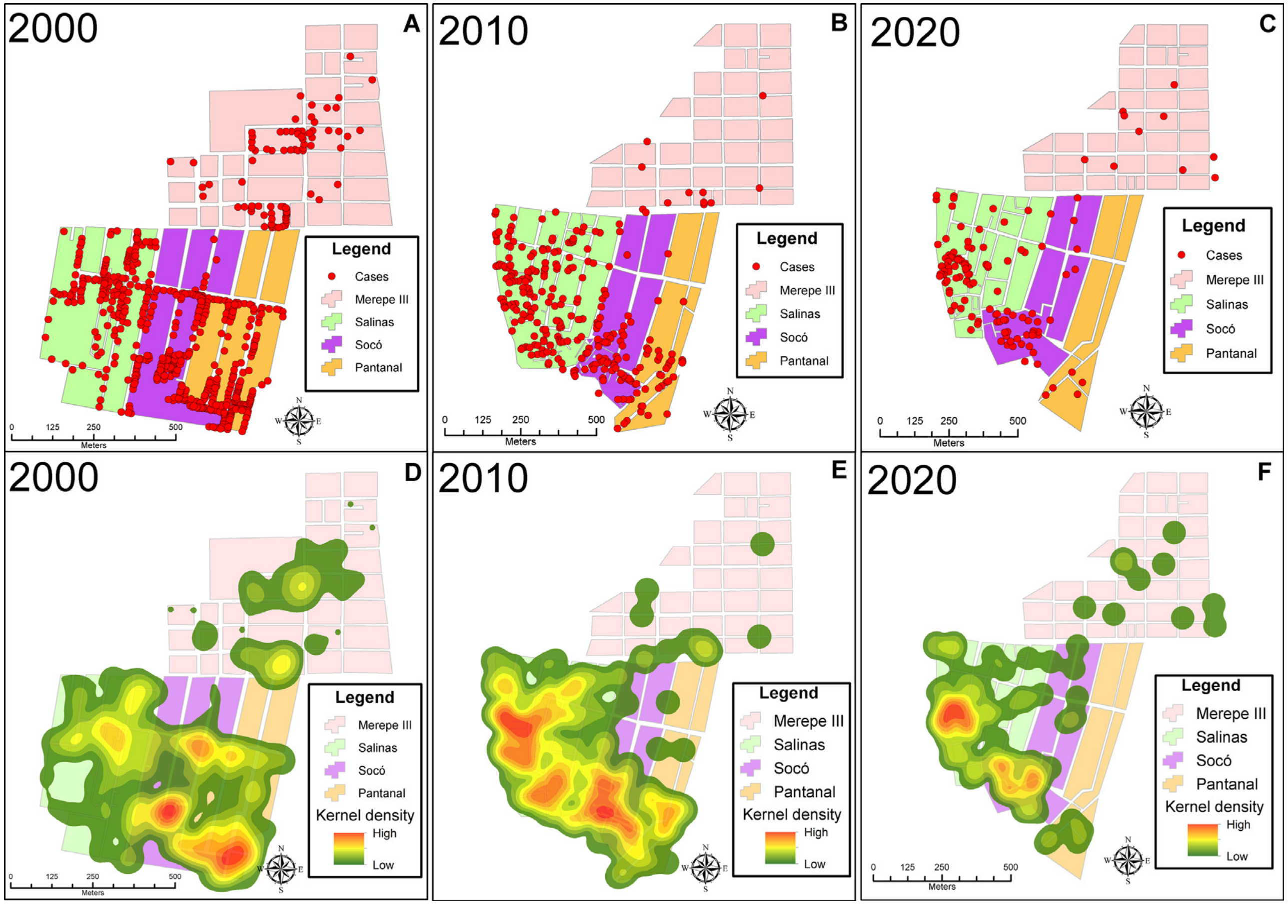


Figure 5. Spatial distribution and risk spatial analysis (kernel maps) of schistosomiasis cases in Porto de Galinhas/Brazil, during the past two decades (2000–2010/2010–2020). In this figure, one can observe in A, B, and C the punctual distribution of the diagnosed cases of schistosomiasis in the study area in 2000, 2010, and 2020, respectively; in D, E, and F present an assessment of the spatial cluster (by Kernel density) of these cases over the same years, respectively.

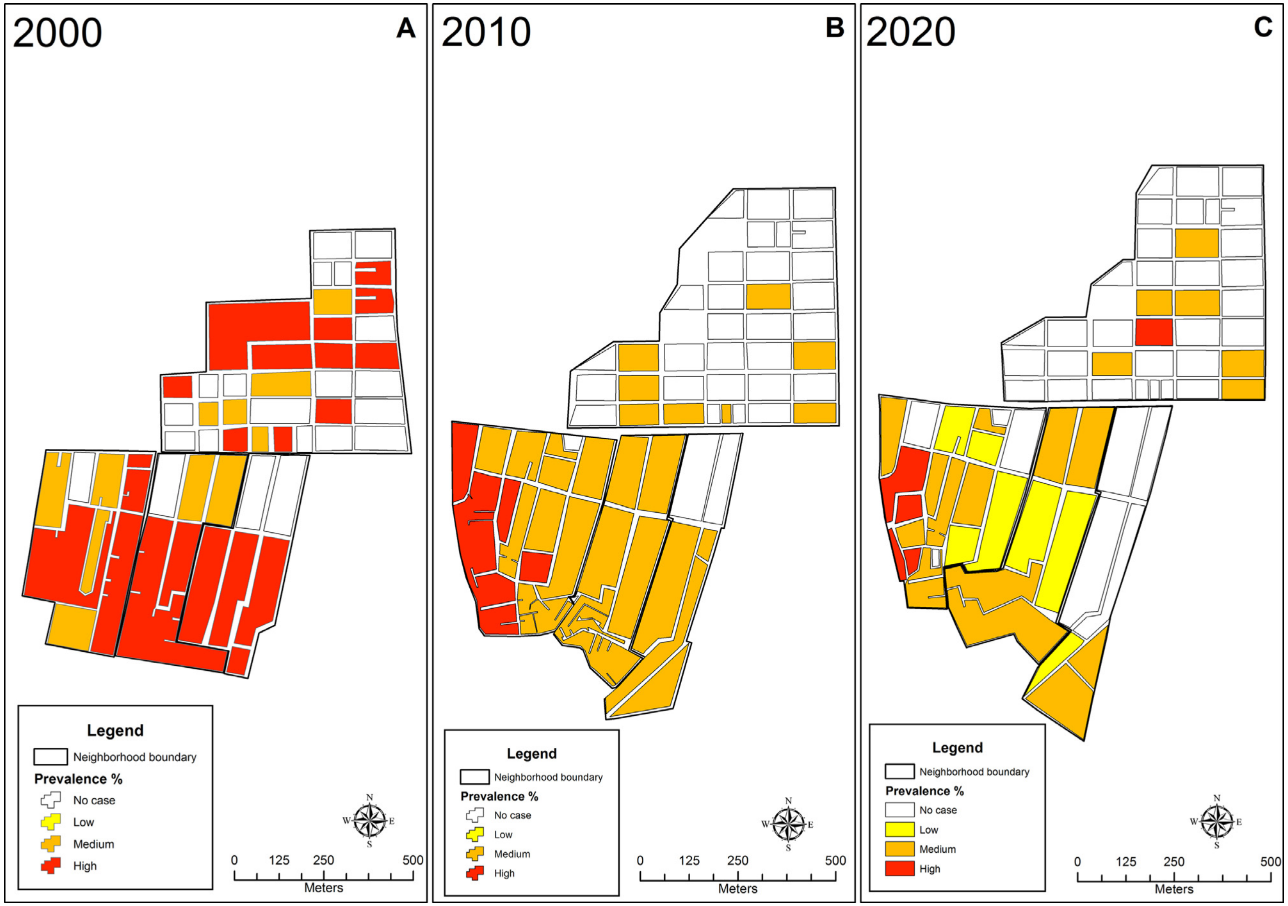


Figure 6. Prevalence of schistosomiasis cases by blocks in Porto de Galinhas/Brazil, during the past two decades (2000−2010/2010−2020). The prevalence of schistosomiasis presented by blocks (ratio of total number of positive individuals per total number of examined individuals by block, multiplied by 100) was calculated for the years 2000 (A), 2010 (B), and 2020 (C). In the figures, the neighborhoods are separated by a darker black outline where the community of Merepe III is the northernmost part, Salinas is the westernmost portion of the blocks, Pantanal is the set of blocks further east, and Socó is the neighborhood between Pantanal and Salinas.

determine the occurrence of cases, as shown the case kernel maps that identified the main hotspots in Pantanal and Socó in 2000, in Socó and Salinas in 2010, and Salinas in 2020. Noteworthy, prevalence by neighbourhood presented the same result; however, kernel maps show that the peripheral areas of these neighborhoods, limited by mangrove, are the most affected area. Nowadays, Salinas represents the most vulnerable area for schistosomiasis occurrence in Porto de Galinhas, and the continuous increase in parasite load over the study years is yet another alarming data for the local health service. Moreover, the high occurrence of cases and prevalence in teenagers and young adults is related to the fact that these individuals are the most economically active, as demonstrated in a previous study,[44] being a target population for health surveillance services.

Despite the observed improvements and epidemiological perspective of reducing the occurrence and prevalence of schistosomiasis - driven by selective treatment and MDA, as well as the reduction in the number of STF over the years, it was not possible to eliminate the transmission of the disease in the locality. Since 2010, moderate prevalence (5 < 25%) persists, and this pattern can be maintained for undetermined time. In a righly comprehensive study, Duarte H de et al., 2014, explored the schistosomiasis transmission and preventive measures using an ecological model for quantitative risk assessment for schistosomiasis. After running a mathematical stochastic model, the study found predictive scenario for 20 years is a cycle of high and low transmission of schistosomiasis in the location. It was also identified that dispersion of *S. mansoni* occurs more frequently through migration of snails transported by tidal streams during rainy months. In addition, the study revealed that drug treatment is not sufficient for eliminating the disease; and sanitation quality improvements are only useful if fully implemented.[49]

Collectively, the results presented in this study show that the dissociation of urbanization and progress culminates in an urban health problem, since cultural and social habits can be imported from rural to urban areas along with infected people from endemic areas of schistosomiasis[50] as happened in Porto de Galinhas and can be replicated worldwide. The negative implication of the rapid urbanization observed in the past decades on global health made the WHO choose 'urbanization' as its theme for the World Health Day in 2010, recognizing its importance.[51] Here we show that, in Porto de Galinhas, the impact of this type of urbanization caused an important change in the natural transmission cycle of the parasite, where people become involuntarily infected in artificial breeding sites, when walking through flooded streets, often the only way to transit through the locality.[20,22,25,36,44,45]

Although the prevalence of schistosomiasis has decreased 50% in each decade of this study, the continuous migration, refusal and contraindications to the treatment, and false-negative cases due to failure in the Kato-Katz method can be pointed as barriers to the elimination of the STF and transmission in the studied area.[49] However, it is important to point out that the increase of some socio-economic indices in the municipality of the study area, such as HDI, schooling and GDP, may have contributed to the prevalence reduction over the last 20 years. Similar results were found in sub-Saharan Africa, with a reduction in the prevalence of soil-transmitted helminths in children aged 5 −14 years from 44% in 2000 to 13% in 2018 by preventive chemotherapy and economic development.[52]

It is important to note that ecological studies have some limitation to estimate risks from aggregated data on geographical basis populational surveys. In this type of study, it is not possible to make inferences of causality at individual levels to avoid 'the ecological bias or fallacy'. In our study, despite the reduction of schistosomiasis prevalence and number of STF over the time, we cannot conclude that transmission is under control or reducing once we also found an increase in infected snails and human parasite load. The aggregated information could be hiding other variables related to individual biological, social, cultural, and economic condition that could be affecting schistosomiasis transmission. However, ecological studies are important to have an overview of the epidemiological status of the diseases within a tight relationship with the environment, such as schistosomiasis.

In conclusion, schistosomiasis control programs are facing a challenge that may be difficult to overcome, because, when transmission is established in a poor urban area, there are new variables that need to be considered: the mobility of people in these areas is more frequent; snail breeding sites and STF are more affected by climatic seasons − disappearing during drought; and reappearing during rainy period, which can also facilitate their dispersion to new areas and increase their size. As it was presented, selective and massive treatments were not enough to control transmission, giving that a small percentage of undiagnosed or untreated people may continue to spread the disease through environmental contamination. Therefore, according to our experience and literature reports, traditional strategies to control schistosomiasis should be paired with improvements in the population's living and housing conditions, and, most importantly, 100% sanitation coverage in focal areas for the transmission of the disease, as well as the supply of drinking water. This will require coordinated actions from the public health system and public administration in a continuous, long-term plan of action to control and, ultimately, eliminate shistosomiasis. It is urgent to think about how to manage urban schistosomiasis transmission worldwide, otherwise, the emergence of this NTD in new non-endemic areas will continue to happen, compromising the health of thousands of individuals, who, due to the loss of Disability-Adjusted Life Years, will indirectly compromise their families and the society.

Contributors

ECSG and CSB designed the research. ECSG, IEPS, ALCD and CSB did the research. ALCD conducted the clinical evaluation and treated the schistosomiasis cases. ECSG, WRCN and RML contributed with analytic tools. ECSG and WRCN analysed data. ECSG, WRCN and CSB wrote the paper. All authors have reviewed the original draft and verified the underlying data.

Data sharing

Data used for this analysis are available upon request to the corresponding author (elainne.gomes@fiocruz.br).

Editorial disclaimer

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Declaration of interests

All authors declare no competing interests.

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