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Spatial Distribution of Leprosy and Schistosomiasis and the Role of Coinfection in Leprosy Disease Severity in Minas Gerais, Brazil

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2016

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An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology

2019

Abstract

Spatial Distribution of Leprosy and Schistosomiasis and the Role of Coinfection in Leprosy Disease Severity in Minas Gerais, Brazil

By Nishanth Parameswaran

Background. Leprosy and schistosomiasis are co-endemic in certain areas of Brazil. It has been demonstrated that leprosy can present in its more infectious and debilitating multibacillary form if the patient concurrently has a helminth infection due to a change in immune response. We hypothesized that this association can be presented spatially and aspatially.

Methods. Aspatial logistic regression was applied to case-control data (n = 126) from a population in Minas Gerais, Brazil to estimate the association between schistosomiasis infection and leprosy infection, as well as multibacillary leprosy. The Kulldorff spatial scan statistic was used to identify clusters of infections and coinfections The Cuzick-Edwards method was used to test for heterogeneity in disease distribution. The local join count statistic was used to identify cluster cores of infections and coinfections by assessing for spatial autocorrelation.

Results. Leprosy was associated with a 4.97 (1.03, 24.09) times higher odds of schistosomiasis infection compared to non-cases. Multibacillary leprosy was associated with a 5.28 (95% CI 1.49, 18.75) times higher odds of schistosomiasis compared to paucibacillary cases. The spatial scan statistic identified schistosomiasis and coinfection clusters, while the local join count statistic identified leprosy and schistosomiasis clusters, albeit in the same general vicinity. The Cuzick-Edwards method results showed global spatial autocorrelation in leprosy cases and schistosomiasis cases. The spatial scan and local join count identified clusters of infected and coinfected individuals in the same section of the study area.

Conclusion. We successfully described aspatial and spatial associations between leprosy and schistosomiasis infection in a coendemic area in Minas Gerais, Brazil. Furthermore, we estimated the aspatial association between multibacillary leprosy and schistosomiasis infection which supports the hypothesis that schistosomiasis may be a factor in the sustained transmission of leprosy in co-endemic areas.

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Background

In 2015, there were 28,761 reported leprosy cases in Brazil, with a case detection rate of 14.07 per 100,000 inhabitants (1, 2). However, a large number of municipalities are still considered hyperendemic (in which case detection rates are > 40/100,000) (1, 2). Although leprosy is on the downturn, it is still a major public health problem in low or middle income countries and is associated with social stigma, disability, as well as loss of productivity if not treated early with multidrug therapy (3).

Leprosy, or Hansen's disease, is a long term infection characterized by initially pale patches of skin, nerve problems such as numbness or tenderness, with potential tissue loss and reabsorption of cartilage (4-6). *Mycobacterium leprae* is the primary causative organism, and there is evidence that a second organism, *Mycobacterium lepromatosis*, can be responsible for leprosy as well. Both organisms are obligate intracellular pathogens, and *M. leprae* can infect dendritic cells, Schwann cells, and macrophages (6). Leprosy is transmitted through close contact between humans, primarily through nasal droplets (7). Household contacts compared to the general population have a higher risk of contracting leprosy (7). Close contact with infected armadillos or consumption of infected armadillo meat can also lead to infection (3). Although *M. leprae* is highly infective, it has a low pathogenicity wherein ~10% of infected actually develop symptoms (2, 8). Furthermore, it is estimated that the majority of the population is resistant (9).

Clinical diagnosis of leprosy is accomplished through a combination of skin lesions and sensory disorders (6, 8, 10-13). For better determination of the clinical type of leprosy, or if the patient presents with purely neurological symptoms, skin and / or nerve biopsiesare the gold standard. This is not always possible in low resourced areas (6). Leprosy can also be characterized using the microscopic examination where bacillary index is calculated on earlobe or skin smears. There are generally three accepted classification systems. The Ridley-Jopling system combines clinical, histopathological, and bacteriological indices as correlates for the host immune response. This system splits up the clinical types into tuberculoid (IT), borderline tuberculoid (BT), borderline borderline (BT), borderline lepromatous (BL), and lepromatous (LL) (13). The World Health Organization (WHO) classification of leprosy involves counting skin lesions, where 1-5 lesions classify as paucibacillary (PB) while 6 or more classify as multibacillary (MB). The WHO classification, in comparison to the Ridley-Jopling system, corresponds to lepromatous at the far end of the MB spectrum and tuberculoid at the far end of the PB side. Finally, the Madrid system lies in between with four clinical categories: indeterminate, tuberculoid, borderline, and lepromatous (3). Contacts of multibacillary cases have a higher relative risk of developing leprosy in comparison to contacts of paucibacillary cases, due to the higher bacillary load in MB cases (7). Multibacillary cases are characterized by an immune response notable for elevated Th2 cytokines, while paucibacillary cases demonstrate a strong cell-mediated or Th1 response (4, 14).

Schistosomiasis is another neglected tropical disease (NTD). It is caused by trematodes carried by freshwater snails, and the species responsible for a large amount of disease burden in Brazil is *Schistosoma mansoni* (1, 15-17). Both leprosy and schistosomiasis are NTDs where the highest burden is often found in areas of poverty, but schistosomiasis in particular is often found in areas with poor water, hygiene, and sanitation (WASH) practices and is driven by environmental factors such as vegetation, land cover, elevation, temperature, and water availability (15, 18-22). Schistosome eggs contaminate water in which infected humans have defecated or urinated. After hatching, the parasites infect and multiply within snails in the water, and then leave the snail to enter the skin of people who enter the freshwater source (20, 22, 23). Schistosomiasis is typically diagnosed by egg counts in stool or urine samples. Immunological methods are also used, such as enzyme-linked immunosorbent assay (ELISA) (24). In Brazil, 700-800 deaths due to schistosomiasis are reported annually, and between 2 and 6 million are infected (21).

Exposure to helminth infections has been shown to raise Th2 levels, and this may be linked to increased likelihood of developing the more severe and infectious MB leprosy, due to potential immune dysregulation and suppression of cell-mediated immunity which is thought to be the primary means of controlling the *M. leprae* (14, 26-28). Diniz et al showed an association with soil-transmitted helminths and leprosy, especially multibacillary leprosy, that was accompanied by a predominant Th2 cytokine response

(29). These differing responses motivate the proposed associations between multibacillary leprosy and schistosomiasis in co-infected individuals (14, 27).

Spatial epidemiological methods are useful for defining clusters of single infections as well as coinfections, and can identify geographic features relevant to these spatial patterns (1, 2, 10, 18-23, 25-27, 30-42). In the case of leprosy and schistosomiasis which are oftentimes driven by environmental factors, data about clusters can help identify contaminated freshwater sources that are nearby. The spatial distribution of leprosy in Brazil is heterogeneous with clear areas with high disease burden in the North, Central-West, and Northeast, where approximately 17% of the country's population reside (1, 10).

Several spatial analyses have been performed to increase understanding of the spatial distribution of leprosy in Brazil, and one with both leprosy and schistosomiasis. The new case detection rates have been analyzed using various methods such as the empirical Bayesian method, spatial autocorrelation assessment, and Kernel density estimation (1, 18, 22, 37, 42). These studies have aggregated data at mesoregion, microregion, neighborhood, district, as well as municipality levels (1). The state of Pará in Brazil is hyperendemic for leprosy and has problems with lack of access to healthcare for large proportions of the population. Serological testing for leprosy and geographic information

system (GIS) techniques were used to assess the heterogeneity of the disease's distribution among schoolchildren, as well as to identify subclinical infections (2, 10, 43). There is reason to believe that there are many hidden cases showing serological signs of infection who have yet to present with leprosy symptoms, specifically anti-PGL-I, LID-I and Ag85B biomarkers (7, 11, 28). In another one of these studies, the authors mapped cases of leprosy, schistosomiasis, and visceral leishmaniasis at the neighborhood level, and conducted a stratified analysis by neighborhood population density. It was found that there was a relative risk (RR) of 6.8 of leprosy in a neighborhood with known schistosomiasis compared to a neighborhood without schistosomiasis, and this association stayed at a high value when controlling for income and population. This association did not appear to be true for leprosy and visceral leishmaniasis, which is another endemic disease in the area with similar risk factors, and is therefore in need of further study (27).

Beyond spatial distributions, cluster analyses can be used to identify areas of high and low burdens so that resources can be effectively utilized, especially in situations of scarcity. Additionally, continuous monitoring using GIS can help with assessment of intervention efficacy (10, 18, 21, 41). Lastly, it can help us better understand infection transmission, especially in the case of leprosy, that could be influenced by other infections and living conditions.

In the present study, we describe the spatial distributions of leprosy, schistosomiasis, and coinfected cases in a town located in Minas Gerais. The high prevalence of

schistosomiasis in this area of Minas Gerais coupled with the hyperendemicity and long latency period of leprosy, also highly endemic in the study region, may contribute to the ongoing reservoir of infection in the community and to a possible preponderance of MB leprosy, which could prolong the transmission cycle of these two NTDs within communities.

Methods

Study Population

The study population was comprised individuals from a small town in eastern Minas Gerais, Brazil. Minas Gerais is the fourth largest by area and second most populous state and is located in southeastern Brazil. In certain municipal areas of Minas Gerais, including the region where this town is located, the case detection for leprosy has been as high as 41/100,000 from 2010-2015, which is just above the hyperendemicity threshold of 40/100,000 (11). As of 2016, Minas Gerais has one of the highest age-adjusted Disability-Adjusted Life Year (DALY) rates due to all NTDs (433.7/100,000) among all the Brazilian states (44). The town of interest has a river in the southeast, which is a likely route of exposure to the freshwater snails, *Biomphalaria*, that carry *S. mansoni*. In Minas Gerais, the distribution of *S. mansoni* is not uniform, and high transmission areas are often found next to areas of little to no transmission or non-endemic areas (19).

Non-pregnant individuals of ages 3 and above were recruited into the study. Cases were identified by inviting community members who were known contacts of former cases to the family health center recruitment. These individuals were examined by a dermatologist with expertise in leprosy and were classified as a case of leprosy if there was evidence of skin lesions or nerve abnormalities consistent with leprosy. Skin smears were performed in all cases to document bacillary index and skin biopsies were performed when the diagnosis was in question. There were two control groups that were divided depending on their contact with known leprosy cases. Healthy controls in the community were matched

with cases by age and sex. These controls had no current or prior leprosy status and no history of undiagnosed skin or nervous disorders. Contacts were controls who had a close contact or family member enrolled in the study, but who did not have signs or symptoms of leprosy. Both groups of controls had extensive dermatologic evaluations to rule out active leprosy.

Ethical Approval

Institutional Review Board (IRB) approval was obtained from both Emory's institutional review board as well as from the local Brazilian university (Universidade Federal de Juiz de Fora, Campus Governador Valadares, Brazil). Informed written consent was obtained from the participants in the study.

Data Collection

All participants were given a basic questionnaire to determine demographic data, which included age, sex, and socioeconomic status. Blood samples were obtained, as well as skin smears or biopsies based on disease status to determine bacillary load and improve diagnosis accuracy. Clinical features of leprosy cases were recorded. Leprosy cases were categorized based on WHO as well as Madrid classification methods. Patients were given instructions as well as requisite supplies to collect their own stool samples. Three separate stool samples on three days were collected and then sent to the microbiology laboratory at Universidad Federal de Juiz de Fora for diagnosis of schistosomiasis and

other helminth infections using the Kato Katz method for egg counts (45). Due to the low sensitivity of stool microscopy for low burden infections, 6 slides (3 per sample) were examined for each participant. Global positioning system (GPS) locations of participants were obtained by study staff or the family health center nurse.

Aspatial Analysis and Logistic Regression

Statistical analysis involving logistic regression was performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

A conditional logistic regression (Model 1) was used to identify the association between schistosomiasis infection and leprosy infection while controlling for matched factors of age and sex.

$$\ln(odds\ of\ leprosy) = \beta_0 + \beta_1 Schisto + \sum_1^{42} \beta_{Mi} V_{Mi} + e$$

Where V_{Mi} denotes dummy variables for the matched individuals.

An unconditional logistic regression (Model 2) was also run, controlling for age and sex conventionally instead of through use of the matching variable.

$$\ln(odds\ of\ leprosy) = \beta_0 + \beta_1 Schisto + \beta_2 Age + \beta_3 Gender + e$$

This was to allow for comparison to the ordinal logistic regression (Model 3) controlling for age and sex, with 3 levels of outcome (0: no leprosy, 1: paucibacillary leprosy, and 2: multibacillary leprosy).

$$\ln\left(\frac{P(LeprosyType \geq g \mid Schisto, Age, Gender)}{P(LeprosyType < g \mid Schisto, Age. Gender)}\right)$$

$$= \propto_g + \beta_1 Schisto + \beta_2 Age + \beta_3 Gender + e$$

$$g = 1, 2$$

The proportional odds assumption was assessed with the Score Test, which followed a χ^2 distribution with 3 degrees of freedom. The null hypothesis of the Score test is that the assumption is met, with all resulting odds ratios being equal regardless of where the cut-point for the outcome is made.

Spatial Analysis

GPS coordinates were imported into QGIS 3.6.1, and projected to World Geographic System 1984, Universal Transverse Mercator Zone 24S (46). Coordinates for households outside the municipality of interest were considered outliers, and subsequently omitted from spatial analyses.

Spatial Scan Statistic

The presence-absence of clinical leprosy and schistosomiasis diagnoses were analyzed in SaTScan 9.6 to calculate the spatial scan statistic using a Bernoulli model (47). The Bernoulli spatial scan utilizes a roaming window that moves throughout the study area with varying sizes to detect most likely clustering of clinically diagnosed leprosy, schistosomiasis, and coinfections as compared to controls (48). High and low clusters were detected using the Log Likelihood Ratio test with the null hypothesis being that

disease risk within the window was equal to the risk outside the window (47-49). The P-value for each cluster was calculated using 999 Monte Carlo simulations (48).

Cuzick and Edwards' Statistic

ClusterSeer 2.5.2 was used to calculate Cuzick and Edwards' Statistic, for up to ten nearest neighbors for clinical leprosy and schistosomiasis (50, 51). The Cuzick and Edward's method uses a case control method to calculate a test statistic T_k by comparing the distribution of the cases to that of the controls to determine if cases are more aggregated. T_k represents the sum of the number of each case's k nearest neighbors that are also cases, so that when cases are clustered the value of T_k will increase (50).

Univariate Local Join Count

Geoda 1.12.1.161 was used to create a K-Nearest Neighbor Weights matrix (k = 4), and to perform a local join count analysis for leprosy diagnoses, schistosomiasis diagnoses, and coinfection status coded as 1 and controls coded as 0 to identify clustering of clinical cases (52). Given two neighboring patients are both cases (both equal 1), they are considered 'joined'. Positive spatial autocorrelation is detected when neighbors are primarily cases with few or no controls (52).

Results

Study Population

In total, there were 126 participants from 63 unique households, with equal numbers of cases, negative controls, and close contacts. Demographic data for the study are summarized in Table 1. Roughly half of the participants (n = 64, 50.7%) were women. The median age of all participants was 42.5 years, with the close contacts being the youngest category with a median age of 34.5 years. 13(~31%) of the 42 leprosy cases were diagnosed as paucibacillary.

Logistic Regression

Point estimates for the covariates are listed in Table 2 and odds ratios are found in Table 3. Among leprosy cases, the odds of having schistosomiasis is 6.32times higher (95% CI 1.60, 24.95) compared to negative controls and close contacts when using an unconditional logistic regression controlling for age and sex. The magnitude of this association was reduced when a conditional logistic regression was used to account for matching – where among leprosy cases, the odds of having schistosomiasis is 4.97 times higher (95% CI 1.03, 24.09) compared to negative controls and close contacts. To further investigate the association between schistosomiasis and leprosy severity, the ordinal logistic regression was performed while controlling for age and sex conventionally. The proportional odds assumption was met, with a chi square value of 0.61 and a p value of 0.89. The odds of having schistosomiasis was 5.28 times higher (95% CI 1.49, 18.75)

among multibacillary leprosy cases compared to paucibacillary cases after controlling for age and sex.

Spatial Scan Statistic

Table 4 contains the various clusters identified by the Bernoulli spatial scan. There was no significant clustering of leprosy cases when the Bernoulli spatial scan was applied. In contrast, there was 1 cluster identified for schistosomiasis cases, and 1 cluster identified for coinfected cases. These two clusters completely overlapped, and are depicted in Figure 2.

Cuzick and Edwards' Test

Cuzick and Edwards' test identified clustering of leprosy cases, schistosomiasis cases, and coinfection cases relative to the distributions of their respective non-cases. Leprosy case distribution was significantly spatially clustered at up to 6 nearest neighbors ($P = 0.03$). Schistosomiasis case distribution was also significantly spatially clustered up to 6 nearest neighbors ($P < 0.01$). For schistosomiasis cases, expected neighboring cases E[T] was much lower than observed neighboring cases T[k] for up to 10 nearest neighbors. There was spatial clustering of coinfected cases at 7 nearest neighbors and above ($P = 0.03$).

Univariate Local Join Count

The cluster cores are presented in Figure 3. The Local Join Count for leprosy cases indicates that there is one significant ($P = 0.048$) cluster. There were 2 clusters of

schistosomiasis cases where significant local spatial autocorrelation was present. There were no clusters of coinfection identified.

Discussion

Aspatial logistic regressions estimated the odds of having schistosomiasis infections among leprosy cases to be 4-6 times higher than close contacts and negative controls after controlling for age and sex. Additionally, among leprosy cases, the odds of having schistosomiasis was approximately 5 times higher among multibacillary cases compared to paucibacilllary cases. However, in all 3 models, the confidence intervals were wide and close to the null value, possibly due to the size of the study. These findings are similar to results seen in other studies. Diniz et al observed the association between intestinal helminth infection and lepromatous leprosy having an OR of 10.88 (29). Oktaria et al found more helminth positive MB leprosy cases than helminth positive PB leprosy cases (11/61 vs 0/20) (53).

The three spatial tests for clustering when taken together indicate that there is heterogeneity in the distribution of cases compared to controls for both leprosy and schistosomiasis. Furthermore, mapping the most likely clusters derived from the spatial scan statistic as well as the statistically significant clusters from the local join count statistic resulted in highlighting the northwest cluster of individuals. However, there is lack of agreement between the methods as to which disease statuses are clustered. The spatial scan statistic identified schistosomiasis and coinfection clusters, while the local join count statistic identified leprosy and schistosomiasis clusters, albeit in the same general vicinity. The Cuzick-Edwards method results showed global spatial

autocorrelation in leprosy cases and schistosomiasis cases. Clustering of these two diseases is associated with common factors. Studies in the literature have shown that leprosy case clustering is often associated with family income, sanitation, and years of schooling (41). Similarly, schistosomiasis case clustering is often associated with poor living conditions and lack of proper sanitation (21). However, this study is the first to demonstrate that there is overlap between the two diseases spatially.

The strengths of the study lie in the relatively small area of interest, where the median age and socioeconomic status were similar across the three groups, with a roughly even gender distribution. However, the small area of interest also creates a situation where the results of the analysis may not be as generalizable to other populations, since there is a greater likelihood that study participants have similar exposures, such as water sources including the river that runs through the southeast part of the town. Furthermore, this was a population who has a dual burden of leprosy and schistosomiasis and thus provides an ideal community to study. The use of the Cuzick and Edwards method was important in this analysis because of the ability to assess clustering in a population that is not evenly distributed (50). As seen in the descriptive mapping in Figure 1, the study population was concentrated in two main areas. However, due to the small study population, there were only 13 schistosomiasis cases (~10% of the population). Of those 13, 8 were leprosy cases. Of the 8 coinfections, 6 were multibacillary leprosy cases, which is 75% of the coinfected population in the study. Another limitation is the inability to assess latent infection of leprosy and low intensity infection in schistosomiasis in individuals.

A next step to study these interactions could be incorporating the use of serological markers to identify areas of increased infection and to better study leprosy cases and those at higher risk of the development of leprosy. Biomarkers such as IDRI diagnostic protein-1 (LID-1) antibodies or anti PGL-1 antibodies can identify latent infections that had not presented with symptoms (2, 10, 11, 28, 43). These methods can determine if close contacts may have latent disease. And due to the long incubation period of leprosy and potentially numerous subclinical infections, interventions can be deployed in areas with positive serological results, so that multidrug therapy can begin before MB leprosy develops and spreads to others in these communities (3, 6, 43). Additionally, due to the semi-quantitative nature of certain serological tests, these immune responses and other parameters of interest such as egg counts from the Kato-Katz method can be used as correlates for disease intensity and help tease out which covariates are responsible for the greatest changes in disease intensity.

The interplay between Th2 cytokines, immune system dysregulation, and helminth infections are hypothesized to affect the development of MB leprosy, and in this study, focus was placed on one helminth infection (14). The use of multiplex serology platforms, which can assess for immune responses to many antigens, is a potent serosurveillance tool that can incorporate additional helminths and other endemic infections of interest (54). Certain assays can be used for both dried blood spots as well as serum samples, which makes them versatile for various study designs (54). Such an assay can be used as part of an integrated serosurveillance strategy, monitoring for

helminth and leprosy infections so that multidrug therapy and other interventions can be delivered and hyperendemicity can be cleared from regions in Brazil.

In the present study, aspatial and spatial analyses were used to describe distributions of disease and assess the effect of coinfection on disease severity. A direct estimate of the association between schistosomiasis infection and leprosy infection was calculated. Moreover, the hypothesized association between schistosomiasis and MB leprosy was found in this study. These findings emphasize the need for more work towards understanding the role of helminths in the development of MB leprosy in coendemic areas. Previous studies in Brazil, Indonesia and Nepal have proposed that this association exists with other helminths (14, 29, 53). This relationship indicates that meeting leprosy reduction targets in these regions requires addressing helminth infections as well as part of a comprehensive integrated strategy.

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Figures and Figure Legends

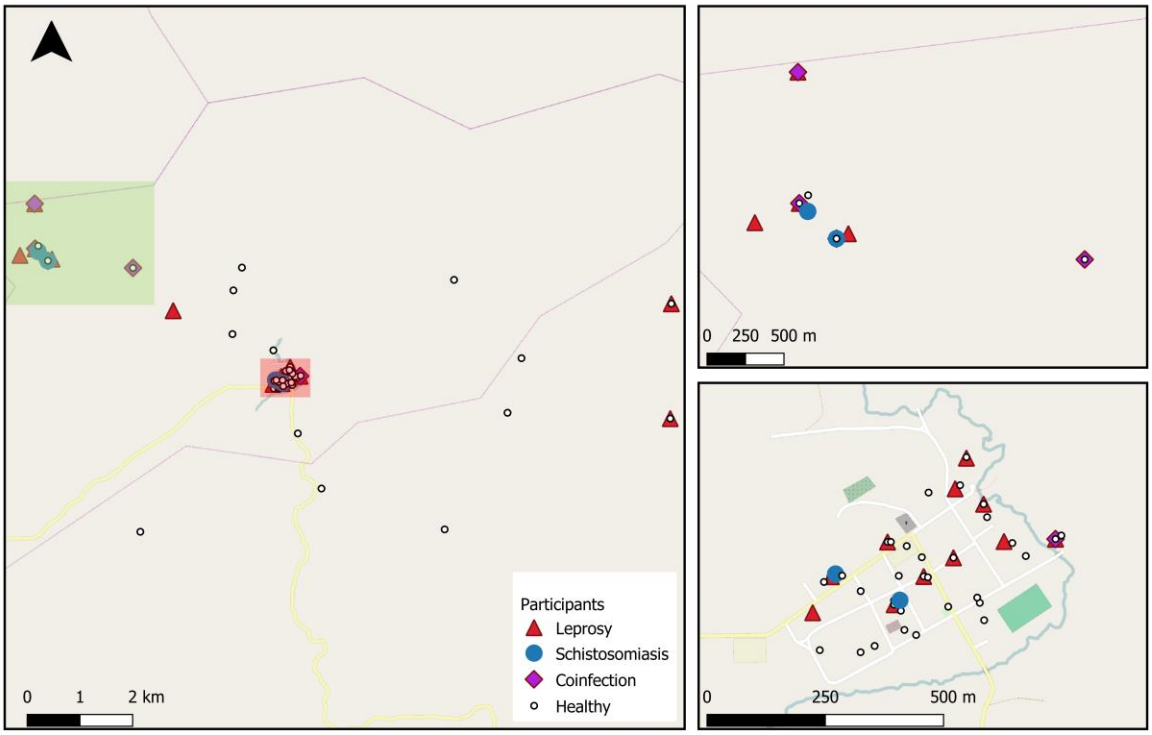

Figure 1. The distribution of study participants in Minas Gerais, Brazil. The distribution of leprosy cases, schistosomiasis cases, coinfected cases, and healthy individuals (n = 113).

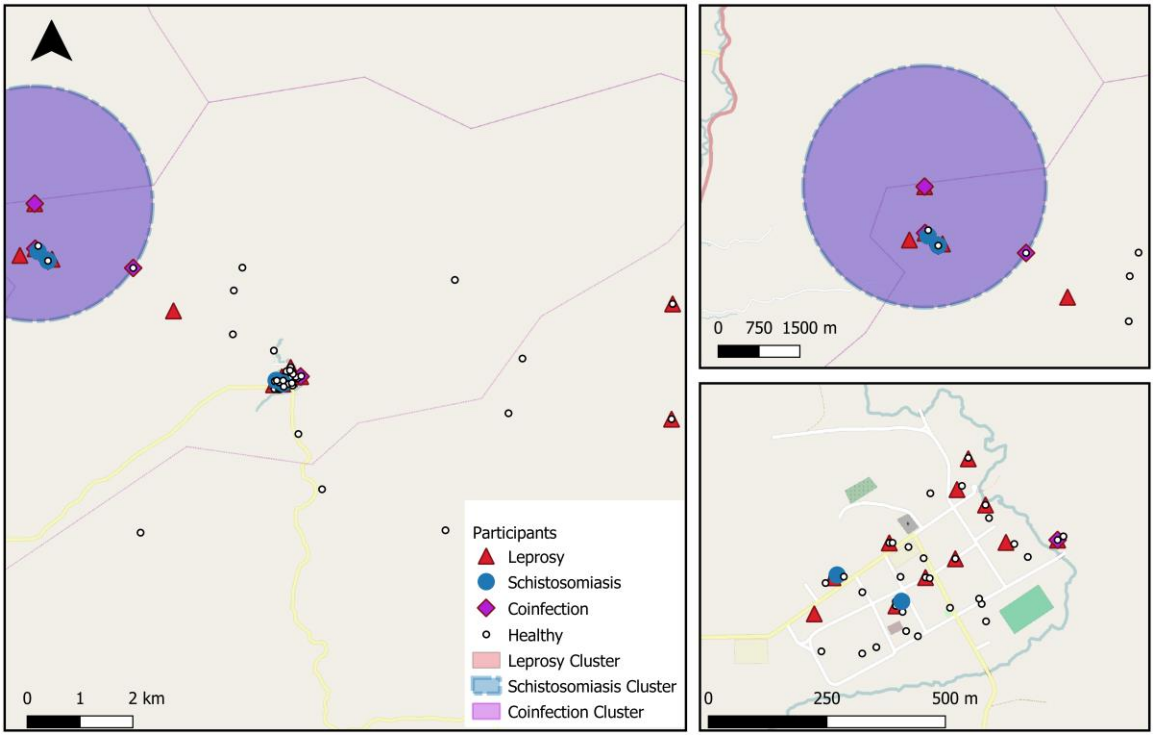

Figure 2. Bernoulli Spatial Scan Clusters of Schistosomiasis and Coinfections. Space-only cluster analysis performed by calculating Kulldorff's spatial scan statistic using SaTScan v. 9.1.1. Mapping of clusters was done in QGIS 3.6. The spatial scan identified a cluster of schistosomiasis and a cluster of coinfections which overlapped.

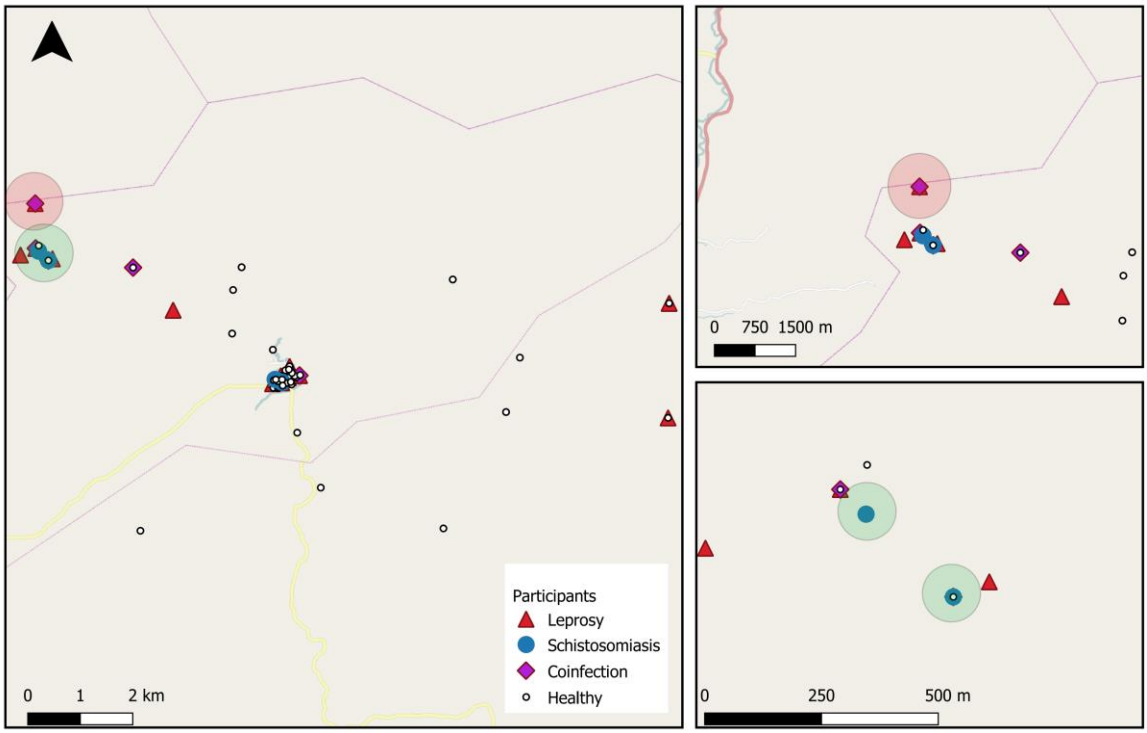

Figure 3. Local Join Count Cluster Cores. The Local Joint Count statistic tested for spatial autocorrelation among leprosy cases, schistosomiasis cases, and coinfected individuals. Statistically significant cluster cores are circled, and color coded by disease (leprosy = red, schistosomiasis = green)

Tables

Table 1. Demographic Data

	Cases	Contacts	Negative Controls	Total
Participants	42	42	42	126
Female (%)	20 (47.6)	23 (54.8)	21 (50)	64 (50.8)
Median Age (IQR)	47.0 (35.3-63.5)	34.5 (20-47.5)	47.0 (28.5-61.8)	42.5 (23.5-56)
Classification of Leprosy Cases				
Paucibacillary (%)	13 (30.9)	0	0	13
Multibacillary (%)	29 (69.1)	0	0	29
Schistosomiasis Positive	8	1	4	13
Location Data Unavailable	5	0	1	6

Table 2. Logistic Regression Parameter Estimates (β's)

		Model 1[1]	Model 2[2]	Model 3[3]
Schistosomiasis	Estimate	1.604	1.84	1.66
	P Value	0.05	0.01	0.01
Age	Estimate		0.03	0.03
	P Value		0.02	0.03
Sex	Estimate		-0.05	-0.08
	P Value		0.91	0.85
Intercept	Estimate		-2.03	
	P Value		<0.01	
Intercept 2 (MB v PB)	Estimate			-2.44
	P Value			<0.01
Intercept 1 (MB & PB v No Leprosy)	Estimate			-1.85
	P Value			<0.01

[1] Conditional Logistic Regression.

[2] Unconditional Logistic Regression.

[3] Ordinal Logistic Regression.

Table 3. Logistic Regression Odds Ratios for Schistosomiasis Infection

Model	Odds Ratio	95% CI
1 (Conditional)	4.97	1.03, 24.10
2 (Unconditional)	6.32	1.60, 24.95
3 (Ordinal)	5.28	1.49, 18.75

Table 4. Bernoulli Spatial Scan Clusters

Cluster Type	Cluster No.	Log Likelihood Ratio	P value	Observed Cases	Expected Cases	Observed/ Expected	Relative Risk
Schisto*	1	9.85	0.004	8	1.850	4.325	13.193
Schisto	2	4.65	0.445	0	3.602	0.000	0.000
Schisto	3	2.52	0.910	0	2.142	0.000	0.000
Schisto	4	2.27	0.958	0	1.947	0.000	0.000
Leprosy	1	6.71	0.059	0	5.115	0.000	0.000
Leprosy	2	4.16	0.522	12	6.319	1.899	2.390
Leprosy	3	3.05	0.862	10	5.416	1.846	2.199
Leprosy	4	2.60	0.966	0	2.106	0.000	0.000
Coinfection*	1	9.53	0.004	5	0.841	5.947	N/A
Coinfection	2	3.54	0.507	0	2.478	0.000	0.000

*statistically significant at $\alpha = 0.05$