

Screening for *Schistosoma mansoni* and *Strongyloides stercoralis* Infection Among Brazilian Immigrants in the United States

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The prevalence of schistosomiasis and strongyloidiasis among Brazilian immigrants in the United States is unknown. We performed a retrospective chart review of serologic screening of asymptomatic Brazilian immigrants during routine physicals. Of 208 eligible patients, 189 were screened: 27.7% (n = 52) had elevated *Schistosoma* antibodies and 5.8% (n = 11) had elevated *Strongyloides stercoralis* antibodies.

Keywords. immigrant health; infectious disease; schistosomiasis; screening; strongyloidiasis.

Schistosoma mansoni and *Strongyloides stercoralis* infections may persist for years, making treatment in the asymptomatic phase of infection an important intervention. It is estimated that 10% of persons infected with *S. mansoni*, the only species of *Schistosoma* found in Brazil, will develop severe complications of infection, including periportal fibrosis and hepatosplenomegaly [1]. Although rare, hyperinfection syndrome with *S. stercoralis* carries mortality rates of 87%–100% [2, 3] and may be triggered by even brief episodes of immunosuppression. Despite the importance of these infections, there are few studies that help guide clinicians when deciding whether to screen asymptomatic immigrants from endemic regions.

We conducted a retrospective chart review of a quality improvement initiative implemented at a community health center

clinic located in Somerville, Massachusetts that is part of an integrated academic, public healthcare system. Over half of the clinic's patients are Brazilian immigrants [4, 5]. The primary objective was to determine the prevalence of, and factors associated with, *Schistosoma* and *S. stercoralis* seropositivity in this population. To our knowledge, this is the first study of serologic screening for schistosomiasis or strongyloidiasis in Brazilian immigrants in the United States.

METHODS

The quality improvement initiative involved a single Portuguese-speaking internist who offered serologic screening for both *Schistosoma* and *S. stercoralis* infection to all Brazilian immigrants completing routine physical exams over a 6-month period. All patients who were not screened at the time of the qualifying office visit were contacted by telephone by a Portuguese-speaking medical assistant and offered screening. Serologic screening was performed using enzyme-linked immunosorbent assay tests detecting levels of immunoglobulin G. All testing for *Schistosoma* and *S. stercoralis* was performed at either ARUP Laboratories (Burlington, North Carolina) or at the local hospital-based clinical laboratory affiliated with the clinic.

Antigen kits for both ARUP tests were provided by SciMedX (Denville, New Jersey) and used soluble egg antigen for *Schistosoma* testing (sensitivity 97%, specificity 92%) and crude larval antigen for *S. stercoralis* testing (sensitivity 85.5%, specificity 82.6%) [6]. Antigen kits for the hospital-based tests were provided by NovaTec (Dietzenbach, Germany) and Bordier Affinity Products (Crissier, Switzerland) for *Schistosoma* testing (purified *S. mansoni* antigens, sensitivity 87%, specificity >95%) and *S. stercoralis* testing (sensitivity 88%, specificity 94%), respectively. Positive *Schistosoma* serology was defined as ≥ 0.20 optical density for the ARUP test and ≥ 11.01 index value (IV) for the hospital-based test. Positive *S. stercoralis* serology was defined as ≥ 2.11 IV for the ARUP test and ≥ 10.01 IV for the hospital-based test.

All patients were informed of their results and treated according to Centers for Disease Control guidelines. Patients with elevated *Schistosoma* antibodies were treated with 40 mg/kg oral praziquantel divided into 2 doses in 1 day [7]. Treatment was deferred if patients reported unexplained seizures or history of neurocysticercosis. Patients with elevated *S. stercoralis* antibodies were treated with 200 $\mu\text{g}/\text{kg}$ per day oral ivermectin for 2 days [8]. Repeat *S. stercoralis* serologic testing was performed at least 6 months after the completion of ivermectin therapy.

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We retrospectively reviewed the electronic medical record (EMR) of all immigrants from Brazil who had presented for complete physical exams between April 1, 2012 and September 30, 2012. We excluded patients who had prior testing or treatment for schistosomiasis or strongyloidiasis in the United States documented in the EMR. The charts of all participants were reviewed for age, sex, number of years in United States since immigration, Brazilian region of origin (North, Northeast, South, Southeast, and Center West) [9], occupation in agricultural versus indoor settings while in Brazil, and *Schistosoma* and *S. stercoralis* serology results. Brazilian regions of origin were then subclassified as high-prevalence (Southeast and Northeast) versus low-prevalence regions (North, South, Center West) for schistosomiasis [10]. No analogous regional prevalence variable was constructed for strongyloidiasis because disease burden is more evenly distributed throughout Brazil [11]. The active problem list for each participant was reviewed for the following clinical characteristics: prior human immunodeficiency virus (HIV) antibody testing results, presence of asthma, alcohol abuse or dependence, or diabetes. Complete blood counts with differential were not performed as part of this quality improvement initiative; however, charts were reviewed for prior complete blood counts with differential to determine the presence of eosinophilia (defined as >7.0% eosinophils).

We calculated the prevalence of a positive serologic test for *Schistosoma* and for *S. stercoralis* antibodies in the study population and then examined bivariate associations between demographic and clinical variables and seropositivity for *Schistosoma* and, separately, for *S. stercoralis* by calculating odds ratios and their associated 95% confidence intervals (CIs) and *P* values using the χ^2 test. Several demographic factors were associated with *Schistosoma* seropositivity at a *P* value of < .05, including sex, region, occupation, and alcohol abuse or dependence. To determine the independent association of these variables with *Schistosoma* seropositivity, we constructed a logistic regression model with seropositivity as the dependent variable and factors from bivariate analyses that were significant (*P* value < .05) as the independent variables (sex, region, occupation, and alcohol abuse or dependence). Logistic regression analysis for *S. stercoralis* seropositivity was not performed, because only a single variable, eosinophilia, was statistically significant in the bivariate analysis. We used Statistical Analysis System software (version 9.3; SAS, Cary, North Carolina) for all calculations. This study received exempt status from the institutional review board of the Cambridge Health Alliance.

RESULTS

Two hundred eight patients met our inclusion criteria. On chart review, we found that 189 of the 208 eligible patients (90.9%) had been screened. One patient was screened only for strongyloidiasis because of an order entry error. There were no

statistically significant differences between the demographic characteristics of the participants who completed screening compared with those who did not complete screening (data not shown).

The mean age of the participants who were screened was 43 years (median, 43; range, 19–81 years; standard deviation [SD], 11.7). Forty-six percent of the patients were male. The mean duration in the United States since immigration from Brazil was 10.9 years (range, 0–29 years; SD, 5.07). Seventy-four percent had immigrated from high-prevalence regions for schistosomiasis in Brazil (Southeast and Northeast). Two thirds of the participants had documentation of prior HIV testing results (all HIV test results were negative); 6.9% had asthma; 5.8% had alcohol abuse or dependence; and 3.7% had diabetes mellitus (data not shown).

Of patients screened for *Schistosoma* spp, 27.7% (52 of 188) had elevated antibodies (Table 1). Patients with elevated *Schistosoma* antibodies were more likely to be male (adjusted odds ratio [AOR] = 3.0; 95% CI, 1.3–6.7), more likely to have worked on a farm in Brazil (AOR = 10.9; 95% CI, 1.1–111.3), and likely to have had immigrated from high-prevalence regions of Brazil (Southeast and Northeast) (AOR = 17.0; 95% CI, 3.3–86.1).

Of patients screened for *S. stercoralis*, 5.8% (11 of 189) had elevated antibodies (Table 1). Patients with elevated *S. stercoralis* antibodies were 17 times more likely to have had elevated eosinophil counts (OR = 17.0; 95% CI, 4.3–68.4). No other demographic factor or clinical characteristic was associated with elevated *S. stercoralis* antibodies.

All patients (*n* = 11) with elevated *S. stercoralis* antibodies were treated, and all had repeat serologies performed 6 to 12 months after treatment. Of these 11 patients, 7 (63.6%) had normal *S. stercoralis* antibody titers when repeated, 2 (18.2%) had titers that decreased to <60% of original values, and 2 (18.2%) had persistently elevated antibody titers.

DISCUSSION

We found that more than one quarter (27.7%) of Brazilian immigrants presenting for routine physical exams had elevated *Schistosoma* antibodies. Those from the high-prevalence Southeastern region of Brazil had a seroprevalence rate of 33.6%. Approximately 6% of patients had elevated *S. stercoralis* antibodies. Serologic testing is more sensitive than stool analysis, and broad serologic testing in Brazil has not been performed; therefore, it is unknown whether our rates are significantly different from those found in Brazil.

Limitations of our study include its single location, relatively small sample size, and variability of *S. mansoni* prevalence within regions. In addition, false-positive results may occur because seropositivity can represent prior infection rather than active infection, and testing reagents may cross-react with antibodies to other parasites. However, 81.8% (9 of 11) of patients retested for *S. stercoralis* had normal titers or titers that had decreased to <60% of original levels, criterion widely accepted as indicating

Table 1. Association of Demographic and Clinical Characteristics of Patients With *Schistosoma* spp and *Strongyloides stercoralis* Antibody Status

	Elevated <i>Schistosoma</i> spp Antibodies N (%)	Normal <i>Schistosoma</i> spp Antibodies N (%)	P Value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (Total N = 188)					
<40	22 (42.3)	59 (43.4)	.89	Ref	
≥40	30 (57.7)	77 (56.6)		1.0 (0.5–1.8)	
Sex (N = 188)					
Women (N = 188)	16 (30.7)	85 (62.5)	<.0001	Ref	
Men	36 (69.2)	51 (37.5)		3.7 (1.9–7.4)	3.0 (1.3–6.7)
Duration in United States (N = 169)					
<10	19 (39.6)	38 (31.4)	.31	Ref	
≥10	29 (60.4)	83 (68.6)		0.7 (0.3–1.4)	
Prevalence of Schistosomiasis in region of residence in Brazil (N = 176)					
Low Prevalence ^a	3 (6.4)	42 (32.6)	.0004	Ref	
High Prevalence ^b	44 (93.6)	87 (67.4)		7.1 (2.1–24.1)	17.0 (3.3–86.1)
Occupation in Brazil (N = 162)					
Indoor Work	41 (89.1)	114 (98.3)	.0098	Ref	
Farm Work	5 (10.9)	2 (1.7)		7.0 (1.3–37.2)	10.9 (1.1–111.3)
Eosinophilia (N = 132) ^c					
No	25 (80.6)	93 (92.1)	.071	Ref	
Yes	6 (19.4)	8 (7.9)		2.8 (0.9–8.8)	
Elevated <i>Strongyloides stercoralis</i> antibodies (N = 188)					
No	49 (94.2)	128 (94.1)	.96	Ref	
Yes	3 (5.8)	8 (5.9)		1.0 (0.3–3.8)	
HIV testing (N = 127) ^d					
Negative	37 (100)	90 (100)	N/A		
Positive	0 (0)	0 (0)			
Asthma (N = 188)					
No	49 (94.2)	127 (93.4)	.83	Ref	
Yes	3 (5.7)	9 (6.6)		0.9 (0.2–3.3)	
Alcohol abuse or dependence (N = 188)					
No	46 (88.5)	131 (96.3)	.04	Ref	
Yes	6 (11.5)	5 (3.7)		3.4 (1.0–11.7)	3.0 (0.5–17.8)
Diabetes (N = 188)					
No	52 (100)	129 (94.8)	.095	Ref	
Yes	0 (0)	7 (5.2)		0.2 (0.009–2.9)	

	Elevated <i>S. stercoralis</i> Antibodies N (%)	Normal <i>S. stercoralis</i> Antibodies N (%)	P Value	Unadjusted OR (95% CI)
Age (total N = 189)				
<40	2 (18.2)	79 (44.4)	.088	Ref
≥40	9 (81.8)	99 (55.6)		0.3 (0.06–1.3)
Sex (N = 189)				
Women	6 (54.5)	96 (53.9)	.97	Ref
Men	5 (45.5)	82 (46.1)		1.0 (0.3–3.3)
Duration in United States (N = 170)				
<10	3 (30)	55 (34.4)	.78	Ref
≥10	7 (70)	105 (65.6)		1.2 (0.3–4.9)
Occupation in Brazil (N = 163)				
Indoor Work	7 (87.5)	149 (96.1)	.24	Ref
Farm Work	1 (12.5)	6 (3.9)		3.5 (0.4–33.6)

Table 1 continued.

	Elevated <i>S. stercoralis</i> Antibodies N (%)	Normal <i>S. stercoralis</i> Antibodies N (%)	P Value	Unadjusted OR (95% CI)
Eosinophilia (N = 133) ^c			<.0001	
No	5 (45.5)	114 (93.4)		Ref
Yes	6 (54.5)	8 (6.6)		17.0 (4.3–68.4)
Elevated <i>Schistosoma</i> spp antibodies (N = 188)			.98	
No	8 (72.7)	128 (72.3)		Ref
Yes	3 (27.3)	49 (27.6)		1.0 (0.2–3.8)
HIV testing (N = 128) ^d			N/A	
Positive	0 (0)	0 (0)		
Negative	8 (100)	120 (100)		
Asthma (N = 189)			.13	
No	9 (81.8)	167 (93.8)		Ref
Yes	2 (18.2)	11 (6.2)		3.4 (0.6–17.5)
Alcohol abuse or dependence (N = 189)			.63	
No	10 (90.9)	168 (94.4)		Ref
Yes	1 (9.1)	10 (5.6)		1.7 (0.2–14.5)
Diabetes (N = 189)			.33	
No	10 (90.9)	172 (96.6)		Ref
Yes	1 (9.1)	6 (3.4)		2.9 (0.3–26.2)

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; N/A, not applicable; OR, odds ratio; Ref, reference.

^a South, North, Center West Regions.

^b Southeast, Northeast Regions.

^c >7.0% eosinophils.

cure [12–14]. This result provides support for the hypothesis that these patients had active infection before treatment.

CONCLUSIONS

If generalizable, our results raise the possibility of a potentially large reservoir of untreated schistosomiasis and strongyloidiasis infection among the hundreds of thousands of Brazilian immigrants as well as immigrants from other endemic countries living in the United States. Our study highlights the need for future research to determine the rate at which positive serologic results in immigrants represent active infections. Determining the optimal approach to screening for these conditions will require confirmation of our findings in larger and more representative patient populations. We would not yet recommend screening for schistosomiasis in Brazilian immigrants until future studies determine the true-positive rate of serologic screening. For strongyloidiasis, we would recommend targeted screening for immunosuppressed Brazilian immigrants and those at-risk for future immunosuppression.

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