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

Citation
Rapoport, Alison B., Danny McCormick, and Pieter A. Cohen. 2015. “Screening for Schistosoma mansoni and Strongyloides stercoralis Infection Among Brazilian Immigrants in the United States.” Open Forum Infectious Diseases 2 (1): ofv003. doi:10.1093/ofid/ofv003. http://dx.doi.org/10.1093/ofid/ofv003.

Published Version
doi:10.1093/ofid/ofv003

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:17295537

Terms of Use
This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

Share Your Story
The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

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

Alison B. Rapoport,1,2 Danny McCormick,2,3 and Pieter A. Cohen2,3

1Department of Infectious Disease, Beth Israel Deaconess Medical Center, 2Harvard Medical School, Boston, and 3Department of Medicine, Cambridge Health Alliance, Massachusetts

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 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 µg/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.
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 $\chi^2$ 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 *Schistosoma* spp Antibodies | Normal *Schistosoma* spp Antibodies | PValue | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|--------------------------------|---------------------------------------|-------------------------------------|--------|------------------------|---------------------|
| **Age (Total N = 188)**        |                                       |                                     | .89    |                        |                     |
| <40                            | 22 (42.3)                             | 59 (43.4)                           | Ref    |                        |                     |
| ≥40                            | 30 (57.7)                             | 77 (56.6)                           | 1.0 (0.5–1.8) |                     |
| **Sex (N = 188)**              |                                       |                                     | <.0001 |                        |                     |
| Women                          | 16 (30.7)                             | 85 (62.5)                           | 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)** |                                 |                                     | .31    |                        |                     |
| <10                            | 19 (39.6)                             | 38 (31.4)                           | 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)** |                                 |                                     | .0004  |                        |                     |
| Low Prevalence                 | 3 (6.4)                               | 42 (32.6)                           | Ref    |                        |                     |
| High Prevalence                | 44 (93.6)                             | 87 (67.4)                           | 7.1 (2.1–24.1) | 17.0 (3.3–86.1) |
| **Occupation in Brazil (N = 162)** |                                 |                                     | .0098  |                        |                     |
| Indoor Work                    | 41 (89.1)                             | 114 (98.3)                          | Ref    |                        |                     |
| Farm Work                      | 5 (10.9)                              | 2 (1.7)                             | 7.0 (1.3–37.2) | 10.9 (1.1–111.3) |
| **Eosinophilia (N = 132)**     |                                       |                                     | .071   |                        |                     |
| No                             | 25 (80.6)                             | 93 (92.1)                           | Ref    |                        |                     |
| Yes                            | 6 (19.4)                              | 8 (7.9)                             | 2.8 (0.9–8.9) |                     |
| **Elevated *S. stercoralis* antibodies (N = 188)** |                                 |                                     | .96    |                        |                     |
| No                             | 49 (94.2)                             | 128 (94.1)                          | Ref    |                        |                     |
| Yes                            | 3 (5.8)                               | 8 (5.9)                             | 1.0 (0.3–3.8) |                     |
| **HIV testing (N = 127)**      |                                       |                                     | N/A    |                        |                     |
| Negative                       | 37 (100)                              | 90 (100)                            | Ref    |                        |                     |
| Positive                       | 0 (0)                                 | 0 (0)                               |        |                        |                     |
| **Asthma (N = 188)**           |                                       |                                     | .83    |                        |                     |
| No                             | 49 (94.2)                             | 127 (93.4)                          | Ref    |                        |                     |
| Yes                            | 3 (5.7)                               | 9 (6.6)                             | 0.9 (0.2–3.3) |                     |
| **Alcohol abuse or dependence (N = 188)** |                                 |                                     | .04    |                        |                     |
| No                             | 46 (88.5)                             | 131 (96.3)                          | Ref    |                        |                     |
| Yes                            | 6 (11.5)                              | 5 (3.7)                             | 3.4 (1.0–11.7) | 3.0 (0.5–17.8) |
| **Diabetes (N = 188)**         |                                       |                                     | .095   |                        |                     |
| No                             | 52 (100)                              | 129 (94.8)                          | Ref    |                        |                     |
| Yes                            | 0 (0)                                 | 7 (5.2)                             | 0.2 (0.009–2.9) |                     |

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

Acknowledgments

We acknowledge Katio Depina for assistance in patient outreach, Dr. Michael C. Payne, who first brought to our attention several cases of active schistosomiasis in Brazilian immigrants, Dr. Rebecca Osgood for assistance and expertise in clinical laboratory sciences, Sarah Messmer for assistance in the initial data analysis, and Dr. Marc Roger Couturier for assistance outlining the testing characteristics for the ARUP Laboratories assays.

References

1. Roca C, Balanzo X, Gascon J, et al. Comparative clinico-epidemiologic study of Schistosoma mansoni infections in travellers and immigrants in Spain. Eur J Clin Microbiol Infect Dis 2002; 21:219–23.
2. Croker C, Reporter R, Redelings M, et al. Strongyloidiasis-related deaths in the United States, 1991–2006. Am J Trop Med Hyg 2010; 83:422–6.
3. Mejia R, Nutman TB. Screening, prevention and treatment of hyperinfection syndrome and disseminated infections by Strongyloides stercoralis. Curr Opin Infect Dis 2012; 25:458–63.
4. Cohen PA, Benner C, McCormick D. Use of a pharmaceutically adulterated dietary supplement, Pai You Guo, among Brazilian-born women in the United States. J Gen Intern Med 2012; 27:51–6.
5. Cohen PA, McCormick D, Casey C, et al. Imported compounded diet pill use among Brazilian women immigrants in the United States. J Immigr Minor Health 2009; 11:229–36.
6. Anderson NW, Klein DM, Dornink SM, et al. Comparison of three immunossays for detection of antibodies to Strongyloides stercoralis. Clin Vaccine Immunol 2014; 21:732–6.
7. Centers for Disease Control and Prevention. Schistosomiasis: Resources for Health Professionals. Available at: http://www.cdc.gov/parasites/schistosomiasis/health_professionals. Accessed 5 May 2014.
8. Centers for Disease Control and Prevention. Strongyloides: Resources for Health Professionals. Available at: http://www.cdc.gov/parasites/strongyloides/health_professionals/. Accessed 5 May 2014.
9. Brazilian Institute of Geography and Statistics. Geography. Division into Regions. Available at: http://www.ibge.gov.br/english/geociencias/geografia/default_div_int.shtm. Accessed 14 December 2014.

10. Amaral RS, Tauil PL, Lima DD, et al. An analysis of the impact of the Schistosomiasis Control Programme in Brazil. Mem Inst Oswaldo Cruz 2006; 101(Suppl 1):79–85.

11. Paula FM, Costa-Cruz JM. Epidemiological aspects of strongyloidiasis in Brazil. Parasitology 2011; 138:1331–40.

12. Biggs BA, Caruana S, Mibrshahi S, et al. Short Report: management of chronic strongyloidiasis in immigrants and refugees: is serologic testing useful? Am J Trop Med Hyg 2009; 80:788–91.

13. Kobayashi J, Sato Y, Toma H, et al. Application of enzyme immunoassay for postchemotherapy evaluation of human strongyloidiasis. Diagn Microbiol Infect Dis 1994; 18:19–23.

14. Loutfy MR, Wilson M, Keystone JS, et al. Serology and eosinophil count in the diagnosis and management of strongyloidiasis in a non-endemic area. Am J Trop Med 2002; 66:749–52.