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Mapping the Prevalence of *Strongyloides stercoralis* Infection in Ecuador: A Serosurvey

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Abstract. Data on the prevalence of strongyloidiasis in Ecuador are patchy. The aim of this study was to document the presence of *Strongyloides stercoralis* infection in rural communities of different provinces of Ecuador. We tested 1,418 serum samples stored at the biobank of the Central University of Ecuador, Quito, with an ELISA test for *Strongyloides*. The samples had been collected in eight different provinces of Ecuador. Two hundred ninety-four samples (20.7%) were positive, and Jipijapa, Manabí Province, was the site with the largest proportion of positive samples (66.7%). Further surveys aimed at estimating the prevalence of the infection should be carried out in areas where the infection seems highly prevalent, and ad hoc control measures should be adopted.

Strongyloidiasis is a soil-transmitted helminthiasis (STH) caused by *Strongyloides stercoralis*, an intestinal nematode widely distributed in the tropics and subtropics.[1] According to recent estimates, the number of infected people could exceed 300 million worldwide.[2] The infection is acquired by skin penetration of the infective larvae living in the soil, and individuals can remain infected for several years (presumably lifelong) if left untreated. The female parasite settles in the intestine, where it lays eggs. The newborn larvae develop into the infective stage when still in the bowel, leading to a cycle of autoinfection and, consequently, to the chronic carrier state.[3]

The burden of morbidity in affected populations is not well defined because studies focusing on this aspect are scant. Nevertheless, a systematic review found that strongyloidiasis can cause urticaria in more than a quarter of the infected individuals in endemic areas.[4] Furthermore, immunocompromised individuals can experience a sudden increase in the parasitic load because of the acceleration of the autoinfection cycle, potentially causing the so-called disseminated strongyloidiasis, that is, extensive invasion of virtually all organs. This very severe complication, usually occurs when the balance between the host and the parasite, maintained by immune mechanisms in an immunocompetent host, is altered because of several risk factors, among which are malignant hematological diseases (especially lymphoma), immunosuppressive therapy (mainly prednisone), organ transplants, and infection by the human T-cell lymphotropic virus (HTLV-1).[3]

Direct smear of feces and Kato-Katz, techniques that are commonly used in prevalence studies carried out in the field, have an exceedingly low sensitivity for *S. stercoralis*.[5] This is the main reason why the prevalence of this parasitic disease has always been underestimated. The Baermann technique and the Koga agar culture have higher sensitivity, although not significantly higher.[5] Moreover, the complexity of these techniques hampers their use for a rapid assessment of prevalence of strongyloidiasis, although their role is important for individual diagnosis (in particular in immunocompromised patients[3]). Conversely, serology is highly sensitive and easy to use in the field, particularly through the collection of blood samples on filter paper.[6] Although its specificity is lower than stool-based tests, a diagnostic study showed that specific cutoff levels can define "proven infection."[7] Moreover, the higher the prevalence in a population, the better the positive predictive value of the serological tests, making their results reliable in a highly endemic setting.[7] Serology is also a suitable tool for posttreatment monitoring, as the titers tend to decrease over time till seroreversion.[8,9] This dynamic of antibody response has also been observed in an observational study carried out in a high-transmission setting.[10]

In Ecuador, there are few data documenting the situation of STH, and particularly of strongyloidiasis.[11–15] A study carried out in 1997 in schoolchildren aged 5 to 14 years from the community of Borbón, Esmeraldas,[15] showed that at least 31% of the children tested were infected with *S. stercoralis*, which is a worrisome figure considering the possible life-threatening complications that have been mentioned. Indeed, in the whole country, there are many areas with climatic and environmental conditions that might favor the presence of the parasite.

The aim of this study was to document the presence of *S. stercoralis* infection in rural communities of different provinces of Ecuador.

This was a cross-sectional study conducted on sera previously collected and available in the serum biobank of the laboratory of the Center of Biomedicine of the Central University of Ecuador, Quito, Ecuador. The biological samples were collected in different provinces of the country, in the context of investigations carried out by the Central University of Ecuador, some of them in collaboration with the Center for Community Epidemiology and Tropical Medicine of Esmeraldas. A brief description of the populations and of the study sites is reported in Table 1. Overall, the samples were collected from 2015 to 2018. The inclusion criterion for samples was all serum samples available in the biobank, belonging to individuals who had given informed consent to the donation of their biological samples for future research purpose. The exclusion criterion was sera belonging to individuals who denied consent. For each patient, information about age, gender, and province of origin was collected in an Excel database, in a strictly anonymous form.

The samples were tested with an immunoenzymatic (ELISA) test for quantitative analysis of *Strongyloides ratti* IgG antibodies

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TABLE 1
Characteristics of the study sites and population

Population	Site	Main characteristics
Entire community	Jipijapa	Coastal Ecuador; broadleaf forest; economy based on cultivation of corn, coffee, and tagua nuts; lack of purified water
	Chiguilpe and Peripa	Indigenous community (Tsachila); area of tropical climate, with varied access to clean water; most workers are farmers/laborers
	Guapcas	Andean rural community; the altitude of the site is between 2,800 and 3,520 m above sea level; agriculture and livestock are main economic activities
	19 de Marzo	Rural community, in equatorial zone; residents are mostly people coming from provinces of Chagas-endemic areas (Manabì and Loja)
	San Antonio de Las Aradas	Andean rural community; economy based on cultivation of coffee; access to purified water
	Awa communities of Esmeraldas Province	Indigenous communities living in rural dispersed areas
	Awa communties of Carchi Province	Indigenous communities; rural communities in the subtropical zone
Schoolchildren	Guayllabamba	Andean area, at 2,142 m above sea level
	Uyumbicho	Andean area, at 2,627 m above sea level
	Cañaribamba	Andean area, suburbs of Cuenca

in serum (*Strongyloides ratti*, Bordier Affinity Products, SA, Crissier, Switzerland. The kits were kindly donated by the manufacturer for this study). This test has previously demonstrated a sensitivity of 90.7% (95% CI: 83.8–95.1) and specificity ranging from 89 (95% CI: 85.1–92.4) to 94.05% (95% CI: 91.2–96.9).[7] For the study purpose, to be able to compare the results from different runs, the results of the ELISA are reported as a normalized optical density (nOD) value, that is, the ratio between the OD of the sample and that of the weak positive control. A test was positive when nOD ≥ 1.

The sample size was based on a convenience and retrospective sampling, the samples having been collected previously and not for the purpose of this study. The protocol received clearance from the Ethics Committee of the Central University of Ecuador on January 16, 2019 (protocol number 038-CE-UCE-2019). Data quality check was performed before

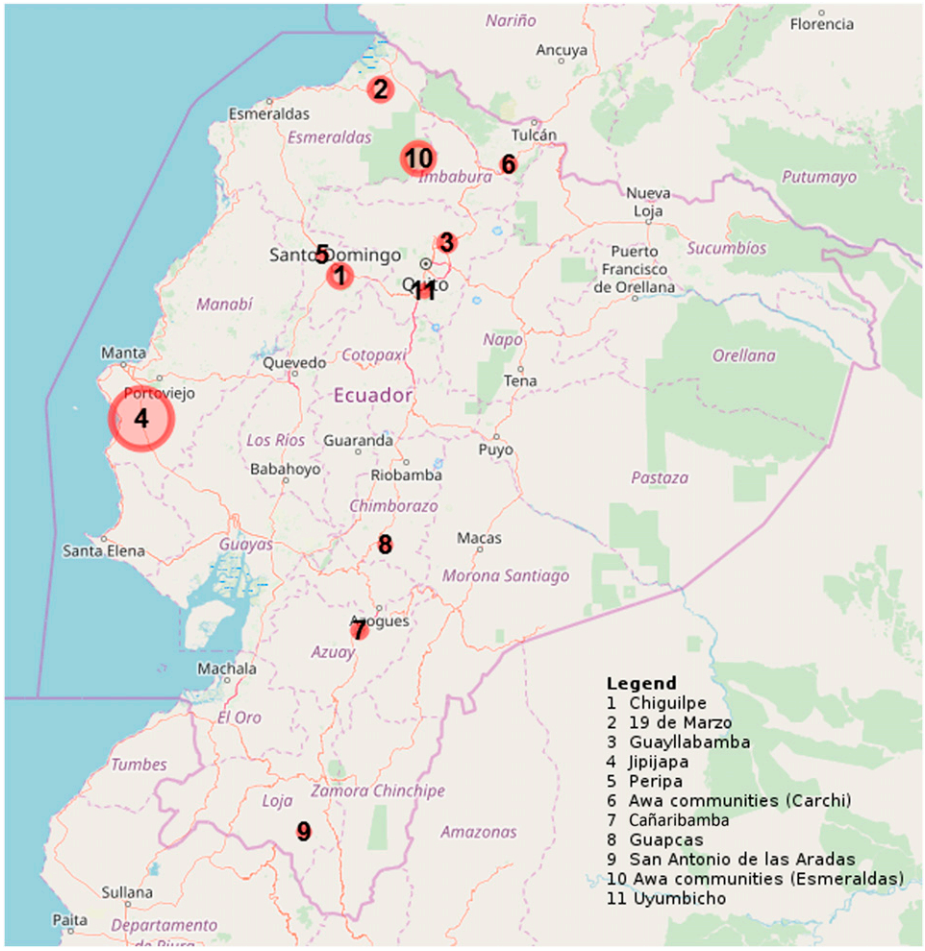

FIGURE 1. Map showing the proportion of positive samples in each study site. This figure appears in color at www.ajtmh.org.

TABLE 2
Geographical distribution of samples in relation to the general population of the area of origin

Site	Province	Population of the study site†	Screened subjects, *n* (% of population)	Positive for *Strongyloides*, *n* (% of screened subjects)
Jipijapa	Manabí	180	24 (13.3)	16 (66.7)
Guapcas	Chimborazo	280	126 (45.0)	11 (8.7)
Guayllabamba†	Pichincha	995	76 (7.6)	13 (17.1)
Uyumbicho†	Pichincha	1,867	92 (4.9)	8 (8.7)
Cañaribamba†	Azuay	702	97 (13.8)	13 (13.4)
Chiguilpe	Santo Domingo de los Tsáchilas	299	26 (8.7)	6 (23.1)
Peripa	Santo Domingo de los Tsáchilas	120	18 (15.0)	1 (5.6)
Awa communities of Esmeraldas Province	Esmeraldas	1,764	506 (28.7)	170 (33.6)
19 de Marzo	Esmeraldas	375	75 (20.0)	17 (22.7)
Awa communities of Carchi Province	Carchi	555	112 (22.9)	16 (14.3)
San Antonio de Las Aradas	Loja	1,263	266 (21.1)	23 (8.6)

* Sources: 1) National Statistical Office and Census, INEC (http://www.ecuadorencifras.gob.ec/estadisticas), World Population Review (http://worldpopulationreview.com/countries/ecuador-population/), and province official websites (Accessed May 2019). 2) https://www.ubica.ec/info/UYUMBICHO. 3) https://www.infoescuelas.com/ecuador/azuay/unidad-educativa-zoila-aurora-palacios-en-cuenca/. 4) https://www.ubica.ec/info/LUIS-PASTEUR.
† School-based survey. For schools, the "population of the study site" is the total number of schoolchildren attending the school.

analysis. Contingence tables and parameter estimations were performed using Stata/SE14. A map was generated using Google API[16] and R4 software.[17]

The study population comprised 1,418 serum samples, each one from a single individual. The samples covered eight provinces. Data regarding gender and age were available for 1,403 and 1,406 individuals, respectively. The median age of the donors was 17 years (IQR 7.4–42.1), and females represented 54.3% of the study population. Specific data on the ethnic group of the individuals tested are not available, although the different groups often reside in definite areas; hence, the information can be partly deduced (but not reported here as we admit it might not be completely accurate). Overall, 294 of 1,418 samples tested (20.7%) were ELISA positive. Distribution of the positive results in relation to the geographical area and to the size of the target population is shown in Figure 1 and Table 2. In particular, Jipijapa, Manabí Province, was the site with the largest proportion of positive samples (66.7%), followed by the Awa communities in Esmeraldas and in Carchi provinces (33.6% and 30.1%, respectively). On the other hand, Peripa, Santo Domingo de los Tsáchilas Province, was the area with the smallest proportion (5.6%) of positive samples. Adults (aged ≥ 18 years) were more frequently positive to *Strongyloides* serology (184 of 684, 26.9% of individuals of that age-group) than children (110 of 734, 14.9%) ($P < 0.0001$).

Individuals positive to *Strongyloides* serology were found in all examined districts, confirming that the infection is an issue that should be seriously considered in the country. The larger proportion of infected individuals are adults (aged ≥ 18 years), probably because of a cumulative exposure over time and of the autoinfection cycle, which does not permit the clearance of the infection without a specific treatment. The lowest proportion was found in a province (Santo Domingo de los Tsáchilas) where mass distribution of ivermectin was delivered for years (up to 2009) in the context of the WHO program for the elimination of onchocercosis; this adds evidence to previous studies demonstrating the usefulness of ivermectin for the community control of strongyloidiasis.[12] Further surveys should be carried out in areas where the infection seems highly prevalent, and ad hoc control measures for this neglected infection should be adopted.

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