Epidemiol. Infect. (2015), **143**, 452–460. © Cambridge University Press 2014
doi:10.1017/S0950268814001563

REVIEW ARTICLE
Prevalence of strongyloidiasis in Latin America: a systematic review of the literature

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Received 20 February 2014; Final revision 20 May 2014; Accepted 30 May 2014; first published online 3 July 2014

SUMMARY

Strongyloides stercoralis is rarely recognized as a major public health issue, probably because its burden is largely underestimated. We reviewed the literature (both PubMed and 'grey' literature) about the prevalence of strongyloidiasis in Latin America, an area of presumable high endemicity. There were finally 88 papers involved in the analysis, covering the period between 1981 and 2011. Studies were heterogeneous in several aspects, such as the populations screened and the diagnostic methods used. Most of the studies relied on direct coproparasitological examination, which has low sensitivity for the detection of *S. stercoralis* larvae. The following countries presented areas of high prevalence (>20%): Argentina, Ecuador, Venezuela, Peru and Brazil. Globally, for most of the included countries it was not possible to define reliable data because of paucity and/or inadequacy of studies. *S. stercoralis* requires specific diagnostic methods for its detection; therefore, surveys should be specifically designed in order to avoid underestimation of the infection.

Key words: Latin America, prevalence, review, *Strongyloides stercoralis*.

INTRODUCTION

Worldwide prevalence of strongyloidiasis has long been estimated to be between 30 and 100 million people [1]; however, in a recent Viewpoint paper [2], we suggest that this is an underestimation (there are probably at least 370 million infected people). In fact, previous data were mostly based on surveys conducted with diagnostic methods with suboptimal sensitivity for the detection of *Strongyloides stercoralis*. For instance, direct faecal smear examination, which is widely used for studies in the field, has very low sensitivity. Concentration techniques (such as the Baermann method) and agar plate culture give better performances, but are cumbersome and seldom used in population-based surveys. Serology is more sensitive than faecal-based methods, but so far only a few prevalence surveys have utilized it [2, 3].

In spite of the potential fatal outcome of strongyloidiasis when larvae disseminate all over the body in immunocompromised subjects [4], this parasite is rarely recognized as a major public health issue, precisely because its burden is underestimated for the reasons explained above. The distribution of the disease

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https://doi.org/10.1017/S0950268814001563 Published online by Cambridge University Press

was poorly known in Latin America (LA) countries: only a few severe (and fatal) cases have been reported [4] and they are considered the tip of the iceberg of an unrecognized and often subclinical chronic disease. In the framework of a project [5] to assess and improve the health status of migrants from LA, we performed this review with the aim of collecting available information about the prevalence of strongyloidiasis in LA countries, where the disease is expected to be highly endemic.

METHODS

Searching

An electronic search in PubMed was done using the following key words, grouped into three main concepts: disease (strongyl*, anguillulose, helminth*, geohelminth*, geo-helminth*, nematod*), epidemiology (preval*, incidenc*, epidemiol*, surve*, rate*, frequenc*), countries of interest (Argentina OR Brazil OR Chile OR Colombia OR Costa Rica OR Cuba OR Dominican Republic OR Ecuador OR El Salvador OR Guatemala OR Guyana OR Honduras OR Mexico OR Nicaragua OR Panama OR Paraguay OR Peru OR Puerto Rico OR Uruguay OR Venezuela). Studies collected were published from 1 January 1981 to 1 January 2011, covering three decades. Search was limited to 'humans' and to the following languages: English, Spanish, Italian, French. The search was done on 16 May 2011. Reference lists of all the articles identified were also examined, and relevant cited references were similarly reviewed. A 'grey' literature search was also conducted, through consultation of libraries of Universidad Peruana Cayetano Heredia and Universidad Nacional Mayor de San Marcos (Lima, Peru).

Selection

Surveys, reports, reviews, epidemiological studies on prevalence of intestinal parasites or specifically strongyloidiasis were collected. The prevalence of *S. stercoralis* was extracted regardless to the type of population (children, immunosuppressed patients, etc.) and diagnostic method used (serology, stool examination, etc.). Moreover, other kind of data (not properly defined as prevalence, e.g. rates, frequencies) were taken into account.

Data abstraction

We identified possibly appropriate papers through titles and abstracts. We then read the whole papers to evaluate their appropriateness for inclusion in the review.

RESULTS

Flow of included papers

The electronic search in PubMed allowed identification of 1071 papers that were evaluated for possible inclusion. The 'grey' literature search provided a further nine studies. After scanning of the abstracts, a total of 223 papers were detected that may relate to our review. Based on the full text of these papers, 135 were rejected since they reported prevalence of other helminthic infections (95 papers) or since they did not report prevalence data (40 papers). Therefore, the total number of papers included was 88. The flow of included papers is shown in Figure 1.

Study characteristics

We found data about the following countries: Argentina (10 papers), Bolivia (2), Brazil (31), Chile (5), Colombia (3), Costa Rica (3), Ecuador (7), Guatemala (1), Guyana (1), Honduras (3), Mexico (2), Nicaragua (1), Peru (12), Puerto Rico (2), Venezuela (5). Most of the studies were cross-sectional, while ten were retrospective and 12 prospective. Most of the studies were not specifically designed to detect *S. stercoralis* but rather to investigate the burden of parasites in general. This is why the diagnostic method used was usually stool examination, frequently without any of the techniques which can enhance the detection of *S. stercoralis* larvae (such as the Baermann method). In just a couple of surveys the authors relied on serology only [6, 7]; in three studies both serology and stool examination were used [8–10], while in one study conducted in Peru, serology (ELISA), stool examination and agar culture were all used [11].

Strongyloidiasis in the different LA countries

Of the 88 studies selected, 31 were conducted in Brazil [6, 8, 12–40]. Studies were characterized by large heterogeneity in several aspects, such as population studied and diagnostic methods used. In Brazil, the lowest proportion of infected individuals was found by Menezes *et al.* [23], who conducted a study in children from municipal day centres in the city of Belo Horizonte from April to November 2006. They found 24·6% children positive for at least one intestinal parasite, but in the 472 stool samples

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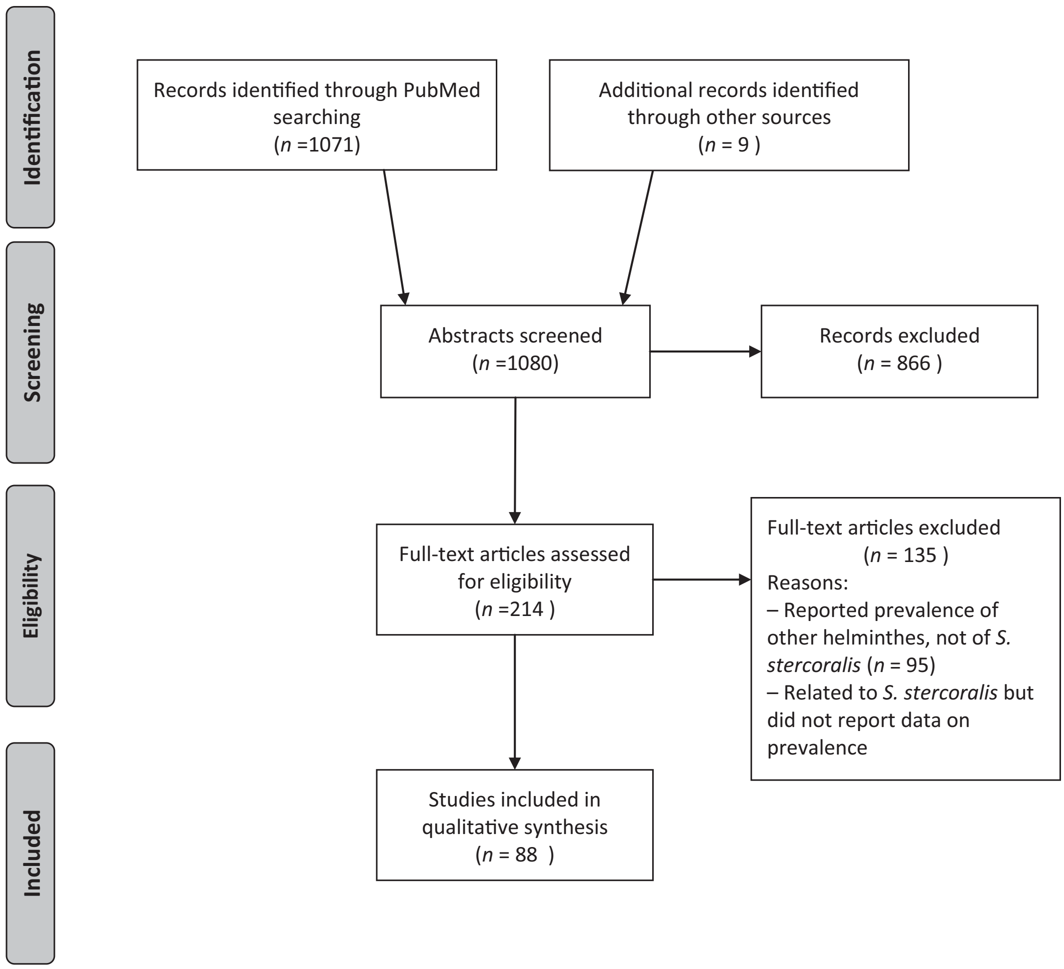

Fig. 1. PRISMA flow chart.

analysed, only one (0·2%) resulted positive for *S. stercoralis*. The diagnostic method used was coproparasitological examination with merthiolate-iodine-formaline concentration. On the other hand, a retrospective study that used faecal examination by the sedimentation method [35] showed the highest percentage (43/198 patients, 21·7% of the examined population) of *S. stercoralis* in alcoholic patients (compared to two control groups). It is of note that one study was not conducted in humans, but it analysed the degree of soil contamination in a couple of indigenous territories in the state of Paraná, Southern Brazil: 111 soil samples were collected in the courtyard of schools and households, and *S. stercoralis* larvae were found in 0·9% and 1·5% of samples, respectively [28]. However, the relationship between soil contamination and intensity of infection in the human population was not analysed. A couple of studies analysed prevalence after treatment: Dorea *et al*. [32] performed stool examination in primary school children at 4 and 6 months after treatment with thiabendazole (with 4·1% prevalence at time 0) and found 50% prevalence reduction. Heukelback *et al*. [15] evaluated prevalence before and after 1 and 9 months from mass treatment with ivermectin (two doses given 10 days apart), finding a reduction from 11% to 0·6% and 0·7%, respectively. A survey conducted in a rural community in the Peruvian Amazon [11] demonstrated *S. stercoralis* larvae in 8·7% of stool samples (combining results from direct smear, Baermann method and simple sedimentation), while the ELISA was positive in 72% of the analysed sera. Given the high negative predictive value of serology (98% according to this study), the authors concluded that despite possible false-positive results (past infections, cross-reactivity) the ELISA was a highly appropriate screening tool. Two other studies conducted in different areas of the Peruvian Amazon found a high percentage of infection in the included subjects (19·5%) [41, 42] by copro-parasitological examination [42]. One of those studies

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concerned subjects who presented symptoms compatible with *S. stercoralis* infection [42]. The proportion of infected subjects was lower (0·8–5%) in two studies conducted in children in different areas of the Peruvian Amazon [43, 44]. Surveys conducted in other areas of Peru [45–50] reported a range of infected people between 0·3% (a study conducted in the small village of Chacas at 3300–3500 m above sea level [45]) and 16% found by Rodriguez & Calderon [48] in children living in a suburb of Tarapoto (which is the largest city in the Department of San Martin, on the edge of the Amazon basin). A study conducted in Lima in HIV-positive patients, found 6% infected people [49]. Of note, a report from the Peruvian Ministry of Health collected a series of transversal studies conducted in different areas of the country between 1981 and 2001; the average prevalence found was 6·6% [51].

The highest rates of strongyloidiasis were found in some areas of Argentina, using only faecal-based methods for diagnosis: a couple of studies performed in the province of Salta [52, 53] found 24% and 50·5% of infected subjects, respectively, and another two studies in the province of Misiones [54, 55] found percentages between 22·2% and 28·6%. In other parts of Argentina [56–61] the figures resulted in a range of 0·2–9·6%, with the lowest rate found in a rural area located at 96 km from Buenos Aires [58].

Large variability in the proportion of *S. stercoralis*-infected subjects was outlined by surveys conducted in Ecuador [9, 62–67] ranging from 0·7% to 24%. Different characteristics of the territories in which the studies were performed might have accounted for part of the disparity; for instance, Peplow [62] found globally 7% of infected people in the Ecuadorian regions analysed, but when we looked at subgroups, we found rates of 8%, 1% and 7% in the Ecuadorian Amazon, the Andean region and on the coast, respectively. A paper by Moncayo *et al.* [63] was particularly interesting: they made a comparison of levels of infection by *S. stercoralis* and other parasites between communities that had received ivermectin mass treatment and communities who were not treated, in Esmeraldas province. Stool samples were examined using a modified Kato-Katz technique and formol-ethyl acetate concentration. They found 35 (1·2%) positive children out of 2878 in the latter group, *vs.* three (0·1%) positive children out of 2528 in those who had received ivermectin. The authors stated that numbers were too small to estimate the impact of ivermectin treatment on strongyloidiasis, while a statistically significant reduction was observed in the ivermectin group when all helminths were considered.

We found five studies conducted in Chile [7, 10, 68–70]. One of which was a survey from 1970 to 1980 in five different geographical areas on the general population [69]. Of the 9489 stool samples, only one (0·01%) was positive at direct examination for *S. stercoralis*. Low infection levels were also demonstrated in a study conducted in children living in a semi-rural county of Santiago province [10] using serology: only one out of 206 children had a positive ELISA test. On the other hand, a couple of studies were conducted in psychiatric institutions [68, 70], where 7–11·6% of patients were found positive. The fourth study was the only one to rely on serology (ELISA) for diagnosis [7]; the authors compared the prevalence in three subgroups: psychiatric patients, health workers and blood donors. Again, percentages of *S. stercoralis* infection were significant only in the psychiatric patients (12%), while strongyloidiasis was almost absent in healthy controls (no infection in health workers, 0·25% in blood donors). The five studies conducted in Venezuela were performed in children (two studies) [71, 72], pregnant women [73], and the general population from different villages [74, 75]. The range found in children and pregnant women was 2·2–7%. Levels of infection in the general population were found to be higher, particularly in the study by Figuera *et al.* [75], where the frequency of strongyloidiasis was investigated by faecal-based methods (13% direct smear, 16% enrichment technique, 24% culture). Moreover, the three studies in Colombia were conducted in heterogeneous populations (general population [76], children [77], immunocompromised patients [78]) and the range was 1·5–3·6%. Two studies conducted in Honduras in HIV patients both found a percentage of infected people around 7·5% [79, 80], while in children living in rural communities and marginal barrios it was 2·6% [81]. All these studies relied on stool examination only.

Range of infection based on the three studies conducted in Costa Rica was between 2% and 5·7%: the lowest figure (2%) was found in a study conducted in the elderly population [82], while the other two studies were conducted in particular subgroups of subjects: patients and health workers from a psychiatric institution [83] (2·5%) and alcoholic patients [84] (5·7%).

We found fewer than three studies each for Bolivia [85, 86], Guatemala [87], Guyana [88], Mexico [89, 90], Nicaragua [91], and Puerto Rico [92, 93]. In all of these studies the percentage of

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Fig. 2. Prevalence of strongyloidiasis in Latin America according to population-based and school-based surveys. Colours are representative of the highest level of prevalence found in the country.

infected subjects was very low, exceeding 2% in only one study in Puerto Rico [92].

Figure 2 shows the detected levels of prevalence of infection with *S. stercoralis* in different LA countries, based on data obtained from school-based and population-based surveys. Each country is coloured after the highest level of prevalence found (which is not necessarily representative of the whole country). Supplementary Table S1 reports in detail the number of patients screened and the percentage of patients found positive. Data are reported only for countries with at least four studies conducted in the general population and/or school children.

DISCUSSION

Globally, we believe that for most countries it is not possible to define a reliable estimation of prevalence because of scarceness and/or inadequacy of studies. In fact, *S. stercoralis* requires specific diagnostic methods, therefore surveys to assess its burden should be specifically designed. As mentioned in the Introduction, direct stool examination without any concentration techniques, or the Kato-Katz method (which is the most widely used method for helminth faecal surveys), are likely to miss most *Strongyloides* infections, as was recently shown by a paper published after the timeframe considered for our review. The authors clearly demonstrated that a survey conducted with inadequate methods provides unreliable figures: in a population living in the Amazon basin of Peru, they detected 0% positive for *Strongyloides* with the Kato-Katz method, while they found 22% of positive samples by agar plate culture. In the same study, the authors showed that alternative techniques, less cumbersome than culture, can also be used, such as

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the spontaneous sedimentation in tube technique (SSTT), which can be applied also for all other helminths. Interestingly, these researchers found the same prevalence with both techniques (Kato-Katz and SSTT) for hookworm as well as for *Ascaris lumbricoides* and *Trichuris trichiura*, while for *S. stercoralis* the prevalence increased from 0% with the Kato-Katz method, to 16% with the alternative method [94].

Serology will be a useful tool, once it is validated and made widely available, especially if blood can be simply collected with a finger prick on filter paper. Different serological techniques are available, and all are more sensitive than faecal-based methods, and also virtually 100% specific above a given cut-off [95]. Alternatively, when resources are limited and ELISA or an alternative serological test can not be used, suitable copro-microscopic methods for *S. stercoralis* should be adopted, such as those mentioned above and in the Introduction. However, it should be borne in mind that the sensitivity of such tests is not perfect, especially when performed on a single faecal specimen, and therefore they are likely to underestimate the real prevalence. There is a need to define a standard protocol to assess the burden of strongyloidiasis, both in terms of diagnostic method and of adequate sampling and statistical analysis. Such recommendations were made for soil-transmitted helminths by the World Health Organization, and mapping guidelines are being elaborated. An attempt to globally map *S. stercoralis* prevalence has just been published [96], confirming our recent view [2] that the global prevalence is probably much higher than previously estimated and that this parasite should be given greater attention by policy makers. We encourage policy makers to include *S. stercoralis* in the soil-transmitted helminths package, as a first step to move forward to the control of strongyloidiasis through an integrated strategic approach.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268814001563.

APPENDIX. COHEMI PROJECT STUDY GROUP

Maurizio Bonati, Francesca Severino, Valeria Confalonieri, Chiara Pandolfini, Zeno Bisoffi, Dora Buonfrate, Andrea Angheben, Marco Albonico, Alessandro Bartoloni, Marianne Strohmeyer, Lorenzo Zammarchi, Jose Muñoz, Robert Pool, Ana Requeña, Maria Roura, Anita Hardon, Christopher Pell, Peter Chiodini, Juan Moreira, Roberto Sempértegui, Mariella Anselmi, Eduardo Gotuzzo, Maria Alejandra Mena, Hector H. Garcia, Javier Bustos, Saul Santiva, Faustino Torrico, Daniel Lozano, Guido Chumiray Rojas, Teresa Hinojosa Cabrera, Javier Ochoa Morón, Ignacio Abapori Cuellar, Jaime Amorós Suarez, Gianni Tognoni, Alessandra Nicoletti, Elisa Bruno.

ACKNOWLEDGEMENTS

This work was supported by the EC within the 7th Framework Programme under the COHEMI project (grant agreement no. FP7-GA-261495).

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