Evaluation of Two Different Strategies for Schistosomiasis Screening in High-Risk Groups in a Non-Endemic Setting. A Retrospective Cohort Study.

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Abstract

Background: to evaluate the real-life performance of direct microscopy techniques and ELISA serology for schistosomiasis screening in a high-risk population in a non-endemic setting.

Methods: a retrospective cohort study was conducted in two out-patient Tropical Medicine units in Barcelona (Spain) from 2014 to 2017. Asymptomatic adults arriving from the Sub-Saharan region were included. Schistosomiasis screening was conducted according to clinical practice following a different strategy in each setting: A) feces and urine direct examination plus *S. mansoni* serology if non-explained eosinophilia was present, B) *S.mansoni* serology plus uroparasitological examination at second-step in case of a positive serology. Demographic, clinical and laboratory features were collected. Schistosomiasis cases, clinical management and 24 months follow-up were recorded for each group.

Results: Four-hundred forty individuals were included: 399 in group A, 41 in group B. The majority of the cohort were male (250, 56.4%), mainly from West African countries. No differences in sex distribution (p=0.57), age (p=0.6) and baseline eosinophilia (p=0.17) were found between both groups. Fifty schistosomiasis cases were detected (11.5% group A vs 4 % group B, p=0.733). When both microscopic and serological techniques were performed, discordant results were recorded in 18.2% (16/88)). Eosinophilia was present in 50% cases. Schistosomiasis cases were younger (p<0.001) and presented more frequently eosinophilia and elevated IgE (p<0.001). Pathological ultrasound was described in 33.3% of examinations performed (4 out of 12)**.**

Conclusions: Similar results were achieved by serology and microscopy techniques -based strategies. Serology might be prioritized for schistosomiasis screening of asymptomatic adults from endemic areas, regardless peripheric eosinophil count or IgE levels.

Background

Human schistosomiasis is a neglected tropical disease caused by trematodes of the gender *Schistosoma sp*. Approximately 240 million people worldwide are affected by this condition (1). Meanwhile, individuals with chronic sequelae after infection are estimated in 440 million (2). Endemic areas are located in tropical and subtropical regions of around 70 countries in Asia, America and Africa, although the Sub-Saharan region gathers up to 90% of cases (1). Six species of *Schistosoma sp.* that affect humans have been identified, whose distribution is linked to the fresh-water snail host habitat (3). *Schistosoma (S)mansoni, S.japonicum*, *S. mekongi, S.intercalatum* and *S. guineensis* cause gastrointestinal manifestations through the invasion of mesenteric plexus, while *S.haematobium* invades the pelvic venus causing genitourinary disease(3). Acute schistosomiasis might evolve to chronic forms, which often remain asymptomatic but may lead to severe consequences in the long-term as result of chronic tissue inflammation. In low-endemic areas, schistosomiasis has gained prominence due to migration streams, increased travelling to endemic regions and variations in climate conditions that affect the intermediate host distribution (5). Prevalence in high-risk groups, such as migrants from endemic areas, could reach

up to 15% and even autochthonous outbreaks in Western countries have been documented (6,7). Implementation of different screening strategies in non-endemic settings have been proposed for high-risk groups (8). Direct microscopic observation of eggs in urine or fecal samples by concentration techniques such as Kato-Katz have been considered the gold standard for diagnosis in endemic populations, despite their scarce sensitivity. Direct observation shows a wide intra and inter-individual variability due to circadian changes in the egg load and throughout the different phases of the infection, as well as to the observer's experience (9,10). Antigenic methods such as circulating cationic antigen detection have shown to improve the detection of *S. mansoni* infections in these high-risk populations (11). On the other hand, antibody detection by commercial non-species-specific tests (mainly enzyme-linked immunosorbent assay, ELISA) is widely used in screening protocols for travelers. However, the clinical interpretation of serological results is often unclear in endemic populations chronically exposed to *Schistosoma sp* (12). As a result, consensus on recommended screening algorithms using available techniques is lacking. The aim of our study was to describe two different screening strategies for a high-risk group in a non-endemic area, using direct microscopy observation and serological detection by ELISA respectively, in order to determine their accuracy and usefulness in a real-world setting.

Methods

Definitions

We use the term *migrant* based on United Nations Educational, Scientific and Cultural Organization (UNESCO) definition as "any person who lives temporarily or permanently in a country where he or she was not born and has acquired some significant social ties to this country*"* (13). Individuals from European origin living in endemic areas were considered *emigrant*, while subjects arriving from endemic areas were considered *immigrants.* The term *recently arrived migrant* was applied to individuals who had arrived to Europe up to 6 months before inclusion. A subgroup of *visiting friends and relatives* (VFR) was categorized according to CDC definition as those migrants who had ever returned to their home country since their arrival to Europe (14).

Study design

A retrospective longitudinal cohort study was performed in order to compare two different screening strategies for schistosomiasis used in the clinical practice.

Settings

The study was conducted in two out-patient units specialized in tropical medicine, part of the International Health Program of Catalan Institute of Health (PROSICS) in Barcelona, Spain. These units provide free medical care to self-referred individuals and referred cases from general practitioners and other medical specialists, public health services and non-governmental organizations (NGOs). Each clinic performs a different schistosomiasis screening strategy: A) hemogram and feces and urine concentration techniques for direct examination followed by *S. mansoni* serology if non-explained eosinophilia was

present, B) *S.mansoni* serology and uroparasitological direct examination at a later time in case of a positive serology. Coproparasitological analysis was also performed in group B patients as part of general parasitosis screening, but not specifically for *Schistosoma* screening. All samples were analysed at the Parasitology Unit of Vall d'Hebron Microbiology Department.

Study population and data collection.

Asymptomatic adults arriving from the Sub-Saharan African (SSA) region from January 2014 to December 2017 were included. Subjects with previously known either eosinophilia or high levels of immunoglobulin E (IgE), past history of schistosomiasis or macrohematuria were excluded. Demographic, clinical and laboratory data at baseline were collected in all subjects.

Laboratory tests included hemogram [with absolute eosinophil count (AEC)] and biochemical panel. Mild eosinophilia was defined as an AEC between 500 and 1000 cells/µl, moderate eosinophilia as AEC between 1000 and 3000 cells/µl and severe eosinophilia as AEC ≥ 3000 cells/µl. The upper normality limit for relative eosinophils count was settled in 4.5%, according to the recommendations of the expert group of the Spanish Society of Tropical Medicine and International Health (SEMTSI) for the diagnosis and treatment of imported eosinophilia (15). Total serum IgE levels were also recorded when available and considered normal below 500KU/L according to the local reference threshold. Routine migrant screening, including hepatitis serology (hepatitis B surface antigen and anti-hepatitis C antibodies), human immunodeficiency virus (HIV) antibodies and antigen-p24 detection and syphilis serology (TPHA and RPR), was performed in all subjects. Asymptomatic individuals aged below 35 years were also tested for tuberculosis infection by either tuberculin skin test or tuberculosis blood test (Quantiferon-TB Gold®). Other latent infections, such as malaria infection and filariasis, were screened based on the patient individual risk assessment. Microscopic examination of stool and urine was performed through concentration techniques; stool examination was carried out using the Ritchie's formalin-ether technique, while urine samples were processed by centrifugation. The identification of the different *Schistosoma* species was carried out according to the morphologic characteristics of the eggs. An ELISA for IgG against *S.mansoni* (Novagnost *S. mansoni* IgG; Siemens Diagnostics, Marburg, Germany) was performed following manufacturer instructions. The results were expressed by index and considered positive when index ≥1.1, negative when index ≤0.9 and grey zone in values ranging from 0.9 to 1.1.

Complementary examinations [abdominal ultrasound (US) and X-ray] were performed at the discretion of the physician in charge. Treatment regimens and follow-up at month 6, 12 and 24 after therapy were also recorded. Figure 1 shows a flowchart of the study design.

Case definition

Confirmed cases were established after direct observation of *Schistosoma* eggs in either feces or urine samples. They were classified as either intestinal or genitourinary disease according to the identified *Schistosoma* species (16). *Probable* schistosomiasis case was defined by a positive serology which was considered true positive by the responsible physician, without parasitological confirmation. The disease

location was considered undetermined due to the inability to identify the parasite species in probable cases. Cases considered false positive according to the medical records were also recorded.

Statistical analysis

Univariate analysis of the dataset included measures of distribution, central tendency (median or mean depending on distribution), and dispersion (standard deviation or interquartile range [IQR]). Normally distributed quantitative variables were compared with Student t-test. Non-normally distributed quantitative variables were analyzed with the Mann-Whitney U test. Categorical variables were described in frequency and percentage. The bivariate analysis was carried out using the $\chi 2$ test or the Fisher's exact test for frequencies below 5%. Hypothesis testing was conducted with a 5% alpha risk and 95% confidence intervals (CI), and considered statistically significant if the two-tailed p-value was below 0.05. Statistical analysis was conducted using IBM SPSS, version 26.0 for Windows (SPSS Inc, Armonk, NY, USA).

Results

Baseline features

A total of 566 patients were tested for schistosomiasis in both settings during study period. Four-hundred and forty patients met inclusion criteria and were included in the analysis: 399 (90.7%) were screened by urine and feces examination (group A), while 41 (9.3%) were screened by serology (group B). Table 1 summarizes baseline characteristics of the overall cohort and by screening strategy.

Table 1
Baseline characteristics in the overall cohort and by screening strategy.

	Overall (n=440)	Group A (n=399)	Group B (n=41)	p-value
Male*	250 (56.8%)	225 (56.4%)	25 (61.0%)	.57
Age (years)**	36.0[20]	36.0[20]	32.0[18]	.06
Country of origin*	190(43.2%)	178 (44.6%)	12(37.1%)	.06
-Equatorial Guinea	86(19.5%)	79(19.8%)	7(17.1%)	
-Senegal	26(5.9%)	23(5.8%)	3(7.3%)	
-Gambia	24(5.5%)	23(5.8%)	1(2.4%)	
-Nigeria	22(5.0%)	16(4.0%)	6(14.6%)	
-Cameroon	15(3.4%)	13(3.3%%)	2(4.9%)	
-Guinea Conakry				
Past medical history*	15(3.4%)	11 (2.8%)	4 (9.8%)	.02
-HIV	16(3.6%)	14(3.5%)	2 (4.9%)	.66
-Chronic viral hepatitis	43(9.8%)	41(10.3%)	2 (4.9%)	.27
-Cardiovascular risk-factors				
Type of migrant*	13(3.0%)	7(1.8%)	6(14.6%)	<.001
-Emigrant	427(97.0%)	392(98.2%)	35(85.4%)	-
-Immigrant	143(32.5%)	136(34.1%)	7(17.1%)	.03
VFR	157(35.7%)	139(34.8%)	18(43.9%)	.26
Newly arrived				
Absolute eosinophilia*	74 (16.8%)	64(16.0%)	10(24.4%)	.17
Relative eosinophilia*	163(37.1%)	142(35.6%)	21(51.22%)	.05
Elevated IgE*	89(20.2%)	88(22.1%)	1(2.4%)	.003

*absolute frequency(%)**median[IQR]. *HIV* human immunodeficiency virus; *IgE* total immunoglobuline E; *VFR* visiting friends and relatives. Absolute eosinophilia was determined as absolute eosinophile count above 500cells/μL; Relative eosinophilia was determined as relative eosinophile count above 4.5%. Elevated IgE was defined as total IgE levels above 500 KU/L.

Most subjects in both cohorts were male (56.4% in group A vs 61.0% in group B), with an overall median age of 36 years (36 vs 32 years, p=0.06). Most subjects arrived from Western African countries, with a predominance in both groups for Equatorial Guinea (190 individuals, 43.2% from overall cohort). The

countries of origin of individuals from the general cohort are represented in Figure 2. A majority of subjects (372, 84.5%) did not have significant past medical history. Fifteen subjects (3.4%) referred medical history of HIV infection, with a significantly higher proportion in group B (2.8 vs 9.8%, p=0.019). Sixteen subjects (3.6%) had previous history of chronic viral hepatitis (9 cases of hepatitis B, 6 cases of hepatitis C and 1 coinfection). Notably, known history of cardiovascular risk factors (i.e. dyslipidemia, arterial hypertension and diabetes mellitus) prevailed over infectious diseases in the general cohort (43 subjects [9.8%] vs 31 [7.0%]).

Schistosomiasis screening outcomes

Fifty subjects (11.4%) were diagnosed with *Schistosoma* infection during the study period. Characteristics of schistosomiasis cases and the comparison with subjects without schistosomiasis are presented in Table 2.

Table 2
Baseline characteristic of schistosomiasis cases compared to subjects without *Schistosoma* infection.

	Schistosomiasis cases			**No schistosomiasis**	**p-value**
	Confirmed (n=40)	Probable (n=10)	Total (n=50)	(n=390)	
Male*	19(47.5%)	6(60%)	25 (50%)	165(42.3%)	.30
Age**	23.5[14.5]	35[30]	24 [16]	37[19]	<.001
Type of migrant*	-	-	-	13(3.3%)	.190
Emigrant	10(25%)	3(30%)	13(26.5%)	130(33.5%)	.327
VFR	21(52.5%)	4(40%)	25(50%)	132(34.0%)	.019
Recently arrived					
Country of origin*	24(60%)	4(40%)	28(56%)	-	-
Equatorial Guinea	4(10%)	1(10%)	5(10%)		
Senegal	1(2.5%)	4(40%)	5(10%)		
Gambia	3(7.5%)	-	3(6%)		
Mali	2(5.0%)	-	2(4.0%)		
Gabon	2(5.0%)	-	2(4.0%)		
Ivory Coast	2(5.0%)	-	2(4.0%)		
Guinea Conakry	1(2.5%)	-	1(1.0%)		
Burkina Faso	-	1(10%)	1(1.0%)		
Cameroon	1(2.5%)	-	1(1.0%)		
HIV infection	4(10%)	1(10%)	5(10%)	24(6.2%)	.297
Eosinophil count**	550[600]	500[400]	550[500]	100[200]	<.001
Absolute eosinophilia*	20(50%)	5(50%)	25(50%)	49(12.6%)	<.001
Relative eosinophilia*	33(82.5%)	8(80%)	41(82%)	122(31.3%)	<.001
IgE levels**	880[3830]	410[872]	741[3156]	147[298]	<.001
Elevated IgE*	17(42.5%)	4(40%)	27(54%)	62(15.9%)	<.001

*absolute frequency(%)**median[IQR]. *HIV* human immunodeficiency virus; *IgE* total immunoglobuline E; *VFR* visiting friends and relatives. Absolute eosinophilia was determined as

Absolute and relative eosinophilia were significantly more frequent in the schistosomiasis group (50% vs 12.6% in absolute count, 82% vs 31.3% in relative count, both p<0.001). Grades of eosinophilia in schistosomiasis cases are represented in Figure 3. The proportion of schistosomiasis cases did not significantly vary between the two strategies (46 cases [11.5%] in group A *vs.* 4 cases [9.8%], p=0.733). According to the screening strategy:

Group A. In group A, based in copro and uroparasitological direct examination, 46 cases (11.5%) of schistosomiasis among 399 screened subjects were detected. Thirty-seven (9.3%) cases were diagnosed by urine and/or feces examination: the vast majority were stool samples (30 cases; 26 subjects presented *S. intercalatum* eggs, 4 cases with *S. mansoni* eggs). Uro-parasitological samples yielded positive results in 6 subjects, in which S. *haematobium* eggs were observed. One case with positive results in both stool (*S.intercalatum*) and urine (*S.haematobium*) examination was detected. Serology was performed in a second-step diagnosis in two subjects with confirmed gastrointestinal schistosomiasis by *S. intercalatum* and *S.mansoni* respectively, and resulted negative in both cases. Serology was performed in a second time in 45 subjects with previous negative results in urine and stool microscopic observation, as part of the study for eosinophilia and/or hyper IgE in baseline blood test. Eleven subjects tested positive, although a probable diagnosis was assumed in 9 cases (81.8% of the cases with a positive ELISA result). The remaining two cases presented a positive serology for *Strongyloides Stercolaris* and were diagnosed as such, considering *Schistosoma spp*. serology as a false positive result due to probable cross-reaction.

Group B. Screening was conducted through baseline *Schistosoma* ELISA serology in 41 cases. Serology resulted positive in 6 individuals, two of them were not assumed as clinically relevant according to medical records. No cases were detected by stool analysis. Among suspected cases, three subjects underwent uroparasitological examination. Genitourinary schistosomiasis was confirmed in all three cases with the observation of *S.haematobium* eggs in urine specimen.

Table 3 summarizes schistosomiasis cases by the two strategies.

Table 3
Schistosomiasis cases diagnosed by screening strategy.

	Group A (n=399)	**Group B (n=41)**
Confirmed cases	37(9.3%)	3(7.3%)
-S. intercalatum	26(6.5%)	3(7.3%)
-S. mansoni	4(1.0%)	-
-S. haematobium	6(1.5%)	-
-Coinfection	1(0.3%)	-
Probable cases	9 (2.0%)	1(2.4%)
Total	46(11.5%)	4(9.8%)

*absolute frequency (%). Probable cases were defined by a positive serology considered true positive by the responsible physician. Confirmed cases were established after direct observation of *Schistosoma spp.* eggs in either feces or urine samples.

Table 4 shows the correlation between serology and coproparasitological or uroparasitological studies when both a direct examination technique and serology were performed.

Table 4
Correlation between serology and copro-uroparasitological examination.

		***S. mansoni.* serology (ELISA IgG) (n=88)**	
		Positive	**Negative**
Copro/uroparasitological examination*	*S.mansoni*	-	1(1.4%)
	S.intercalatum	-	1(1.4%)
	S.haematobium	3(17.6%)	-
	No eggs	14(82.4%)	69(97.1%)
	Total	17(100%)	71(100%)

*Absolute frequency (%). *ELISA* enzyme-linked immunosorbent assay; *S. mansoni/intercalatum/haematobium*: Schistosoma mansoni/intercalatum/haematobium.

Among 88 subjects in whom both tests were performed, 18.2% showed discordance between techniques (either positive serology with negative uroparasitological examination or positive microscopic observation with negative serology). Out of the 17 patients with positive serology, no *Schistosoma spp*. eggs were found in 14 (82.4%); among 71 patients with negative serology, eggs were found in 2 (2.9%).

Schistosomiasis treatment, complementary examinations and follow-up

Among 50 subjects with schistosomiasis diagnosis, 46 received antiparasitic treatment with praziquantel. Four (8.0%) were lost of follow-up before receiving treatment. Treatment regimens were non systematically collected in medical records. The most commonly therapeutic scheme was a daily dose of 40mg/kg, given twice a day for two days (34 cases, 68%). Concerning complementary examinations, 12 (24%) underwent abdominal US, which showed pathological findings in four of them (33.3%). Pathological US findings consisted in all four cases in irregularities and thickening of bladder walls.

Schistosoma serology was performed in 7 subjects at6 months follow-up in subjects who had previously tested positive. Serological test persisted positive in 6 of them, and titles had not significantly decreased. In two subjects, serology was repeated after 12 months, with persistent positive result. Re-treatment was decided in one case due to persistent eosinophilia and positive serological result.

General screening results

From the overall cohort, 188 subjects (42.7%) were diagnosed with 215 other infections during systematic screening: 23.9% individuals (45 out of 188) showed any simultaneous coinfection. Among *Schistosoma*-infected subjects, 26 (52.0%) presented other infectious disease. The main infections are summarized in figure 4 and Table 5.

Table 5

Absolute and relative frequency of newly diagnosed infections in the general cohort (n=440).

New diagnosed infections	Frequency (%)
Trichuris Trichuria	33(7.5%)
Chronic viral hepatitis	30(6.8%)
HBV	25 (11.6%)
HCV	5 (2.3%)
Filarias	29 (6.6%)
Latent TB infection	24 (5.5%)
Strongyloides stercolaris	20 (4.5%)
Ancylostoma	15 (3.4%)
Ascaris lumbricoides	14 (3.2%)
HIV	14 (3.2%)
Syphilis	10 (2.3%)
Malaria	8 (1.8%)
Giardia	6 (1.4%)
Entamoeba	5 (2.3%)
Mansonella	3 (1.4%)
Gonorrhea	1 (0.5%)
Toxocara canis	1 (0.5%)
Taenia solium	1 (0.5%)
Dicroelium dendriticum	1 (0.5%)

*Absolute frequency (%). *HBV* hepatitis B virus; *HCV* hepatitis C virus; *HIV* human immunodeficiency virus; *TB* tuberculosis.

The presence of coinfections was significantly higher in subjects with baseline eosinophilia (71.6% vs 36.9%, p<0.001). Among the twenty-five schistosomiasis cases who presented absolute eosinophilia at baseline, 14 (56%) were diagnosed with other infectious diseases. Considering previously known and newly diagnosed cases, chronic conditions such as chronic viral hepatitis and HIV reached a prevalence of 10.5% and 6.6% respectively in the general cohort.

Discussion

Our study analyzes two schistosomiasis screening strategies used in the clinical practice of an International Health Institution in Barcelona, Spain, from 2014 to 2017. All diagnosed cases correspond to immigrants, mostly from Equatorial Guinea. This country is probably over-represented due to historical and cultural ties with Spain and the high degree of awareness of the importance of screening in this group. Similar demographic characteristics have been reported in cohorts within the Spanish territory (17,18).

The rationale for screening schistosomiasis in a population from endemic areas is that the disease is highly prevalent, and that treatment with praziquantel is safe and effective[18,19]. In studies in endemic populations, the rate of schistosomiasis varies between 20-40% (19,20). In migrants, the prevalence varied between 1% and 18% depending on the screening technique (parasitological vs serological study), according to a recent meta-analysis (21–23). In our study the overall prevalence, including both screening strategies, was 11.5%.

It should be noted that the effectiveness of the parasitological study depends largely on the experience of the observer, and therefore may vary significantly between laboratories; moreover, in contexts with a low egg burden, egg excretion may vary at different times of the day; even in the same sample the eggs may be unevenly distributed (24,25). The use of more objective techniques would allow screening to be expanded and performed in primary care units, and not necessarily in specialized centers.

In this situation, the sensitivity of the technique should be prioritized over specificity, although performing two tests in parallel could be used to increase the accuracy of detection and inform schistosome specy (8). In our study, the percentage of diagnosed cases in our cohort resulted similar in both described strategies. A possible explanation could be the high specialization of the reference laboratory, which optimizes the sensitivity of direct observation techniques. This condition might not be generalized to other contexts with less specialized laboratory personnel.

In this study, the serology used was an ELISA based on crude antigens of *S. mansoni*. Several studies show that this technique is more sensitive than direct visualization of eggs, mainly in adults in non-endemic areas with light infections (26,27). Nevertheless, the sensitivity of commercial tests for other *Schistosoma* species could be compromised. Thus, sensitivity varies between 50 and 90% for *S. mansoni* and 20 and 70% for *S. haematobium* (28).

Prevalence of imported eosinophilia among travelers and immigrants is reported between 8% and 28.5%, that is consistent with the reported prevalence of 16.8% in our cohort. Etiological diagnosis is often troublesome and, depending on the depth of the study and on the population analyzed, a parasitic cause is identified in 17–75.9% of the individuals. Among the difficulties encountered to compare studies are the heterogeneity of the studied populations, the study designs and the different diagnostic protocols (15). In schistosomiasis, eosinophilia is not a consistent finding (29,30), mainly in adult migrant patients, with initial infection probably in childhood, and low parasite load. In our study, 50% had eosinophilia. However, this finding could be influenced by the usual presence of coinfections in these patients, such as

strongyloidiasis, filariasis and soil-transmitted infections. Consistently with other studies (18,31), IgE elevation was higher (68%); however, one third of the patients diagnosed had no abnormality. Therefore, screening for the disease should be based primarily on origin in the case of migrants, and on risk activities in the case of travelers, rather than on the presence of these parameters (21).

Once screening has been performed, the question of what the exact procedure is to follow once individuals are considered positive is not clear. There are few guidelines on the management of these patients, either symptomatic or asymptomatic. Some guidelines recommend performing a parasitological examination in the case of a positive serology, and performing an ultrasound only if eggs are found (32). Although this is essential to differentiate the species, the low sensitivity of the parasitological test and the presence of lesions in patients without egg detection suggest that an ultrasound should be performed in all patients, regardless of the parasitological result and the presence of symptoms (33,34). In our study, in all patients diagnosed, either by parasitological study or by serology, treatment was considered. However, the percentage of ultrasounds performed was very low, reflecting the difficulties on an appropriate follow-up in many contexts. One third of the performed ultrasound showed pathological findings in relation to the infection.

One limitation of schistosomiasis serology is that its use to differentiate between current and past infection is very limited, since antibody titers vary significantly after adequate treatment (35). In our study, only 2.5% of patients underwent control serology, of which 73% were positive. In general, the follow-up of migrant patients is difficult, especially in the screening of asymptomatic population, due to socioeconomic and idiomatic limitations, high mobility and lack of disease perception (36). Mechanisms need to be in place to ensure non-discrimination in health care access, such as access to cultural mediators, improvement of health literacy through targeted health promotion interventions, supranational communication system and effective asylum policies, among others (37,38).

Due to the limitations of both techniques currently used, new tests with higher sensitivity, higher specificity, and capable of differentiating current from past infections, should be developed. Meanwhile, the combination of several serological techniques, the western blot technique, or the immuno-chromatographic test (ICT) have shown a higher sensitivity (28).

A recent evaluation of several diagnostic tools found that a rapid commercial serological ICT test with 96% sensitivity would have the potential for being used as a single screening test for migrants from Sub-Saharan Africa (39). Molecular techniques (serum or excreta PCR) also have a high performance, improving the sensitivity of serology and allowing confirmation of the *Schistosoma* species involved. Furthermore, they can be useful for monitoring outcome (40). More efforts should be made to make these tests widely available for their use in daily practice.

Regarding general screening, an important proportion of the cohort was diagnosed with some infectious diseases, which encourages the maintenance of screening programs with the active participation of actors such as NGOs, community organizations and other health care departments. The lower rate of infections in our study compared to similar publications could be probably explained due to the exclusion

of individuals with symptoms or known eosinophilia/elevated IgE (17,18). Concerning general migrant health status, it is worthy reported the high prevalence of cardiovascular conditions, even among such a young population as the included in this cohort (41). Specific, culturally oriented strategies and resources should be available to ensure also detection and management of non-communicable diseases in these vulnerable populations (42).

This study presents important limitations mainly due to its retrospective design. Information bias due to incomplete data in medical records could have influenced the results concerning serological interpretation. As foresaid, selection bias might not be completely avoided despite tight inclusion criteria. Also, the sample size of both strategies considerably differs, making difficult a significant comparison between groups. In the same line, the sample of schistosomiasis cases is too limited to draw robust conclusions. The high rate of loss to follow-up, related to the precarious life conditions, is the cause of a substantial amount of data losses, especially concerning follow-up information. Finally, it is worthy remarking that inclusion was limited to asymptomatic subjects coming from SSA and thus, results might not be generalized to other populations. Despite these remarkable limitations, we believe that this study provides valuable data on the screening of Sub-Saharan migrants in the clinical practice.

Conclusions

Serology achieves a similar performance to direct diagnosis for the screening of schistosomiasis in a high-risk population. Due to the standardization of serology technique and its availability at all levels of care, facilitating access to all patients, this strategy is recommended. Screening should be based primarily on origin rather than on the presence of eosinophilia and/or elevated IgE levels, due the inconsistence of these parameters.

Abbreviations

S
Schistosoma
ELISA
enzyme-linked immunosorbent assay
UNESCO
United Nations Educational, Scientific and Cultural Organization
VFR visiting friends and relatives
NGO
non-governmental organizations
IgE
immunoglobulin E
AEC
absolute eosinophil count
SEMTSI

Spanish Society of Tropical Medicine and International Health
HIV
human immunodeficiency virus, US:ultrasound
IQR
interquartile range
ICT
immuno-chromatographic test.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethical Committee of the University Hospital Vall d'Hebron PR(AG)112/2016. All data of the subjects participating in the study was anonymized. The need for informed consent was waived, due to the study's design.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LR collected, analyzed and drafted the manuscript; ES conceived the study designs and revised the manuscript; CB conceived the study designed, analyzed and drafted the manuscript;FS contributed to the interpretation of the data and revision of the manuscript; BT contributed to the interpretation of the data and revision of the manuscript , FZ contributed to the revision of the manuscript, LG , NS-D contributed to the interpretation of the data and revision of the manuscript, IO-S contributed to the interpretation of the data and revision of the manuscript, MLA contributed to the interpretation of the data and revision of the manuscript, DP contributed to the interpretation of the data and revision of the manuscript, AS-M contributed to the interpretation of the data and revision of the manuscript, PB-N contributed to the

interpretation of the data and revision of the manuscrip, JE contributed to the interpretation of the data and revision of the manuscript, IM contributed to the interpretation of the data and revision of the manuscript. All authors read and approved the final manuscript

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Figures

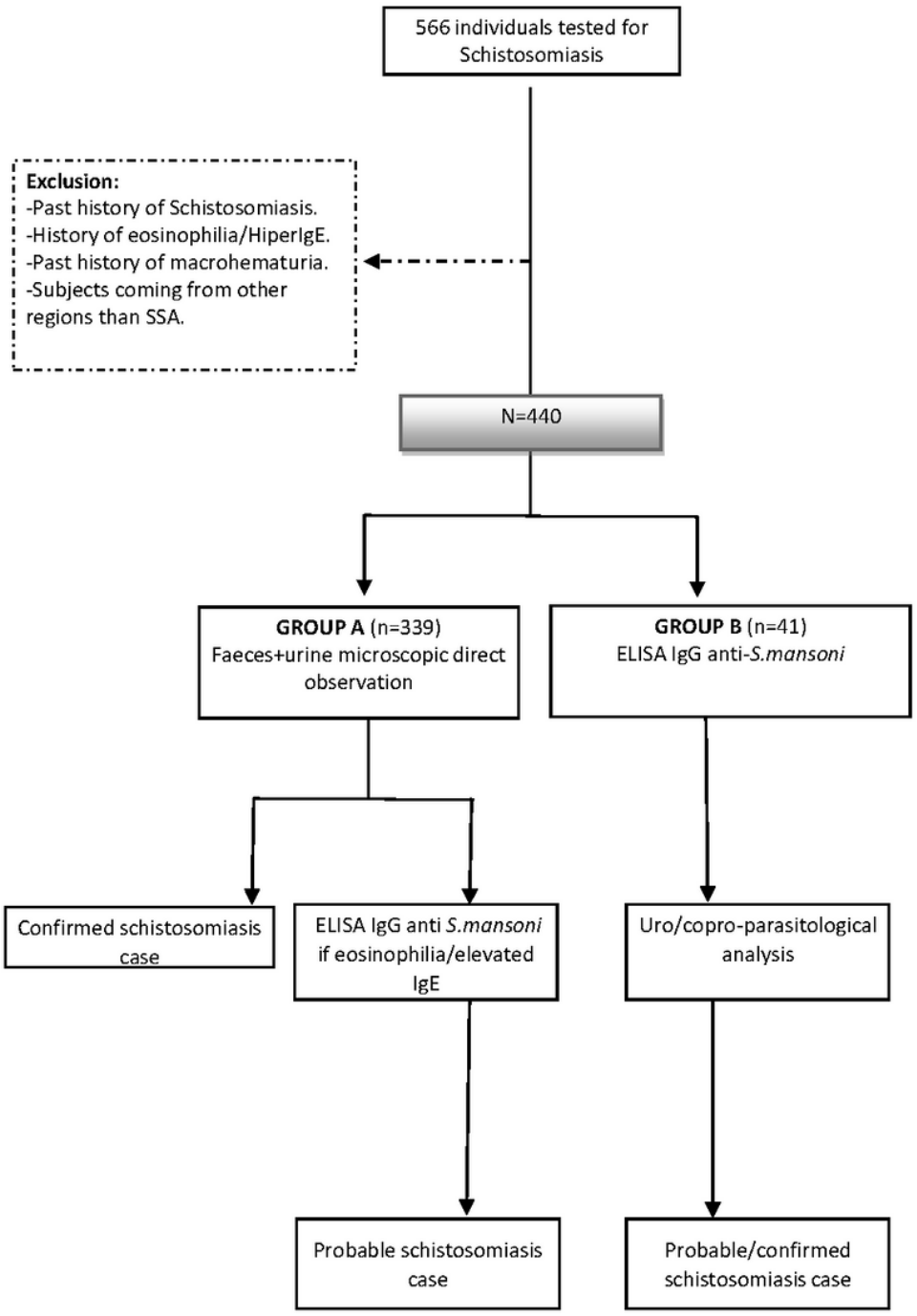
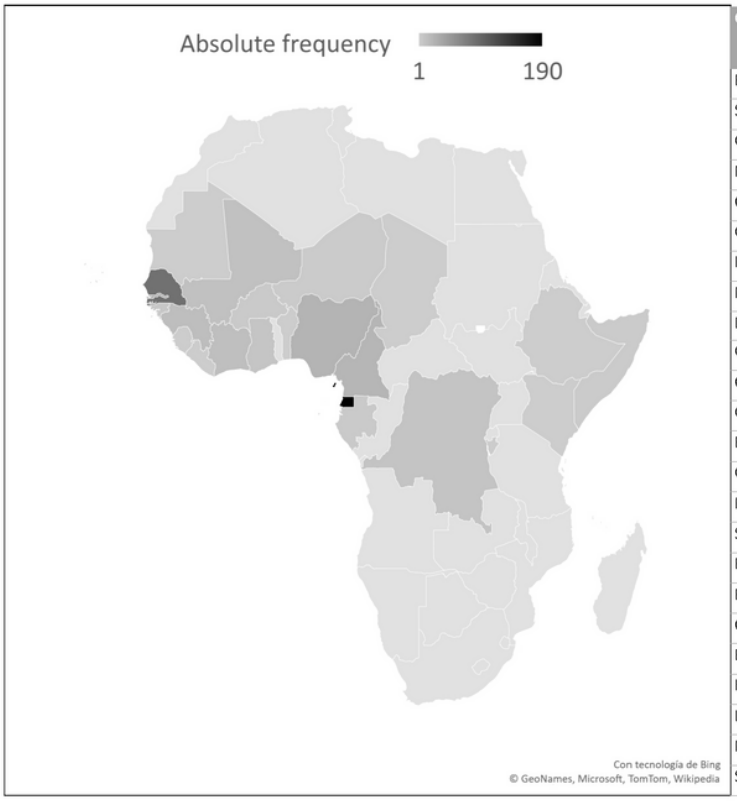


Figure 1

Study design and flowchart. ELISA enzyme-linked immunosorbent assay; IgE immunoglobulin E; IgG immunoglobulin G; S.mansoni Schistosoma mansoni; SSA Subsaharan Africa



Country of origin	Frequency (%)
Equatorial Guinea	190 (43.2%)
Senegal	86 (19.5%)
Gambia	26 (5.9%)
Nigeria	24 (5.5%)
Cameroon	22 (5.0%)
Guinea Conakry	15 (3.4%)
Ivory Coast	14 (3.2%)
Mali	12 (2.7%)
Democratic Republic of Congo	9 (2.0%)
Ghana	8 (1.8%)
Centro African Republic	6 (1.4%)
Guinea Bissau	6 (1.4%)
Burkina Faso	4 (0.9%)
Gabon	4 (0.9%)
Niger	3 (6.8%)
Somalia	3 (6.8%)
Benin	1 (0.5%)
Burundi	1 (0.5%)
Chad	1 (0.5%)
Ethiopia	1 (0.5%)
Kenya	1 (0.5%)
Liberia	1 (0.5%)
Mauritania	1 (0.5%)
Sierra Leone	1 (0.5%)

Figure 2

Country of origin of screened individuals in overall cohort (n=440) by absolute and relative frequency.

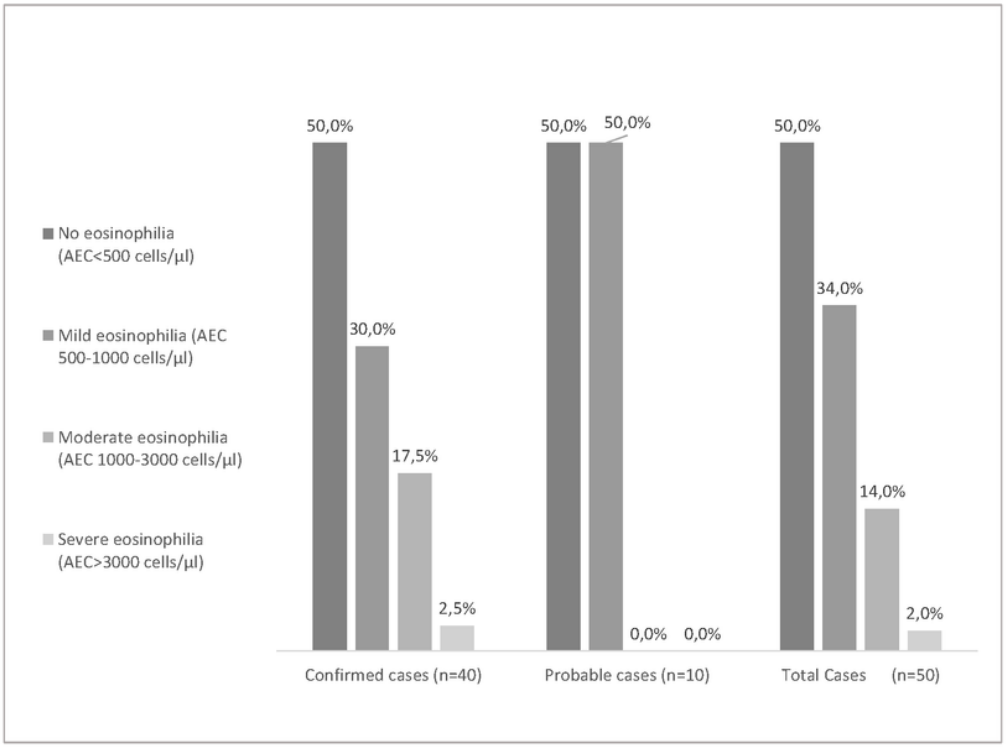


Figure 3

Grades of eosinophilia (by relative frequency) in schistosomiasis cases. AEC absolute eosinophil count in peripheric blood.

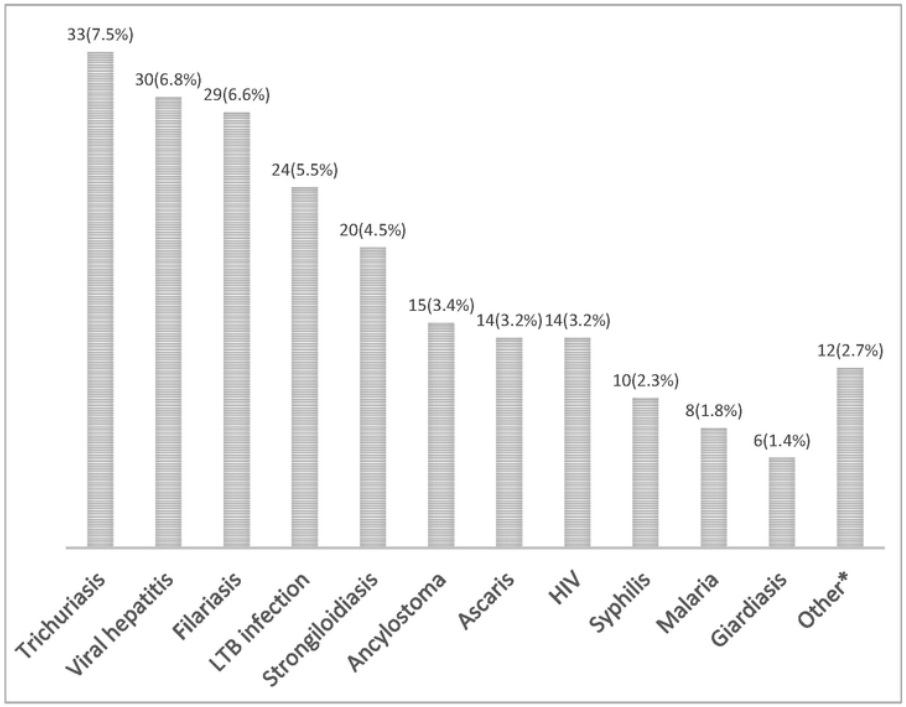


Figure 4

Relative frequency of newly diagnosed infections in the general cohort (n=440). HIV human immunodeficiency virus; LTB latent tuberculosis. *The category “other” included cases of amebiasis, gonorrhea and Mansonella, Toxocara canis, Taenia solium and Dicrocoelium dendriticum infections