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► To cite this version:

Emma Oliosi, Adéla Angoulvant, Anthony Marteau, Luc Paris, Olivier Bouchaud, et al.. Chronic schistosomiasis imported in France: A retrospective multicentre analysis of 532 patients, calling for international recommendations. *Travel Medicine and Infectious Disease*, 2023, 56, pp.102644. 10.1016/j.tmaid.2023.102644 . hal-04282967

HAL Id: hal-04282967

<https://hal.science/hal-04282967>

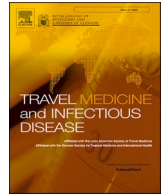
Submitted on 29 May 2024

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Chronic schistosomiasis imported in France: A retrospective multicentre analysis of 532 patients, calling for international recommendations

Emma Oliosi^{a,*}, Adela Angoulvant^b, Anthony Marteau^{a,c}, Luc Paris^d, Olivier Bouchaud^e,
Hélène Guegan^f, Pascaline Choinier^g, Pierre Tattevin^h, Jean-Pierre Gangneux^f,
Gaylord Delobreⁱ, Sandrine Houzé^j, Stéphane Jauréguiberry^{a,k,**}

^a Université Paris-Saclay, Service des Maladies Infectieuses et Tropicales, AP-HP, Hôpital Bicêtre, Le Kremlin Bicêtre, 94270, France

^b Université Paris-Saclay, Laboratoire de Parasitologie-mycologie, AP-HP, Hôpital Bicêtre, Le Kremlin Bicêtre, 94270, France

^c Université Sorbonne Paris Nord, Service de Parasitologie-Mycologie, AP-HP, Hôpital Avicenne, Bobigny, 93000, France

^d Sorbonne Université, Service de Parasitologie-Mycologie, AP-HP, Hôpital Pitié-Salpêtrière, Paris, 75013, France

^e Université Sorbonne Paris Nord, Service des Maladies Infectieuses et Tropicales, AP-HP, Hôpital Avicenne, Bobigny, 93000, France

^f Université Rennes, CHU de Rennes, Inserm, Irset (Institut de Recherche en Santé, Environnement et Travail) UMR_S 1085, Rennes, 35000, France

^g Sorbonne Université, Service de Pneumologie, AP-HP, Hôpital Tenon, Paris, 75020, France

^h Université Rennes 1, Service des Maladies Infectieuses et Tropicales, Hôpital Pontchaillou, Rennes, 35000, France

ⁱ Réseau Louis Guilloux, Rennes, 35000, France

^j Université Paris-Cité, Laboratoire de Parasitologie-Mycologie, AP-HP, Hôpital Bichat-Claude Bernard, Paris, 75018, France

^k Société Française de Médecine des Voyages, France

ARTICLE INFO

Keywords:

Bilharzia
Migrants
Parasitic diseases

ABSTRACT

Background: Schistosomiasis is a major public health issue for migrants. This study aims to describe the clinical presentation and management of imported schistosomiasis in France.

Methods: We included all new cases of schistosomiasis in patients aged ≥ 18 years, defined by a positive specific Western blot and/or a positive parasitological analysis of urine, stool or biopsy, between January 1, 2016, and December 31, 2019, in 4 laboratories in Paris and Western France.

Results: Over the study period, 532 patients were included. Mean age was 37 years (18–91), and 461/532 (87 %) were men. Among 476/532 (89 %) patients born in an endemic area, 433 (91 %) were born in sub-Saharan Africa. Most of the patients (405/532, 76 %) had only a positive serology, and 127/532 (24 %) had ova on microscopic examination. Among 361/532 (68 %) who had at least one urine, stool or biopsy analysis, microscopic analysis was positive in 127 (35 %). Imaging showed lesions compatible with schistosomiasis in 88/164 (54 %) patients with clinical symptoms and 13/29 (45 %) patients without ($p = 0.5$). Patients who arrived in France less than one year before diagnosis were more likely to have clinical symptoms than those who arrived in France 1–5 years and >5 years prior to diagnosis (52 %, 41 % and 43 %, respectively, $p = 0.03$). Two-hundred and seventeen patients (40.8 %) were left untreated.

Conclusion: Approximately 50 % of patients with imported chronic schistosomiasis have radiological abnormalities, whether they are symptomatic or not, and management is heterogeneous. Multidisciplinary international guidelines are requested to clarify the management of this neglected disease.

Emma OliosiStéphane JauréguiberryLuc ParisPascaline Choinier-
Adela AngoulvantAnthony MarteauSandrine HouzéPierre
TattevinHélène GueganOlivier BouchaudJean-Pierre GangneuxGaylord
Delobre

1. Introduction

Schistosomiasis is a major public health issue in tropical areas [1]. Active transmission is documented in 78 countries, and current estimates suggest that approximately 240 million people are infected

* Corresponding author. Service des maladies infectieuses et tropicales, Hôpital Bicêtre, APHP, Kremlin Bicêtre, France.

** Corresponding author. Service des maladies infectieuses et tropicales, Hôpital Bicêtre, APHP, Kremlin Bicêtre, France.

E-mail addresses: emma.oliosi@aphp.fr (E. Oliosi), stephane.jaureguiberry@aphp.fr (S. Jauréguiberry).

worldwide [1–3]. Over 90 % of infected people live in Sub-Saharan Africa. In nonendemic settings, schistosomiasis is more frequently diagnosed among migrants than among travellers returning from endemic areas [4,5]. A recent meta-analysis reported a seroprevalence of 24.1 % among Sub-Saharan African migrants in nonendemic countries [6]. Chronic schistosomiasis is the most common presentation. It can lead to life-threatening complications such as periportal fibrosis and bladder carcinoma [7,8]. However, awareness of the burden of schistosomiasis in the migrant population appears to be low among European health professionals.

European Centre for Disease Prevention and Control guidelines recommend only serological screening for newly arrived migrants [9]. French guidelines suggest performing direct parasitological exams of urine and stools as well as biopsies [10,11]. Serology is the most sensitive method but does not assess morbidity, while parasitological examination of urine and stools is associated with close to 100 % specificity but suboptimal sensitivity [12]. In patients who test positive, ultrasonography and CT scans are valuable tools to explore schistosomiasis-related morbidity. The description of lesions should rely on the Niamey classification, which is still poorly known by physicians and radiologists [13]. Overall, the stratification and indications of these exams are not well established. Thus, the diagnostic workup is a challenging combination of clinical, biological and radiological methods.

The standard treatment for schistosomiasis consists of a single oral dose of 40 mg/kg praziquantel [1,8]. However, a single agent may fail to achieve parasitological eradication. In endemic areas, it is clearly demonstrated that the repetition of doses is necessary to significantly lower the parasite load [14]. In nonendemic areas, one to three doses of praziquantel have been associated with treatment failures in 9.5–35 % of patients in several studies [15–17]. One recent review has shown the wide heterogeneity of therapeutic regimens reported in nonendemic settings [18]. To date, no prospective study has compared the efficacy of single and repeated doses in nonendemic areas. Considering the absence of recent guidelines concerning chronic schistosomiasis in nonendemic countries and the suboptimal awareness of this disease by most physicians, we aimed to describe the presentation, diagnosis and treatment of chronic schistosomiasis imported into France.

2. Methods

2.1. Study design and setting

This retrospective observational study was conducted using data from four parasitology labs in four referral centres for tropical medicine: Bicêtre Hospital, Avicenne Hospital and Bichat Hospital in the greater Paris region and Rennes Teaching Hospital in Brittany, Western France. These laboratories analysed samples from inpatients and outpatients followed up in 7 hospitals and 36 wards that recruit cases of schistosomiasis and immigrant-related diseases. We followed the STROBE guidelines for observational studies.

2.2. Participants

We selected all cases of schistosomiasis diagnosed by these laboratories from January 1, 2016, to December 31, 2019. The main inclusion criteria were (i) age ≥ 18 years at the time of diagnosis and (ii) diagnosis of schistosomiasis by at least one positive *Schistosoma*-specific test among the following: Western blot (WB) detection of anti-*Schistosoma* antibodies, microscopic *Schistosoma* spp. egg identification in urine, stool or histopathological samples. The exclusion criteria were (i) diagnosis of schistosomiasis before 2016, (ii) cases of acute schistosomiasis (based on the review of medical files), (iii) cases with missing clinical data and (iv) lack of consent. The diagnosis was defined as confirmed (positive microscopic analysis) or probable (positive WB assay). Patients with clinical symptoms compatible with schistosomiasis and/or a positive urine strip test for blood or leucocytes were

categorized as symptomatic. Immigrants were categorized into three groups depending on the time since arrival in France: <1 year, 1–5 years or >5 years.

2.3. Parasitological methods

Four serological methods were used.

- ELISA Bordier*, considered positive if the ratio of patient optical density over control optical density was greater than 1;
- Hemagglutination Cellognost Schistosomiase Dade Behring*, considered positive if the titre was $>$ or $=$ to 1/32;
- Hemagglutination ELL.H. A *Schistosoma* by ELITech group*, considered positive if the titre was $>$ or $=$ to 1/160;
- *Schistosoma* western blot IgG LDBIO Diagnostics*, with the presence of a 22–24 kDa band and/or a 30–34 kDa band considered positive.

In all participating laboratories, first-line serological testing was performed with ELISA and/or haemagglutination. If the first-line test was positive, WB was used as confirmation. In certain cases of strong suspicion, WB could be performed even if first-line tests were negative. If WB was negative, the final serology was deemed as negative.

Urine specimens were examined both fresh and after concentration. Stool specimens were examined both fresh and after concentration along with two different diphasic methods: Belanger (with ethyl acetate instead of ether) and MIF (Merthiolate-Iode-Formol solution, for the aqueous phase).

2.4. Variables and data sources

We collected inclusion criteria, demographic and clinical data (gender, age, country of origin or endemic regions visited, clinical symptoms), the results of imaging studies when performed, and biological data (serology, microscopic examination, and eosinophil count), as well as anti-schistosomiasis treatment and follow-up. All the data were collected anonymously in a password-protected Excel file. All medical records were reviewed by 2 infectious and tropical diseases specialists (E.O. and S.J.).

2.5. Statistical analysis

Qualitative variables were described using numbers and percentages (%). The mean, maximum and minimum were used for quantitative variables. Analysis was first performed on the whole study population. Then, subgroup analyses were performed, and variables were compared between subgroups by univariate analyses. To compare symptomatic and asymptomatic patients, as well as newly arrived immigrants and other immigrants, we used a two-sided χ^2 test for categorical variables and Student's *t*-test for continuous variables. We considered a *p* value < 0.05 as significant. All statistical analyses were performed with R studio© version 3.3.3 (The R Foundation for Statistical Computing).

2.6. Missing data

Patients with entirely missing files were excluded from the study. To assess that this would not generate too much bias, we compared excluded and included patients in terms of demography and microbiology tests. The number of missing data for each variable was specified.

2.7. Ethical statement

This study was conducted with the approval of the Ethical Committee of Paris-Saclay University (CER-Paris-Saclay-2020-092). In line with French legislation, it was also registered under the direction of the Clinical Research Department of APHP (Assistance Publique-Hôpitaux de Paris), reference 201071, and on [ClinicalTrials.gov](https://www.clinicaltrials.gov) under the number

NCT04810741. No individual written consent was sought, but an information letter was sent to all patients with the option of withdrawing from the study.

3. Results

3.1. Diagnosis

We analysed the data of 532 patients (Fig. 1). There was no significant difference between patients included and those excluded due to missing data (Supplementary Table 1). Patient characteristics, comorbidities and countries of origin are displayed in Table 1 and Supplementary Figure 1.

There were 405/532 (76.1 %) probable cases and 127/532 (23.9 %) confirmed cases. Anti-*Schistosoma* antibody detection was performed for 499/532 (93.8 %) patients. Different serological methods were used: enzyme-linked immunosorbent assay for 491/532 (92.3 %) patients, haemagglutination for 317/532 (59.6 %) patients and WB for 497/532 (93.4 %) patients. The positivity rates for ELISA and haemagglutination tests were 457/491 (93.1 %) and 138/317 (43.5 %), respectively. Western blot was positive for 493/497 (98.8 %) tested patients. Microscopic examination of stool, urine and/or histopathological samples was performed for 361/532 (67.9 %) patients: 127 patients had at least one positive microscopic examination with ova identification (127/361, 35.2 %). Table 2 shows details of the findings of the microscopic examination. Three different species of *Schistosoma* were identified: *Schistosoma mansoni* (*Sm*), *Schistosoma haematobium* (*Sh*) and *Schistosoma intercalatum* (*Si*). Mixed infections were identified in 6 samples: one stool sample with *Si* and *Sm* eggs, one stool sample with *Sh* and *Sm* eggs, one urine sample with *Si* and *Sh* eggs, two urine samples with *Sh* and *Sm* eggs and one intestinal biopsy with *Sh* and *Sm* eggs. Quality and quantity of samples was not routinely notified. Only one hospital always specified the urine sample quantity among the 71 samples analysed there. Among those, 32/71 (45.1 %) lacked quality due to an insufficient quantity of urine. Concerning stool analysis, 124 patients had at least two available stool samples, and the mean interval between samples was 2.8 days. Among patients with only two available stool examinations (N = 29), 6/29 (20.7 %) had a negative first sample but a positive second sample, and 23/29 (79.3 %) had two negative samples. Among patients with three available stool examinations (N = 95), 7/95 (7.4 %) had a negative first sample but a positive second sample, and 2/95 (2.1 %) had a negative first and second sample but a positive third sample.

3.2. Clinical, biological, and imaging study data, and treatment

Two hundred forty patients (45.1 %) had at least one clinical

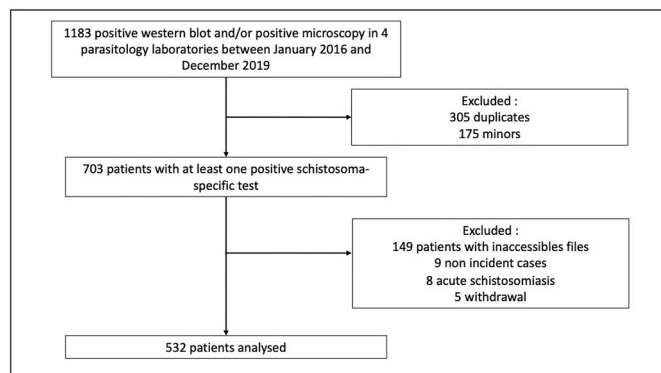


Fig. 1. – Study flow chart of selected adult cases (≥ 18) of chronic schistosomiasis in 4 parasitology laboratories providing results for 36 wards in metropolitan France.

Table 1

Epidemiological and biological features of 532 patients diagnosed with chronic schistosomiasis.

Characteristics	No (%) of patients
Mean age in years (min-max)	37.2 (18–91)
Male	461/532 (87)
Region of origin ^a	
Sub-Saharan Africa	433/491 (88.2)
North Africa	31/491 (6.3)
Metropolitan France	15/491 (3.1)
French West Indies (Antilles: Guadeloupe or Martinique)	9/491 (1.8)
Other ^b	3/491 (0.6)
Type of patient	
Traveller	15/532 (2.9)
Native of an endemic country	476/532 (89.5)
Living in an endemic country	1/476 (0.2)
Immigrant < 1 year ^c	155/476 (32.6)
Immigrant 1–5 years ^c	119/476 (25)
Immigrant > 5 years ^c	115/476 (24.2)
Comorbidities ^d	
HIV	62/532 (11.7)
Hepatitis B virus seropositivity	139/532 (26.1)
Hepatitis C virus seropositivity	19/532 (3.6)
Tuberculosis ^e	59/532 (11.1)
Chronic kidney disease ^f	15/532 (2.8)
Mean weight in kg (min-max)	71.2 (40–138)
Biological results at baseline	
Median eosinophil count/mm ³ (Q1-Q3)	271 (130–670)
Patients with eosinophils > 500/mm ^{3g}	182/514 (35.4 %)
Mean creatinine in $\mu\text{mol/L}$ (IQR)	83 (70–93)
Patients with creatinine > 100 $\mu\text{mol/L}^h$	58/397 (14.6 %)
Mean SGPT in U/L (Q1-Q3)	25 (18–38)
Mean SGOT in U/L (Q1-Q3)	27 (21–35)
Patients with cytolysis ⁱ	142/375 (37.9)
Mean gamma-glutamyl transferase in U/L (Q1-Q3)	32 (20–61)
Mean alkaline phosphatase in U/L (Q1-Q3)	72 (59–90)
Patients with cholestasis ^j	156/342 (45.6)
Mean haemoglobin in g/dL (Q1-Q3)	14.1 (12.7–15.2)
Patients with anaemia ^k	73/439 (16.6)

^a Information was available for 491 (92.3 %) patients.

^b Irak, Philippines, Brazil.

^c Immigrant arrived for less than one year/between 1 and 5 years/more than 5 years at the time of diagnosis.

^d Most relevant comorbidities are presented in this table. Concerning cardiovascular risk factors, 15/532 (2.8 %) patients had type 2 diabetes, 27/532 (7 %) had hypertension and 5/532 (0.9 %) had dyslipidaemia.

^e Past medical history or active infection.

^f Two patients had vascular nephropathy: the other case was of undetermined cause (chronic schistosomiasis could not be excluded).

^g Eosinophils above 500/mm³ either on biological examination or only reported in clinical files. Information was available for 514 patients.

^h Creatinine was available for 397 patients.

ⁱ Cytolysis was defined as either SGPT or SGOT above 35 U/L. SGPT and SGOT were available for 375 patients.

^j Cholestasis was defined as either GGT >36 U/L or PAL >116 U/L. GGT and PAL were available for 342 patients.

^k Anaemia was defined as haemoglobin <12.5 g/dL. Haemoglobin was available for 439 patients.

symptom compatible with chronic schistosomiasis. Fifty-five patients (10.3 %) had no symptoms and a negative urine strip test. The clinical examination was fully missing for 39/532 patients (7.3 %), and the urine strip test was missing for 198/532 patients (37.2 %). Symptoms are detailed in Supplementary Table 2. One hundred eighty-two patients (182/514 with available information, i.e., 35.4 %) had eosinophilia above 500/mm³.

Two hundred eighty patients (52.6 %) had at least one imaging study, which was abnormal in 131/280 (46.8 %). Different imaging techniques were performed: 186/532 patients (35 %) underwent ultrasonography, the results of which were abnormal in 52/186 (28 %) cases; 138/532 patients (25.9 %) had a CT scan, the results of which were abnormal in 93/138 (70.3 %) cases; and 16/532 patients (3 %) had an

Table 2

Microscopic examination in 532 patients with a diagnosis of chronic schistosomiasis before treatment (stool and/or urine and/or biopsy).

	Patients with a microscopic analysis	Patients with a positive microscopic analysis
		No (% of the number of patients with a positive microscopic analysis)
Stool examination	242/532 (45.5)	45/242 (18.6) ^(a)
Stool examination n°1	242/242 (100)	30/242 (12.4) ^(b)
Stool examination n°2	124/242 (51.2)	22/124 (17.7)
Stool examination n°3	95/242 (39.3)	15/95 (15.8)
Urine examination ^(a)	275/532 (51.7 %)	65/275 (23.6)
Urine examination n°1	275/275 (100)	61/275 (22.2)
Urine examination n°2	52/275 (18.9)	6/52 (11.5)
Urine examination n°3	22/275 (8)	5/22 (22.7)
Bladder biopsy	30/532 (5.6)	27/30 (90)
Hepatic biopsy	11/532 (2.1)	7/11 (63.6)
Intestinal biopsy	13/532 (2.4)	6/13 (46.2)
Colposcopy	1/532 (0.2)	1/1 (100)

^a Number of patients with at least one positive microscopic result.

^b Number of patients with first microscopy positivity.

abdominal X-ray, the results of which were abnormal in 11/16 (68.8 %) cases. Table 3 details the abnormalities attributable to schistosomiasis identified by imaging studies. Among patients with clinical symptoms, 164/240 (70 %) had at least one ultrasonography or CT scan, compared to 29/55 (52.7 %) patients with no clinical symptoms ($p = 0.03$). Ultrasonography or CT scans showed lesions compatible with schistosomiasis in 88/164 (53.7 %) patients with clinical symptoms and 13/29 (44.8 %) patients with no clinical symptoms ($p = 0.5$).

Treatment was prescribed for 315/532 patients (59.2 %), who predominantly received praziquantel (312/315, 99 %). Information was missing for the 3 other patients. Different treatment strategies were used: 191/315 (60 %) patients received one dose of praziquantel 40 mg/kg; 92/315 (30 %) patients received two doses of praziquantel, with a mean interval of 57.9 days; and 18/315 (6 %) patients received other

Table 3

Imaging abnormalities compatible with schistosomiasis in patients with a diagnosis of chronic schistosomiasis among patients with at least one imaging exam (regardless of the imaging exam performed).

Type of abnormalities	Total number of patients with abnormalities (%) (N = 131)
Urological abnormalities	89/131 (67.9 %)
Urinary tract calcifications	54/89 (60.7 %)
Urinary tract thickening	31/89 (34.8 %)
Kidney atrophy	5/89 (5.6 %)
Pyelocalyceal dilatation	14/89 (15.7 %)
Hepatosplenic abnormalities^a	43/131 (32.8 %)
Hepatomegaly	29/43 (67.4 %)
Splenohegaly and portal hypertension	21/43 (48.8 %)
Other lesions	
Colitis/ileitis	3/131 (2.3 %)
Abdominal lymphadenopathy	5/131 (3.8 %)
Pulmonary nodules ^b	3/131 (2.3 %)
Myelitis/epiduritis	2/131 (1.5 %)

^a Of 43 patients with hepatosplenic abnormalities, 18 were also infected with HBV or HCV without liver biopsy, so the hepatosplenic abnormalities could have been due to both viral and parasitic lesions.

^b Pulmonary lesions described in the table were considered by the radiology team as secondary to schistosomiasis rather than other diagnosis such as tuberculosis or other differential diagnosis.

treatment regimens (Supplementary Table 3). The treatment strategy with praziquantel prescription was not specified for 11 patients. No severe side effects were reported: 7 patients reported mild side effects such as abdominal discomfort and rash. Among the 315 treated patients, 178 (56.5 %) went to a follow-up visit, 51 (16.2 %) had a visit planned but did not show up, and 86 (27.3 %) had no visit planned. In the subgroup of 127 patients with a positive microscopic examination, 96 (75.6 %) were treated. Among those with a posttreatment sample (52/96, 54.2 %), eggs were still found in 19 patients (36.5 %). Supplementary Table 4 shows the details of the microscopic exams after treatment.

Fig. 2 shows a subgroup comparison of the clinical presentation and management of patients depending on (2-A) the time between arrival in France and schistosomiasis diagnosis and (2-B) clinical symptoms. The mean age was 30.7, 33.4, and 45.5 years for immigrants diagnosed within one year, 1–5 years, and more than 5 years after arrival in France, respectively ($p < 0.001$).

4. Discussion

This study highlights the heterogeneity of the clinical presentation and management of chronic schistosomiasis in a nonendemic country. A

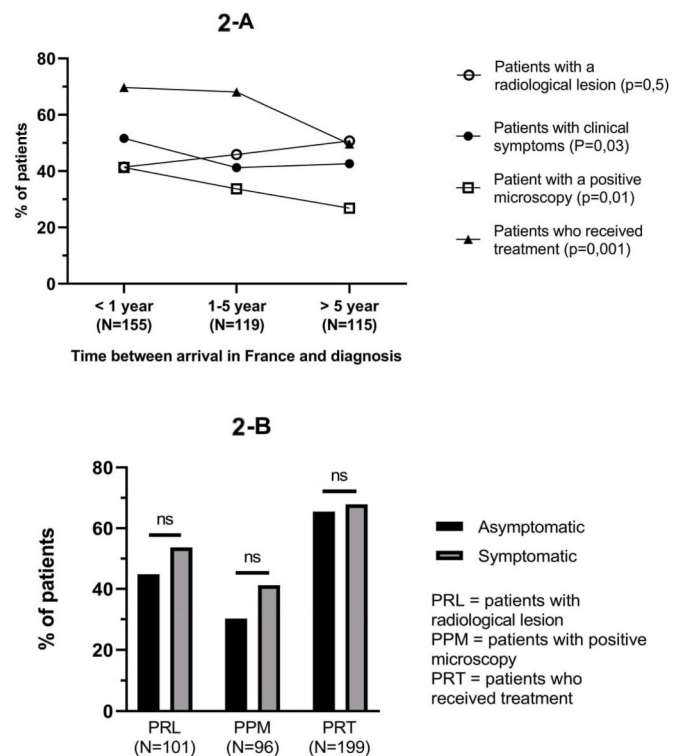


Fig. 2. Comparison of the clinical presentation and management of patients depending on (2-A) the time between arrival in France and schistosomiasis diagnosis among patients with a diagnosis of chronic schistosomiasis and (2-B) clinical symptoms. 2-A shows a subgroup comparison using a two-sided chi-2 test between newly arrived migrants (less than one year before diagnosis), migrants who arrived between one to five years before diagnosis and migrants who arrived more than 5 years before diagnosis. The three groups are independent but represent also the potential evolution over time of schistosomiasis. Variables statistically associated with the time between arrival in France and schistosomiasis diagnosis were the presence of clinical symptoms, a positive microscopic examination and praziquantel treatment ($p = 0.03$, $p = 0.01$, $p = 0.001$, respectively). 2-B shows a subgroup comparison between asymptomatic and symptomatic patients. Patients with clinical symptoms compatible with schistosomiasis and/or a positive urine strip test for blood or leucocytes were categorized as symptomatic. There was no significant difference between symptomatic patients compared to asymptomatic patients in terms of radiological lesions, positive microscopy and treatment received.

majority of patients had no clinical symptoms and no positive microscopic examination, but asymptomatic radiological lesions were frequent, almost 50 %. Ultimately, the few patients treated and the loss to follow-up are other major issues in this precarious immigrant population. Although European and French recommendations exist, they are not well known by colleagues because the disease remains rare and is not well adapted to the clinical situations of these patients [9–11,19]. Specific and adapted guidelines are now needed.

In our study, the mean age (i.e., 37 years) and sex ratio (87 % of males) were different from data found in demographic studies of newly arrived immigrants from Africa in France, which revealed a mean age of 23 years and a 1:1 sex ratio [20]. However, our findings are consistent with data from medical studies of schistosomiasis, since a higher proportion of males has been frequently reported among patients with schistosomiasis in nonendemic countries but not in African series [21–25]. Male prevalence could be the consequence of better access to medical care among men compared to women. We had only one confirmed case of female genital schistosomiasis, despite a supposedly high prevalence among women from endemic countries [26].

We found no correlation between clinical symptoms and imaging abnormalities. Nearly half of the asymptomatic patients (44.8 %) had urinary tract and/or hepatosplenic lesions visible on imaging studies, whether or not eggs were identified through microscopic examination. A recent Italian study on urogenital schistosomiasis found a similar proportion of abnormal ultrasonography in patients without clinical symptoms (67 %) but focused only on urogenital schistosomiasis [15]. Additionally, in this study, there was a significant difference compared to patients with clinical symptoms (83 % of whom had imaging abnormalities, $p < 0.02$), whereas in our population, this difference was not significant (55 % had imaging abnormalities, $p = 0.5$) [15]. This illustrates the lack of correlation between symptoms and anatomical anomalies due to the disease and should be taken into account. The question of routine imaging, such as ultrasound or CT scan, for all patients regardless of presenting symptoms arises.

Serology was the main diagnostic tool in our cohort, whereas microscopic examination was not often performed (51.7 % had at least one urine sample). When it was performed, it was not very sensitive (23.6 % for urine analysis and 18.6 % for stool analysis). This is consistent with other studies reporting sensitivities between 20.0 and 44.5 % for both types of microscopic examination [27,28]. Repeating stool samples may improve sensitivity [29]. In our study, almost one-third of patients with more than one stool exam had eggs identified through the second or third stool sample, whereas the first sample was negative. However, in real life, it is complicated to obtain several samples because of erratic follow-up, low acceptability of this type of sampling and the price of biological analysis. The quantity and timing of urine samples are also essential. Our study was not designed to analyse the quantity of urine collection, but data from one of the hospitals suggested that the quantity was inadequate in 45.1 % of the cases. The WHO guidelines recommended exercising before urine collection [1]. However, a recent comparative study conducted in Ivory Coast did not find any association between *S. haematobium* egg excretion and exercise [30]. It is nonetheless advisable to perform microscopic examination tests, as they may allow us to determine the species of *Schistosoma* involved, the parasite load and the follow-up if initially positive. PCR techniques are being developed and will likely improve the diagnosis. Such methods clearly outperformed microscopic examination in recent studies while providing species identification [31–34]. Moreover, sampling is easier, as PCR can be performed on small quantities of stool and urine. Finally, PCR could be relevant for follow-up after treatment. Antigenic techniques are being developed also, as detection of circulating cathodic antigen in urine. Sensitivity is quite variable between studies and seems to depend on the parasite load [8,12].

The treatment of choice for schistosomiasis remains praziquantel, as recommended by international guidelines [9]. However, 40 % of the patients were not treated despite proper diagnosis in this real-life study.

Lack of knowledge concerning schistosomiasis and proper follow-up can lead to undertreatment. Follow-up after treatment with parasitological exams showed presence of egg in 36.5 % of patients, however the laboratories did not distinguish between viable and dead eggs so we cannot assert that all these patients had treatment failure. However, many studies have shown that failure rates are significant in nonendemic settings, from 9.5 % to 35 % [15–17]. According to studies in endemic countries, repeated doses may be necessary to sterilize urine and stools, especially when the parasite load is high [35–37]. The repetition of doses and intervals between doses have not been properly evaluated in nonendemic countries. Finally, we highlighted the difference between younger and newly arrived immigrants compared to older immigrants (Fig. 2). The subgroup of newly arrived immigrants stood out as more symptomatic, with more frequent identification of eggs through microscopic examination of stools and urine. This is consistent with data from another study where the prevalence was maximal in patients aged 10–30 years compared to older patients [38]. Infections in younger immigrants were probably more recent and had higher parasite loads, but these characteristics did not result in more anomalies on imaging studies. Comparatively, older immigrants had fewer symptoms or positive microscopy and were thus treated less frequently even if they had radiological lesions as younger immigrants. The subgroup analysis comparing symptomatic and asymptomatic patients showed no significant difference in terms of radiological lesions, positive microscopy and treatment received (Fig. 2).

This study has some limitations. First, the retrospective design poses the risk of missing data, especially in such a precarious population. Follow-up can be particularly difficult in migrants without any resources or social assistance. We had to exclude some patients because we missed too much data in their files. However, in terms of demography and diagnosis, their data did not differ from the included patients, which suggests a fair global representativity. Inclusions through laboratory results were quite exhaustive, although we might have missed some outpatients who were managed in the hospital but were diagnosed in other laboratories. Most of the cases were classified as probable and not confirmed, which could be a limit but also reflects the real-life management of this disease. Sensitivity of microscopic examination is limited and it seemed relevant to include probable cases in order to question how medical doctors deal with them. The heterogeneity in the choice of imaging studies, microscopic examinations, and treatment may be related to limited knowledge about this neglected disease among many medical doctors. Also, we could not rule out the possibility that part of the results might partly be linked to differential diagnosis, for example other helminthiasis responsible for eosinophilia, or viral hepatitis and haemoglobinopathies for abnormal liver and spleen exams. First-line serological techniques were also slightly different between laboratories. Haemagglutination was used mostly in one of the laboratories and was less sensitive in our study. Finally, we were not able to evaluate the effectiveness of the treatments received, with the exception of patients with a positive urine or stool test before treatment. There is no clear definition for cure in asymptomatic patients, and the improvement of lesions on imaging requires clinical follow-up and repeated radiological assessment [13]. Improvement on CT scan or echography requires follow-up after treatment, and we were unable to determine such evolution. Despite these limitations, this study provides a comprehensive overview of the management of chronic schistosomiasis in a nonendemic country. The multicentric design and the large number of patients included reinforce the external validity of our results.

From a medico-economic point of view, a recent study highlighted that presumptive treatment of all immigrants from endemic countries was an effective alternative in terms of costs, survival and sequelae [39]. However, this attitude prevents morbidity assessment, which is essential to detect preclinical lesions (such as carcinoma) and implement follow-up. The distinction between different nosological frameworks, such as newly arrived and more-symptomatic immigrants compared to older immigrants, may help clinicians choose the best strategy of

diagnosis and treatment. Our data suggest that imaging studies should be systematically performed when schistosomiasis is diagnosed, whether or not the patient has compatible symptoms or eggs identified on microscopic examination. Treatment options such as the repetition of praziquantel doses should be discussed thoroughly to implement new guidelines. In our center, we implemented systematic microscopic examination and imaging for all seropositive patients, and treatment with 3 doses of praziquantel at 2 months intervals.

In conclusion, the management of chronic schistosomiasis in non-endemic countries can be challenging to nonspecialists. Optimal management would require more specific guidelines to take into consideration the diversity of clinical presentations. Screening, imaging assessment and treatment of all newly arrived immigrants from endemic countries but also for all patients without previous history of screening is essential.

Meetings at which some preliminary results were presented

Journées Nationales d'Infectiologie 2021, TropNet meeting Madrid 2022.

Grants or financial support

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

The data that support the findings of this study are available from the corresponding author, E. O., upon reasonable request.

Declaration of competing interest

The authors declare no conflicts of interest related to the subject of the article.

Acknowledgements

We thank all patients, staff, clinicians, and biologists at all the participating centres.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tmaid.2023.102644>.

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