Morbidity associated with *Schistosoma mansoni* infection in northeastern Democratic Republic of the Congo

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Short title: Schistosomiasis morbidity burden in Ituri province in northeastern Congo

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Abstract

Background

Controlling morbidity is the main target of schistosomiasis control. Yet, only rarely do we assess morbidity linked to Schistosoma sp. infection. In the Democratic Republic of Congo (DRC), and particularly in the northeastern Ituri province, morbidity associated with Schistosoma mansoni infection is unknown. For this reason, we aimed to assess intestinal and hepatosplenic morbidity associated with S. mansoni infection in Ituri province.

Methods / Principal Findings

In 2017, we conducted a cross-sectional study in 13 villages in Ituri province, DRC. S. mansoni infection was assessed with a Kato-Katz stool test (2 smears) and a point-of-care circulating cathodic antigen (POC-CCA) test in urine. A questionnaire was used to obtain demographic data and information about experienced intestinal morbidity. Each participant underwent an abdominal ultrasonography examination to diagnose hepatosplenic morbidity. Of the 586 study participants, 76.6% tested positive for S. mansoni. Intestinal morbidity, such as abdominal pain (52.7%), diarrhea (23.4%) and blood in the stool (21.5%) in the previous two weeks, was very frequent, as was hepatosplenic morbidity, such as splenomegaly (60.1%), hepatomegaly (23.2%) and abnormal liver parenchyma pattern (52.6%). Hepatomegaly (adjusted odds ratio [aOR] 2.04, 95% confidence interval [CI] 1.27–3.26, P=0.003) and splenomegaly (aOR 1.69, 95% CI 1.17–2.45, P=0.005) were positively associated with S. mansoni infection at the individual level. At the village level, S. mansoni prevalence was positively associated with the prevalence of hepatomegaly and splenomegaly. Higher S. mansoni infection intensities were associated with diarrhea, blood in the
stool, hepatomegaly, splenomegaly and with liver parenchyma, pathology pattern D-E. Four study participants were diagnosed with ascites and five reported hematemesis.

Conclusions/Significance: Our study documents a high burden of intestinal and hepatosplenic morbidity associated with *S. mansoni* infection status in Ituri province. The results call for targeted interventions to address both *S. mansoni* infection and related morbidity.

Keywords: *Schistosoma mansoni*; Ituri province; Democratic Republic of Congo; infection prevalence; infection intensity; hepatosplenic morbidity
Author Summary

Schistosomiasis caused by *Schistosoma mansoni* is of great public health importance in sub-Saharan Africa. The World Health Organisation (WHO) recommends that control efforts aim to reduce morbidity through large scale intervention programmes. However, intestinal and liver morbidity is rarely assessed in such control programmes. Hence, little is known about (i) the magnitude of the intestinal and liver morbidity burden in a given community, or about (ii) the morbidity associated with *S. mansoni* infection, specifically. We conducted a (cross-sectional) study in which we assessed intestinal morbidity by questionnaire and liver morbidity by abdominal ultrasonography. Further, we determined the infection status of the study participants using standard diagnostic procedures (Kato-Katz technique and point-of-care cathodic circulating *S. mansoni* antigen [POC-CCA] test in urine). Among 586 study participants, six years and older, from 13 villages in Ituri province, DRC, we observed a high degree of intestinal (e.g. 23.4% with diarrhoea, 21.5% with blood in stool) and hepatosplenic morbidity (e.g. 60.1% with enlarged spleen, 23.2% with enlarged liver). *S. mansoni* infection was associated with liver and spleen enlargement. Likewise, *S. mansoni* infection intensity was linked to diarrhoea, to liver and spleen enlargement and to pathological changes in the liver parenchyma. At village level, we observed that the prevalence of enlarged liver and spleen among patients increased with the prevalence of *S. mansoni* infection. We conclude that the population of Ituri province carries an alarming burden of intestinal, liver and spleen morbidity associated with *S. mansoni* infection. Therefore, a comprehensive control programme to address this infection and disease burden is urgently required.
Introduction

Schistosomiasis is a neglected tropical disease (NTD) caused by several Schistosoma species. Chronic infection may result in damage to multiple organs, depending on the species and other factors, such as infection intensity. The adult worm of Schistosoma mansoni dwells in portal veins. The daily migration to the mesenteric veinlets that drain the intestines are used to deposit the eggs. Eggs release enzymes that provoke inflammation, which in turn facilitates the transition of the egg into the intestinal lumen. Some eggs may be carried in the blood stream to the liver, where they remain in the liver tissue. The immunopathological processes around the eggs trapped in the intestinal and hepatic tissues are the basic components of schistosomiasis’ pathological development [1]. The pathology results from immune-mediated damage to host cells and tissues. Eggs release enzymes that trigger the formation of granulomas. These granulomas have both a protective and frequently pathological role. Once the granulomas are formed, the excess collagen and other extracellular matrix material deposited around them cause scarring. In the intestines, inflammation may induce diarrhoea, whereas granulomas may cause polyposis with ulcers and recurrent bleeding. In the liver, the scars may disrupt liver function. In severe cases, they can obstruct the portal veins, leading to portal hypertension and, later, to oesophageal varices and then to haematemesis and melena, the main direct causes of death with S. mansoni infection. The granulomatous reaction triggered by S. mansoni infection may lead to splenomegaly, hepatomegaly, liver fibrosis, and ultimately, to accumulation of tissue fluid in the mesenteries and abdominal cavity, known as ascites [2]. Chronic schistosomiasis can lead to anaemia, stunted growth and impairment of cognitive development [3, 4]. Many infected people, even those with considerable infection intensity, may remain
asymptomatic or experience only non-specific symptoms, such as nausea, headaches, fever, fatigue
and abdominal pain [5].

In the Democratic Republic of Congo (DRC), little information about the infection burden of schistosomiasis is available and no reports on morbidity due to *S. mansoni* exist. Several studies conducted in neighbouring Uganda, however, show high morbidity and considerable mortality linked to *S. mansoni* infection [2, 6, 7]. In our study, we determined the infection burden of *S. mansoni* in Ituri province, DRC, and report on its association with morbidity.
Materials and Methods

Ethics statement

This study was approved by the Swiss Ethical Commission (Ref. No. UBE-15/78) and by the University of Kisangani’s Research Ethical Commission, (Ref No: CER/003/GEAK/2016). Research authorization was granted by the Nyankunde Higher Institute of Medical Techniques (Ref No 70/ISTM-N/SGAC/2017), Bunia, DRC. Permission for field work was obtained from the Ituri Provincial Health Division (Ref. 054/433/DPS/IT/06/2016 and Ref. 054/472/DPS/IT/06/2017) and from all relevant health districts. Prior to enrolment, the study objectives and procedures were explained to each participant in the local language and all of their questions were answered. Written informed consent was obtained from all study participants aged 15 years and older. Parents or legal guardians signed consent forms for participants aged <14 years. Participants diagnosed with S. mansoni were treated with praziquantel (40mg/kg) [8]. All participants received Mebendazole (500mg, single dose, Vermox®) for general deworming, in accordance with the DRC national deworming guidelines.

Study area

The study was conducted in 13 villages in Ituri province, northeastern DRC (geographical coordinates: 1.30°–3.60° latitude and 27.00°–31.40° longitude). Ituri province has an area of about 65,658 km² and is home to 5.2 million inhabitants from five different ethnic groups (Nilo-Hamites, Bantu, Nilotic, Sudanese, and Pygmy). The province is bordered by Lake Albert in the east, while several streams and rivers irrigate the province. These waterways are suitable environments for schistosome’s intermediate host snails. Schistosomiasis transmission has been documented in the province since colonial times, and mainly occurs along Lake Albert’s shores [9]. Only a small
proportion of the population residing in Bunia city has access to an adequate water supply. The majority of the population uses natural water bodies (springs, ponds, streams) as its main water source.

Study design and population

We conducted a cross-sectional, household-based, in-depth study of 13 purposively-selected villages across six health districts in Ituri province. The thirteen villages were Bankoko, Lumumba, Simbilyabo, Mangenengene, Kadjugi, Kindia, Gupe, Sukisa, Ngezi, Mambau, Mandima, Pekele, and Ndaru-Muswa. Households were randomly selected in each village and all willing household members aged 6 years and older, and present on the day of the survey were enrolled. Household visitors, as well as mentally and terminally ill persons were excluded.

The study incorporated household and individual questionnaires; anthropometric assessments; and parasitological, clinical, and abdominal ultrasonographic examinations.

Procedures

Individual questionnaires

All participants were invited to participate in an interview, conducted using a pre-tested questionnaire. This individual questionnaire focused on demographic, anthropometric, occupational, educational and religious characteristics, as well as on knowledge, attitude and practices related to *S. mansoni* infection and disease. The questionnaire also helped to assess for signs and symptoms related to schistosomiasis, such as diarrhoea or blood in the stool in the previous two weeks, and a history of hematemesis at any time, at least once.
Anthropometric measurements

Participants’ height and weight were measured by a Seca analog bathroom scale and height rod, and reported to the nearest half kilogram (0.5 kg) and half centimetre (0.5 cm), respectively. Participants’ body mass index (BMI) was also calculated (weight in kilograms divided by the square of the person’s height in metres, kg/m²).

Parasitological examination

Participants were asked to provide one faecal sample (approx. 5 grams of morning stool) in a labelled plastic container for testing with the Kato-Katz technique [10]. From each stool specimen, two thick smears of 41.7 mg [10] were prepared and examined by experienced technicians. To allow for hookworm assessment, all smears were examined by microscope within one hour after preparation. All slides were examined for *S. mansoni* within 24 hours after stool collection. One third of the prepared smears were checked by the principal investigator. All helminth eggs were counted and recorded for each species separately. The intensity of the helminth infection was calculated by multiplying the mean number of eggs found on the two slides by 24. The result was expressed as eggs per gram (EPG) of stool [4].

Participants were also asked to provide a urine sample (approx. 60 ml) in a pre-labelled, wide-mouth, plastic container, for the detection of circulating *S. mansoni* antigens using a point-of-care circulating cathodic antigen (POC-CCA) test. Both the stool and urine examinations were performed at the relevant village health centre facility.

The POC-CCA tests were performed according to the manufacturer’s guidelines (Rapid Medical Diagnostics, Pretoria, South Africa). Urine was examined on the day of collection. In cases where
the test was postponed until the next day, urine samples were kept in a solar fridge, at 2–8°C (Steca, Germany). Test results were deemed negative if the POC-CCA band did not appear within 20 minutes. Trace, weak, medium and strong coloured CCA bands were recorded as positive results. Questionable results were discussed among at least two technicians and the principal investigator.

Clinical examination

All participants underwent clinical and abdominal ultrasonography examinations. Clinical examinations consisted of physical examinations performed by an experienced physician and assisted by an experienced nurse.

Abdominal ultrasound examination

An abdominal ultrasound was performed for each participant, according to a pre-established protocol and using a 1.0 Mhz probe U-Lite Sonoscanner Ultraportable HD Ultrasound Unit (U-Lite, Sonoscanner, 6, Rue André Voguet, Paris, France). A portable generator (MK, China) and solar powered batteries (for remote villages) were used as electricity sources.

Participants were examined in a supine position. The size of the left and right liver lobe, the portal vein diameter, and the gall bladder length and width were measured. Organ parenchyma was observed. Liver parenchyma patterns (Figure S1) were assessed following the WHO/TDR guidelines [11]. The length and the width of the spleen were measured and its texture evaluated.

Data management and analysis

Data was entered in Excel and cross-checked against the data sheet. STATA, version14.2 software (Stata Corp, College Station, USA) was used for data management and analysis. Only participants
with a complete dataset were retained in the analysis (Figure 1). Seven age groups were established: (i) 6–9 years, (ii) 10–14 years, (iii) 15–19 years, (iv) 20–29 years, (v) 30–39 years, (vi) 40–49 years, and ≥50 years. Body mass index (BMI) was calculated and four categories were set: underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥30 kg/m²). Infection prevalence was expressed as the number of *S. mansoni*-positive individuals divided by the total number of participants examined. Infection intensity was estimated based on helminth egg counts per gram of stool (EPG) when examined with the Kato-Katz technique [10]. *S. mansoni* infection intensities were classified as light (1–99 EPG), moderate (100–399 EPG), and heavy (≥400 EPG) [4].

Arithmetic mean infection intensity was calculated. Categorical variables were presented as frequencies and percentages. Pearson’s chi-square ($\chi^2$) test was used to compare frequency distributions. A univariate logistic regression analysis was carried out to identify associations between *S. mansoni* infection status (outcome) and morbidity indicators (predictors) and/or demographic factors (age, gender). Predictors with a significance level of 20% or less, and age and gender variables were included in the multivariable logistic regression models. Odds ratios (OR), adjusted OR (aOR), and corresponding 95% confidence intervals (95% CI) were calculated. *P*-values <0.05 were considered statistically significant.
RESULTS

Study population

Data were collected between June and September, 2017. We enrolled participants from 13 purposely-selected villages across six health districts with an anticipated high prevalence of S. mansoni infection. Of the 949 individuals enrolled (Figure 1), 586 completed all study procedures and had a complete dataset, that is, one stool sample examined with two Kato-Katz smears, a urine sample tested with POC-CCA, two completed questionnaires, and a clinical and abdominal ultrasound examination.

Among those with a complete dataset, 342 (58.4%) were females, 330 (56.3%) were under 20 years of age, and 268 (45.7%) were underweight (Table 1). The prevalence of S. mansoni was 59.2%, 65.7%, and 76.6% according to Kato-Katz, POC-CCA and combined test results, respectively. Thirty-seven percent, 15.2% and 7.2% of the population had light-, moderate- and heavy-intensity infections, respectively. Infection with soil transmitted helminths (STH) was not common among participants, with only eight participants diagnosed with an STH infection. In contrast, intestinal symptoms were very common, with 52.7%, 23.4% and 21.5%, reporting abdominal pain, diarrhoea, and blood in the stool within the two weeks preceding the survey, respectively. Five participants (0.9%) had experienced hematemesis at least once in his/her life. Abdominal ultrasound examinations revealed that 60.1% of participants had splenomegaly, 23.2% had hepatomegaly, and 0.7% had ascites. Only 47.4% of the participants had a normal liver parenchyma (pattern A).
949 individuals from 13 selected villages enrolled

- 22 without questionnaire data
- 41 without stool samples

886 completed questionnaires

- 2 insufficient stool samples

884 provided at least 1 stool sample

- 254 without urine sample
- 44 without clinical and/or ultrasound examination

586 study participants with:
- one stool sample sufficient for 2 Kato-Katz smears
- urine sample
- completed questionnaires
- clinical examination
- ultrasound examination
Figure 1: Flowchart of participant inclusion/exclusion in the 2017 Ituri morbidity study across 13 villages.

Table 1: Study sample characteristics in the 2017 Ituri infection and morbidity study. Study conducted in 13 purposively-selected villages in Ituri province (n=586).

| Characteristics                              | N    | %    |
|----------------------------------------------|------|------|
| Gender                                       |      |      |
| Females                                      | 342  | 58.4 |
| Males                                        | 244  | 41.6 |
| Age categories (years)                       |      |      |
| 6 – 9                                        | 123  | 21.0 |
| 10 – 14                                       | 140  | 23.9 |
| 15 – 19                                       | 67   | 11.4 |
| 20 – 29                                       | 77   | 13.1 |
| 30 – 39                                       | 68   | 11.6 |
| 40 – 49                                       | 52   | 8.9  |
| ≥50                                          | 59   | 10.1 |
| Body mass index (kg/m² - categories)         |      |      |
| Obese (≥30.0)                                | 58   | 9.9  |
| Overweight (25.0–29.9)                       | 24   | 4.1  |
| Normal weight (18.5–24.9)                    | 236  | 40.3 |
| Underweight (<18.5)                          | 268  | 45.7 |
| S. mansoni infection                         |      |      |
| Kato-Katz test                               | 347  | 59.2 |
| CCA test                                     | 385  | 65.7 |
| KK+CCA*                                      | 449  | 76.6 |
| Infection intensity (KK only)                |      |      |
| Light                                        | 216  | 36.9 |
| Moderate                                     | 89   | 15.2 |
| Heavy                                        | 42   | 7.2  |
| Soil transmitted helminths                   |      |      |
| Trichuris trichiura                          | 3    | 0.5  |
| Ascaris lumbricoides                         | 1    | 0.2  |
| Hookworm                                     | 4    | 0.7  |
| Clinical findings                            |      |      |
| Diarrhoea                                    | 137  | 23.4 |
| Blood in stool                               | 126  | 21.5 |
| Abdominal pain                               | 309  | 52.7 |
| Hematemesis                                  | 5    | 0.9  |
| Ultrasound findings                          |      |      |
| Hepatomegaly (US)                            | 136  | 23.2 |
| Splenomegaly (US)                            | 352  | 60.1 |
| Ascites                                      | 4    | 0.7  |
| Pattern A                                    | 278  | 47.4 |
| Pattern B/C                                  | 214  | 36.6 |
| Pattern D/E                                  | 79   | 13.5 |
| Pattern F                                    | 15   | 2.5  |
* KK+CCA, combined any positive result by Kato-Katz and/or by point-of-care circulating cathodic antigen (POC-CCA); KK only, Kato-Katz results only with at least one egg in at least one of two smears.

**Morbidity associated with S. mansoni infection**

The results of the univariable risk analysis are presented in Table 2. Male participants were more likely to be infected with *S. mansoni* but the increased risk was not statistically significant (OR 1.22, 95% CI 0.82–1.81, *P*=0.318). *S. mansoni* infection was observed more frequently in younger age groups, with prevalence peaking among young adults (Figure 3). Participants aged 50 years and older had a statistically significant reduced risk of infection compared to children aged 6–9 years (Table 2, OR 0.49, 95% CI 0.26–0.92, *P*=0.024).

Hookworm infection was negatively associated with *S. mansoni* infection status (OR 0.10, 95% CI 0.10–0.98, *P*=0.015). Participants with a normal BMI (OR 2.11, 95% CI 1.14–3.92, *P*=0.016) and underweight individuals (OR 2.31, 95% CI 1.25–4.28, *P*=0.006) had a significantly higher risk of becoming infected with *S. mansoni* than those who were overweight. Study participants who reported an episode of diarrhoea within the preceding two weeks also had an increased risk of receiving an *S. mansoni* diagnosis (OR 1.69, 95% CI 1.03–2.78, *P*=0.038).

Diagnosed hepatomegaly (OR 1.67, 95% CI 1.01–2.74, *P*=0.042), splenomegaly (OR 1.50, 95% CI 1.02–2.20, *P*=0.040) and D/E liver parenchyma pattern (OR 1.87, 95% CI 1.04–3.36, *P*=0.032) were significantly associated with an *S. mansoni* infection.

The age distribution of reported diarrhoea and blood in stool, as well as the ultrasonographically assessed hepato- and splenomegaly displayed an age distribution resembling the *S. mansoni* infection with peaks in the adolescent and adult age groups (Figure 3).
Table 2: Morbidity associated with *S. mansoni* infection in the 2017 study. Results of the univariable analysis of data from 13 purposively-selected villages in Ituri province (n=586).

| Characteristics          | *S. mansoni* (+) | *S. mansoni* (-) | OR (95% CI)  | p-value |
|--------------------------|------------------|------------------|--------------|---------|
|                          | N=449            | N=137            |              |         |
|                          | n %              | n %              |              |         |
| Gender*                  |                  |                  |              |         |
| Females                  | 257 (57.2)       | 85 (62.0)        | 1.0          |         |
| Males                    | 192 (42.8)       | 52 (38.0)        | 1.22 (0.82–1.81) | 0.318   |
| Age categories (years)*  |                  |                  |              |         |
| 6 – 9                    | 92 (20.5)        | 31 (22.6)        | 1.0          |         |
| 10 – 14                  | 119 (26.5)       | 21 (15.3)        | 1.61 (0.94–2.76) | 0.078   |
| 15 – 19                  | 54 (12.0)        | 13 (9.5)         | 1.10 (0.58–2.07) | 0.769   |
| 20 – 29                  | 63 (14.0)        | 14 (10.2)        | 1.53 (0.81–2.89) | 0.184   |
| 30 – 39                  | 48 (10.7)        | 20 (14.6)        | 0.77 (0.42–1.42) | 0.396   |
| 40 – 49                  | 35 (7.8)         | 17 (12.4)        | 0.73 (0.38–1.43) | 0.359   |
| ≥50                      | 38 (8.5)         | 21 (15.3)        | 0.49 (0.26–0.92) | 0.024   |
| STH                      |                  |                  |              |         |
| *T. trichiura* (Y/N)*    | 1 (0.2)          | 2 (1.5)          | 0.15 (0.01–1.69) | 0.076   |
| *A. lumbricoides* (Y/N)  | 1 (0.2)          | 0 (0.0)          | na           |         |
| Hookworm (Y/N)*          | 4 (0.2)          | 3 (2.2)          | 0.10 (0.01–0.98) | 0.015   |
| Anthropometry*           |                  |                  |              |         |
| Obese (Y/N)              | 36 (8.0)         | 22 (16.1)        | 1.0          |         |
| Overweight (Y/N)         | 18 (4.0)         | 6 (4.4)          | 1.83 (0.62–5.40) | 0.264   |
| Normal weight (Y/N)      | 183 (40.8)       | 53 (38.7)        | 2.11 (1.14–3.92) | 0.016   |
| Underweight (Y/N)        | 212 (47.2)       | 56 (40.9)        | 2.31 (1.25–4.28) | 0.006   |
| Clinical findings        |                  |                  |              |         |
| Diarrhoea (Y/N)*         | 114 (25.4)       | 23 (16.8)        | 1.69 (1.03–2.78) | 0.038   |
| Blood in stool (Y/N)     | 99 (22.1)        | 27 (19.7)        | 1.15 (0.72–1.86) | 0.560   |
| Abdominal pain (Y/N)     | 238 (53.0)       | 71 (51.8)        | 1.05 (0.72–1.54) | 0.808   |
| Hematemesis (Y/N)        | 4 (0.9)          | 1 (0.7)          | 1.22 (0.14–11.05) | 0.858   |
| Ultrasound findings      |                  |                  |              |         |
| Hepatomegaly (Y/N)*      | 113 (25.2)       | 23 (16.8)        | 1.67 (1.01–2.74) | 0.042   |
| Splenomegaly (Y/N)*      | 280 (62.4)       | 72 (52.6)        | 1.50 (1.02–2.20) | 0.040   |
| Ascites (Y/N)*           | 2 (0.5)          | 2 (1.5)          | 0.30 (0.04–2.17) | 0.207   |
| Pattern A (Y/N)*         | 205 (45.7)       | 73 (53.3)        | 1.0          |         |
| Pattern B/C (Y/N)        | 168 (37.4)       | 46 (33.6)        | 1.00 (0.69–1.46) | 0.982   |
| Pattern D/E (Y/N)        | 67 (14.9)        | 12 (8.8)         | 1.87 (1.04–3.36) | 0.032   |
| Pattern F (Y/N)          | 9 (2.0)          | 6 (4.4)          | 0.48 (0.17–1.38) | 0.166   |

* Included in the multivariable analysis. PE, physical examination; US, ultrasound examination; na, not applicable; Pattern A: normal; Pattern B: “starry sky”; Pattern C: “rings and pipe-stems”; Pattern DE: “ruff around portal bifurcation and patches”; Pattern F: “bird’s claw” [11].
Figure 2: *S. mansoni* infection prevalence by age in the 2017 Ituri province morbidity study (n=586). Overall (green-solide line), female (red-dash line), and male (maroon-long-dash line).

Ten variables were included in the multivariable logistic regression analysis, the results of which are displayed in Table 3. Age was negatively associated with *S. mansoni* infection (adjusted odds ratio [aOR] 0.85; 95% CI 0.76–0.94, *P*=0.003) while gender showed no association (aOR 0.95; 95% CI 0.66–1.34, *P*=0.785).

Of the morbidity indicators investigated, hepatomegaly (aOR 2.04; 95% CI 1.27–3.26, *P*=0.003) and splenomegaly (aOR 1.69; 95% CI 1.17–2.45, *P*=0.005) had highly and statistically significant associations with *S. mansoni* infection. Patients with abnormal liver parenchyma patterns (aOR 1.06; 95% CI 0.84–1.34, *P*=0.648) did not have an increased risk for *S. mansoni* infection.
The risk analysis considered the results of the Kato-Katz diagnostic tests only. The outcomes of the risk analysis (Table S1, S2) were largely consistent with those obtained using the combined diagnostic test results (Kato-Katz and POC-CCA) but there were three differences. First, intestinal morbidity indicators, such as diarrhoea, were significantly associated with an *S. mansoni* infection (aOR 1.78, 95% CI 1.14–2.77, *P*=0.012). Second, only hepatomegaly was associated with an *S. mansoni* infection (aOR 1.72, 95% CI 1.10–2.71, *P*=0.018), not splenomegaly (aOR 1.36, 95% CI 0.94–1.95, *P*=0.099). Third, an abnormal liver parenchyma pathology (patterns) was significantly associated with *S. mansoni* infection (aOR 1.41, 95% CI 1.11–1.78, *P*=0.004).

### Table 3. Morbidity associated with *S. mansoni* infection in the 2017 study.

Results of the multivariable analysis of data from 13 purposively-selected villages in Ituri province (n=586).

| Risk factors                      | aOR (95% CI) | Std. Err. | z      | p-value |
|-----------------------------------|--------------|-----------|--------|---------|
| **Demographic risk factors**      |              |           |        |         |
| Age groups                         | 0.85 (0.76–0.94) | 0.047 | -3.00  | 0.003   |
| Gender (Male/Female)               | 0.95 (0.66–1.38) | 0.179 | -0.27  | 0.785   |
| **Anthropometric risk factors**    |              |           |        |         |
| BMI                               | 1.12 (0.92–1.36) | 0.113 | 1.11   | 0.267   |
| **Clinical finding**               |              |           |        |         |
| Diarrhoea                         | 1.37 (0.88–2.11) | 0.303 | 1.40   | 0.160   |
| **Ultrasound findings**           |              |           |        |         |
| Hepatomegaly (Yes/No)             | 2.04 (1.27–3.26) | 0.489 | 2.97   | 0.003   |
| Splenomegaly (Yes/No)             | 1.69 (1.17–2.45) | 0.320 | 2.80   | 0.005   |
| Ascites (Yes/No)                  | 0.55 (0.07–4.48) | 0.591 | -0.55  | 0.580   |
| Liver pathology (Yes/No)          | 1.06 (0.84–1.34) | 0.126 | 0.46   | 0.648   |
| **Co-infection**                  |              |           |        |         |
| *Trichuris trichiura* (Yes/No)    | 0.23 (0.02–2.72) | 0.290 | -1.17  | 0.244   |
| Hookworm (Yes/No)                 | 0.21 (0.02–2.13) | 0.247 | -1.32  | 0.186   |

aOR: adjusted odds ratio in multivariable analysis; CI: confidence interval.
At the village level, the prevalence of hepatomegaly (Figure 4) and splenomegaly (Figure 5) increased with the prevalence of *S. mansoni* infection. Four patients were diagnosed with ascites; all of whom were residents of villages where overall *S. mansoni* prevalence exceeded 80%.

**Figure 4**: Association of hepatomegaly and *S. mansoni* infection prevalence at village level in the 2017 Ituri morbidity study (n=586).

**Figure 5**: Association of splenomegaly and *S. mansoni* infection prevalence at village level in the 2017 Ituri morbidity study (n=586).
*S. mansoni* infection intensity varied greatly among individuals, with a maximum of 4,497.6 EPG and a mean infection intensity of 109.7 EPG. Table 4 presents the infection intensity according to gender, age, helminth co-infection and morbidity categories. Infection intensity levels were similar in the two gender groups (P=0.198). The age distribution of the infection intensity levels followed the age-infection prevalence curve. Heavy-intensity infections were mostly found (12.9%) among adolescents aged 10–14 years, while no one in the oldest age group (50 years and older) had a heavy-intensity infection (P=0.006). Heavy-intensity infections were significantly higher among patients co-infected with *Ascaris lumbricoides* (13.0%, P=0.005) and underweight participants (10.1%, P=0.033).

There was a significantly higher prevalence of reported diarrhoea (40.5%, P=0.004) and blood in the stool (52.4%, P<0.001) among patients in the heavy-intensity infection group compared to the other infection intensity groups.

Among patients with heavy-intensity infections, the prevalence of splenomegaly (81.0%) was significantly higher than among other infection intensity groups (P=0.008), while the prevalence of hepatomegaly was similar among all infection intensity groups (P=0.273). When stratified by age, patients with an enlarged liver and/or spleen bore a higher infection intensity burden compared to those with a normal-sized liver and spleen in the same age group (Figure 6). In general, younger patients (aged ≤19 years) experienced more high-intensity infections compared to those in older age groups (aged ≥ 20 years).
Table 4: *S. mansoni* infection intensity by morbidity in the 2017 study. Study conducted in 13 purposively-selected villages in Ituri province (n=586). Only results of the Kato-Katz test have been taken into account in this analysis.

| Characteristics | Negative | *S. mansoni* infection intensity |  |
|-----------------|----------|---------------------------------|---|
|                 | n  | %   | Light | n  | %   | Moderate | n  | %   | Heavy | n  | %   | χ² | p-value |
| Overall         | 239 | 216 | 89 | 42 |  |
| Gender          |  |
| Females         | 152 | 44.4 | 117 | 34.2 | 50 | 14.6 | 23 | 6.7 |  |
| Males           | 87  | 35.7 | 99  | 40.6 | 39 | 16.0 | 19 | 7.8 | 4.66 | 0.198 |
| Age categories  |  |
| (years)         |  |
| 6 – 9           | 50  | 40.7 | 47  | 38.2 | 18 | 14.6 | 8  | 6.5 |  |
| 10 – 14         | 49  | 35.0 | 49  | 35.0 | 24 | 17.1 | 18 | 12.9 |  |
| 15 – 19         | 19  | 28.0 | 25  | 37.3 | 17 | 25.4 | 6  | 9.0 |  |
| 20 – 29         | 27  | 35.0 | 32  | 41.6 | 11 | 14.3 | 7  | 9.1 |  |
| 30 – 39         | 31  | 45.6 | 26  | 38.2 | 9  | 13.3 | 2  | 2.9 |  |
| 40 – 49         | 27  | 51.9 | 18  | 34.6 | 6  | 11.6 | 1  | 1.9 |  |
| ≥50             | 36  | 61.0 | 19  | 32.2 | 4  | 6.8  | 0  | 0.0 | 36.68 | 0.006 |
| Soil-transmitted helminths |  |
| *T. trichiura* (Y/N) | 2  | 0.8 | 1  | 0.5 | 0  | 0.0 | 0  | 0.0 | 1.18 | 0.758 |
| *Ascaris* (Y/N) | 0   | 0.0 | 0  | 0.0 | 0  | 0.0 | 1  | 2.4 | 13.0 | 0.005 |
| Hookworm (Y/N) | 3   | 1.3 | 1  | 0.5 | 0  | 0.0 | 0  | 0.0 | 2.21 | 0.530 |
| Anthropometry   |  |
| Obese           | 33  | 56.9 | 20 | 34.5 | 4  | 6.9  | 1  | 1.7 |  |
| Overweight      | 13  | 54.2 | 9  | 37.5 | 2  | 8.3  | 0  | 0.0 |  |
| Normal weight   | 96  | 40.7 | 89 | 37.7 | 37 | 15.7 | 14 | 5.9 |  |
| Underweight     | 97  | 36.2 | 98 | 36.5 | 46 | 17.2 | 27 | 10.1 | 18.15 | 0.033 |
| Clinical findings |  |
| Diarrhoea (Y/N) | 41  | 17.2 | 56 | 25.9 | 23 | 25.8 | 17 | 40.5 | 13.11 | 0.004 |
| Blood in stool  | 42  | 17.6 | 32 | 14.8 | 30 | 33.7 | 22 | 52.4 | 39.49 | <0.001 |
| Abdom. pain (Y/N) | 124 | 51.9 | 107 | 49.5 | 52 | 58.4 | 26 | 61.9 | 3.53 | 0.317 |
| Hematemesis (Y/N) | 3  | 1.3 | 1  | 0.5 | 1  | 1.1  | 0  | 0.0 | 1.28 | 0.733 |
| Ultrasound findings |  |
| Hepatomegaly (Y/N) | 47  | 19.7 | 52 | 24.1 | 24 | 27.0 | 13 | 31.0 | 3.89 | 0.273 |
| Splenomegaly (Y/N) | 134 | 56.1 | 124 | 57.4 | 60 | 67.4 | 34 | 81.0 | 11.87 | 0.008 |
| Ascites (Y/N) | 3   | 1.3 | 0  | 0.0 | 1  | 1.1  | 0  | 0.0 | 3.19 | 0.364 |
| Pattern A (Y/N) | 131 | 47.1 | 96 | 34.5 | 36 | 13.0 | 15 | 5.4 |  |
| Pattern B (Y/N) | 20  | 33.9 | 28 | 47.4 | 7  | 11.9 | 4  | 6.8 |  |
| Pattern C (Y/N) | 60  | 38.7 | 56 | 36.1 | 26 | 16.8 | 13 | 8.4 |  |
| Pattern D/E (Y/N) | 21  | 26.6 | 31 | 39.2 | 19 | 24.1 | 8  | 10.1 |  |
| Pattern F (Y/N) | 7   | 46.7 | 5  | 33.3 | 1  | 6.7  | 2  | 13.3 | 19.74 | 0.072 |

Pattern A: normal; Pattern B: “starry sky”; Pattern C: “rings and pipe-stems”; Pattern DE: “ruff around portal bifurcation and patches”; Pattern F: “bird’s claw”. [Ref.].


S. mansoni infection intensity varied considerably among patients with different liver parenchyma pathologies. In general, more heavy-intensity infections were observed among patients with more severe liver morbidity patterns. That is, the number of individuals with heavy-intensity infections increased with the severity of the liver parenchyma pattern, from normal liver parenchyma pattern A (5.4%) to the most severe “bird’s claw” pattern F (13.3%). The association was borderline significant (P=0.072). When stratified by age, a clear association emerged between increased number of high-intensity infections and increasingly abnormal liver pathologies (Figure 7). Liver parenchyma worsened, from normal pattern A to pattern DE, the median infection intensity increased. Patients with pattern F had similar- or lower-intensity infections than patients with less severe morbidity patterns.

![Figure 6: S. mansoni infection intensity by hepatomegaly and splenomegaly and age in the 2017 Ituri morbidity study (n=586). Hepatomegaly (brown) and splenomegaly (cranberry).](image-url)
Figure 7: *S. mansoni* infection intensity by liver parenchyma patterns and age in the 2017 Ituri morbidity study (n=586). Pattern A: normal (lime); Pattern B/C (magenta): “starry sky” and “rings and pipe-stems”; Pattern D/E (red): “ruff and patches around portal bifurcation”; Pattern F (orange): “bird’s claw”.
Discussion

Today, the World Health Organisation’s recommended control strategy for schistosomiasis focuses on controlling morbidity, with preventive chemotherapy being a key concept. The aim is to prevent morbidities from developing by regularly treating the exposed population, and thereby avoiding the development of severe infection intensities and hence, morbidity. Regular mass-drug administration is the recommended control activity [12].

Although minimizing morbidity is the target of schistosomiasis control efforts, control programmes rarely collect (baseline) and monitor morbidity data. Instead, they largely rely on monitoring infection intensities, which are linked to morbidity and much easier to assess than intestinal and hepatosplenic morbidity. Consequently, little is known about the morbidity burden of schistosomiasis.

In this study, we assessed the magnitude of the intestinal and hepatosplenic morbidity burden in Ituri province, DRC, and investigated its associations with S. mansoni infection status. To that end, we conducted a cross-sectional study in 13 S. mansoni endemic villages. We enrolled all household member six years and older, and assessed their S. mansoni infection status and their intestinal and hepatosplenic morbidity.

We found a high degree of intestinal and hepatosplenic morbidity. About one quarter of the study participants reported diarrhoea (23.4%) and blood in the stool (21.5%). Upon ultrasonography examination, almost one-quarter was diagnosed with hepatomegaly (23.2%); almost two-thirds (60.1%) had splenomegaly, and more than half (52.6%) had abnormal liver parenchyma (pattern B–F). Five patients reported an experience of hematemesis and four patients had ascites.
In our study population, we found a high prevalence of *S. mansoni* infection (76.6%). Light-, moderate- and heavy-intensity infections were diagnosed in high frequencies of 36.9%, 15.2% and 7.2%, respectively. *S. mansoni* infection prevalence and intensity was highest in the adolescent and young adult age groups. The prevalence of intestinal and hepatosplenic morbidity indicators showed a very similar age distribution (although hepato- and splenomegaly peaked in older age groups), and at village level, hepatosplenic morbidity prevalence increased with infection prevalence. Both observations suggesting a close link between morbidity and *S. mansoni* infection.

Furthermore, at individual level, we found an increased risk of hepatomegaly and splenomegaly in *S. mansoni*-infected patients, confirming the association found at village level and the similarly shaped age distributions. The findings are also consistent with documented hepatosplenic morbidity associated with *S. mansoni* infection [13, 14]. Hence, providing further evidence that *S. mansoni* infection is a major contributor to the overall observed morbidity.

We found three notable differences in the risk results when relying on the diagnostic results from the Kato-Katz technique only. First, reported diarrhoea was significantly associated with *S. mansoni* infection; second, pathological changes of the liver parenchyma were associated with *S. mansoni* infection as was hepatomegaly; and, third, splenomegaly was not associated with *S. mansoni* infection. Using the Kato-Katz technique alone to diagnose *S. mansoni* infection reduces the overall sensitivity of the diagnostic approach due to the low sensitivity of the technique itself [15, 16]. Hence, on average, those diagnosed with an *S. mansoni* infection are more likely to have a higher infection intensity in comparison to the combined diagnostic approach. From these observations, we see that subtle morbidity increases — such as reported diarrhoea and pathological changes in the liver parenchyma — become statistically significant. Indeed, for both morbidity indicators, we observed an association with *S. mansoni* infection intensity. Patients with diarrhoea
had the highest prevalence of heavy-intensity infections (Table 2) and those with abnormal liver parenchyma patterns D–E had the highest mean infection intensities (Figure 4).

Quantifying schistosomiasis morbidity is a challenging [17, 18] and controversial matter [19]. Morbidity associated with Schistosoma infection is unspecific. Hence, the observed morbidity pattern might be provoked partially by or in combination with other pathogens, such as other helminth species, protozoa, bacteria and viruses. Given that multiple infections are frequent in tropical Africa, a combination of infections is most likely responsible for the observed morbidity. In Ituri province, other parasitic infections, such as malaria (i.e. Plasmodium falciparum), and other infections with hepatosplenic affinity, such as viral hepatitis, are prevalent [2, 6, 20, 21] and may have contributed to the hepatosplenic morbidity pattern observed. The time gap between infection and the occurrence of measurable morbidity further complicates efforts to assess the association between infection and morbidity. Furthermore, organomegaly is sometimes described as normally present in children; it then regresses and disappears in adulthood [2, 22-24].

In our study, we encountered patients with severe complications from S. mansoni infection, which further underscore the importance of the infection’s morbidity burden. Four people (0.9%) reported a history of hematemesis. The finding appears to corroborate the health service’s statistics report from the Angumu health district (on the shore of Lake Albert), which declares that hematemesis is a frequent medical emergency and that adults have died after vomiting blood in this area. Oesophageal varices remain silent until they rupture and irreversible damage occurs [21]. Angumu health district is a remote area and well known for its high blood transfusion rates. Patients vomiting blood often reach the hospital too late, leading to the worst medical outcome.
The morbidity levels we observed are consistent with those measured by Ongom and Bradley [7], who found serious morbidity, including diarrhoea and abdominal pain, in a schistosomiasis endemic community on Lake Albert in Uganda. Other studies of *S. mansoni* endemic communities outside of the DRC present similar morbidity levels [24-26]. Very few studies of morbidity due to schistosome infection in DRC exist [21, 27]. Our study contributes to the country’s knowledge base and may offer a baseline for future intervention studies to determine the exact extent of morbidity associated with *S. mansoni* infection.

We conducted our study in purposively-sampled villages known to have a high prevalence of *S. mansoni*. Thus, the examined population is not representative of the entire province but rather of high transmission areas. Furthermore, ongoing civil unrest in Ituri province creates a challenging security situation, which only afforded us a short time in each village. For this reason, only one stool sample could be collected from each study participant. Finally, limited available resources did not allow us to examine participants for parasitic, bacterial and viral co-infections, which could have helped to better explain the degree of morbidity linked to *S. mansoni* infection.

Our study provides, for the first time, comprehensive baseline data showing a high intestinal and hepatosplenic morbidity burden in Ituri province; a burden that is associated with *S. mansoni* infection at both the individual and community level. At present, we cannot quantify the extent to which *S. mansoni* infection alone is responsible for the observed morbidity (or whether other infections contribute). To answer this question, additional investigations are needed. However, the high degree of intestinal and hepatosplenic morbidity present in Ituri province warrants immediate and comprehensive control activities.
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References

1. Loker ES, Hofkin BV. Parasite Versus Host: Pathology and Disease. Parasitology: A Conceptual Approach. 2015:159-92.

2. Kabatereine NB, Kemijumbi J, Ouma JH, Kariuki HC, Richter J, Kadzo H, et al. Epidemiology and morbidity of Schistosoma mansoni infection in a fishing community along Lake Albert in Uganda. T Roy Soc Trop Med H. 2004;98(12):711-8.

3. Savioli L, Albonico M, Engels D, Montresor A. Progress in the prevention and control of schistosomiasis and soil-transmitted helminth infections: forging control efforts. T Roy Soc Trop Med H. 2002;96(6):577-9.

4. Savioli L, Stansfield S, Bundy DAP, Mitchell A, Bhatia R, Engels D, et al. Schistosomiasis and soil-transmitted helminth infections: forging control efforts. T Roy Soc Trop Med H. 2002;96(6):577-9.

5. Gray DJ, Ross AG, Li YS, McManus DP. CLINICAL REVIEW Diagnosis and management of schistosomiasis. Brit Med J. 2011:342.

6. Tukahebwa EM, Magnussen P, Madsen H, Kabatereine NB, Nuwaha F, Wilson S, et al. A Very High Infection Intensity of Schistosoma mansoni in a Ugandan Lake Victoria Fishing Community Is Required for Association with Highly Prevalent Organ Related Morbidity. Plos Neglect Trop D. 2013;7(7).

7. Ongom VL, Owor R, Grundy R, Bradley DJ. Epidemiology and Consequences of Schistosoma-Mansoni Infection in West Nile, Uganda .2. Hospital Investigation of a Sample from Panyagoro Community. T Roy Soc Trop Med H. 1972;66(6):852-63.

8. WHO. Preventive chemotherapy in human helminthiasis. 2006.

9. WHO. Les bilharzioses humaines au Congo Belge et au Ruanda-Urundi. 1954.

10. Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique in Schistosomiasis mansoni. Rev Inst Med Trop Sao Paulo. 1972;14(6):397-400.

11. Richter J, Domingues ALC, Barata CH, Prata AR, Lambertucci JR. Report of the second satellite symposium on ultrasound in schistosomiasis. Mem I Oswaldo Cruz. 2001;96:151-6.

12. Ross AGP, Li YS. Mass Drug Administration (MDA) for Schistosomiasis Reply. J Infect Dis. 2015;211(5):849-60.

13. Kaatano GM, Min D-Y, Siza JE, Yong T-S, Chai J-Y, Ko Y, et al. Schistosoma mansoni-Related Hepatosplenic Morbidity in Adult Population on Kome Island, Sengerema District, Tanzania. Korean J Parasitol. 2015;53(5):545-51.

14. Booth M, Vennervald BJ, Kabatereine NB, Kazibwe F, Ouma JH, Kariuki CH, et al. Hepatosplenic morbidity in two neighbouring communities in Uganda with high levels of Schistosoma mansoni infection but very different durations of residence. T Roy Soc Trop Med H. 2004;98(2):125-36.

15. Maurice Mutro Nigo GBS-B, Manuel Battegay, Peter Odermatt, Patrick Hunziker. Schistosomiasis: from established diagnostic assays to emerging micro/nanotechnology-based rapid field testing for clinical management and epidemiology. Prec Nanomed. 2020;3(1):439-58.

16. Mazigo HD, Heukelbach J. Diagnostic Performance of Kato Katz Technique and Point-of-Care Circulating Cathodic Antigen Rapid Test in Diagnosing Schistosoma mansoni Infection in HIV-1 Co-Infected Adults on the Shoreline of Lake Victoria, Tanzania. Tropical medicine and infectious disease. 2018;3(2).

17. Samuels AM, Matey E, Mwinzi PNM, Wiegand RE, Muchiri G, Ireri E, et al. Schistosoma mansoni morbidity among school-aged children: a SCORE project in Kenya. The American journal of tropical medicine and hygiene. 2012;87(5):874-82.

18. van der Werf MJ, de Vlas SJ, Brooker S, Looman CW, Nagelkerke NJ, Habbema JD, et al. Quantification of clinical morbidity associated with schistosome infection in sub-Saharan Africa. Acta Trop. 2003;86(2-3):125-39. Epub 2003/05/15.
19. Asztely MS, Eriksson B, Gabone RM, Nilsson LA. Is ultrasonography useful for population studies on schistosomiasis mansoni? An evaluation based on a survey on a population from Kome Island, Tanzania. Acta Radiol Open. 2016;5(12):2058460116686392. Epub 2017/03/14.

20. Davis SM, Wiegand RE, Mulama F, Kareko EI, Harris R, Ochola E, et al. Morbidity associated with schistosomiasis before and after treatment in young children in Rusinga Island, western Kenya. Am J Trop Med Hyg. 2015;92(5):952-8. Epub 2015/03/12.

21. Gryseels B, Polderman AM. The Morbidity of Schistosomiasis-Mansoni in Maniema (Zaire). T Roy Soc Trop Med H. 1987;81(2):202-9.

22. Gryseels B. Morbidity and Dynamics of Schistosomiasis after Chemotherapy - Implications for Control. Eur J Pharmacol. 1990;183(3):670-.

23. Gryseels B, Nkuliyinka L. The Morbidity of Schistosomiasis-Mansoni in the Highland Focus of Lake Cohoha, Burundi. T Roy Soc Trop Med H. 1990;84(4):542-7.

24. Abdel-Wahab MF, Esmat G, El-Boraey Y, Ramzy I, Medhat E, Strickland GT. The epidemiology of schistosomiasis in Egypt: Methods, training, and quality control of clinical and ultrasound examinations. Am J Trop Med Hyg. 2000;62(2):17-20.

25. El-Hawey AM, Amr MM, Abdel-Rahman AH, El-Ibiary SA, Agina AM, Abdel-Hafez MA, et al. The epidemiology of schistosomiasis in Egypt: Gharbia Governorate. Am J Trop Med Hyg. 2000;62(2 Suppl):42-8.

26. El-Khoby T, Galal N, Fenwick A, Barakat R, El-Hawey A, Nooman Z, et al. The epidemiology of schistosomiasis in Egypt: summary findings in nine governorates. Am J Trop Med Hyg. 2000;62(2 Suppl):88-99.

27. Gryseels B, Polderman AM. Schistosoma-Mansoni Morbidity in 3 Central-Africa Foci - Intrapopulation Vs Interpopulation Analysis. Trop Med Parasitol. 1987;38(3):263-.

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Competing interest

No authors have competing interests.
Supplementary information captions

Tables

**Table S1:** Univariable associations with *S. mansoni* infection in the 2017 morbidity study.
Study conducted in 13 purposively-selected villages in Ituri province (n=586). Only diagnostic results of Kato-Katz (KK) test have been taken into account.

**Table S2:** Risk factors for morbidity due to *Schistosoma mansoni* infection, 2017 study.
Results of the multivariable analysis of risk factors for morbidity due to *Schistosoma mansoni* infection among participants from 13 villages in Ituri province (n=586). Only diagnostic results of Kato-Katz (KK) test have been taken into account.

Figures

**Figure S1:** Liver image patterns associated with schistosomiasis, by [11].