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Prevalence and risk distribution of schistosomiasis among adults in Madagascar: a cross-sectional study

Dissertation

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Infectious Diseases of Poverty

SHORT REPORT

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Prevalence and risk distribution of schistosomiasis among adults in Madagascar: a cross-sectional study

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Abstract

Background The goal to eliminate the parasitic disease of poverty schistosomiasis as a public health problem is aligned with the 2030 United Nations agenda for sustainable development goals, including universal health coverage (UHC). Current control strategies focus on school-aged children, systematically neglecting adults. We aimed at providing evidence for the need of shifting the paradigm of schistosomiasis control programs from targeted to generalized approaches as key element for both the elimination of schistosomiasis as a public health problem and the promotion of UHC.

Methods In a cross-sectional study performed between March 2020 and January 2021 at three primary health care centers in Andina, Tsiroanomandidy and Ankazomborona in Madagascar, we determined prevalence and risk factors for schistosomiasis by a semi-quantitative PCR assay from specimens collected from 1482 adult participants. Univariable and multivariable logistic regression were performed to evaluate odd ratios.

Results The highest prevalence of *S. mansoni, S. haematobium* and co-infection of both species was 59.5%, 61.3% and 3.3%, in Andina and Ankazomborona respectively. Higher prevalence was observed among males (52.4%) and main contributors to the family income (68.1%). Not working as a farmer and higher age were found to be protective factors for infection.

Conclusions Our findings provide evidence that adults are a high-risk group for schistosomiasis. Our data suggests that, for ensuring basic health as a human right, current public health strategies for schistosomiasis prevention and control need to be re-addressed towards more context specific, holistic and integrated approaches.

Keywords Schistosomiasis, *Schistosoma haematobium*, *Schistosoma mansoni*, Universal health coverage, Madagascar

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Background

Access to health care is a human right and the urge of achieving universal health coverage (UHC) is emphasized by the United Nations (UN) in the sustainable development goals (SDGs) [1, 2]. The control of infectious diseases of poverty, and particularly those characterized by long term consequences, have been suggested as indicators towards UHC [3–5].

Schistosomiasis is a waterborne neglected disease of poverty prevalent in tropical areas but not limited to them [6]. It is caused by different species of the trematode schistosome, of which *S. mansoni* and *S. haematobium* are the most frequent worldwide [7]. The Neglected Tropical Diseases (NTDs) roadmap, released by the World Health Organization (WHO) in 2021 [8], targets the elimination of the disease as a public health problem by 2030 in all endemic countries. Progress on morbidity control has been made through vertical control strategies, especially by preventive chemotherapy through mass drug administration (MDA) with praziquantel in school aged children [9–11]. However, it has been reported that the implementation of vertical control programs can exacerbate health inequalities amplifying disparities based on sex, gender, socio-economic status and age [3, 12–14], hampering the achievement of UHC. Even though adults in high-risk areas and with occupational risk are theoretically eligible to receive annual MDA [15], campaigns including adults are rare [16]. In 2019, the WHO reported a global coverage rate of 67.2% in school aged children, while it was only 17.7% in adults [17]. The limited availability of praziquantel on the market alongside with the low MDA uptake of adults because of occupational duties, fear of side effects and understanding schistosomiasis as a pediatric disease, exclude de facto adults from national programs [16]. As a consequence, untreated adults do not only serve as infection reservoir for the community, but are also under risk to develop severe chronic forms of the disease [16].

Chronic intestinal schistosomiasis caused by *S. mansoni* can lead to hepato-splenomegaly and portal hypertension, chronic urogenital schistosomiasis caused by *S. haematobium* carries high risk of squamous bladder cancer and manifestations like genital schistosomiasis [7]. Both forms may present symptoms like chronic pain, fatigue and morbidities like anemia and undernutrition, resulting in a great loss of quality-adjusted life-years (QALY) [18, 19], impaired work capacity of adults [20] and finally reduced economic productivity [7]. Adapted guidelines for the diagnosis and treatment of chronic forms of schistosomiasis are often missing in endemic countries generating a lack of services aggravated by the low knowledge among the health-care workers of signs, symptoms and management of chronic forms of the disease, such as female genital schistosomiasis [8, 21]. Preventive chemotherapy at early stages of life, early diagnosis and treatment can prevent long-term consequences and increase QALY [22]. Diagnostic services are still limited in low resource settings because of a lack of affordable and easy to implement diagnostic tools [23]. Moreover, the health seeking behaviors for schistosomiasis care show several barriers as for example social stigma or opening hours of health services that often overlap with the working hours of the users limiting their accessibility [24, 25]. Even though treatment of chronic forms in adults might be available, it can be linked to out-of-pocket expenses as health interventions and transport costs to the health care centers are frequently not affordable for the affected populations [26]. Further, patients, especially women, with morbidities of chronic genital schistosomiasis, like infertility and vaginal discharge, fear marginalization when accessing health services as the symptoms resemble those of sexually transmitted diseases [27].

The life cycle of schistosome infection [7] justifies the adoption of a holistic approach combining MDA with health education programs and improved water, sanitation and hygiene (WASH) [28] measures in a One Health-oriented [29] approach to tackle the disease at its sources [8, 10]. Infection control measures should be encouraged in low resource settings to control morbidity, prevent chronic forms of the disease and meet the ambitious goal of the NTD roadmap [8]. However, several infection control interventions have so far proven to be ineffective for schistosomiasis prevention and control due to contextual barriers that demand the synergistic implementation of multiple measures in order to impact on the transmission of the disease [7, 30].

This study is based on data collected in Madagascar, a country highly endemic for schistosomiasis where both, *S. mansoni* and *S. haematobium* exist in distinct geographic areas [31, 32]. With the exception of few surveys conducted among adults the most of the existing data in the country refers to school-aged children with prevalence ranging between 15.2% and 87.7% [33–36].

Our study aims to provide prevalence estimates, describe risk associations of schistosomiasis in adults in the country and motivate a shift in the paradigm of schistosomiasis control programs from targeted to broader approaches as key element for both the elimination of schistosomiasis as a public health problem and the promotion of UHC.

Materials and methods

Study design, area and population

The planning, organization, implementation and analysis of this cross-sectional study was conducted by eight

interdisciplinary collaborating institutes: the Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany; the German Centre for Infection Research, Hamburg-Borstel-Lübeck-Riems, Germany; the *Centre d'Infectiologie Charles Mérieux*, University of Antananarivo, Madagascar; University of Fianarantsoa Andrainjato, Madagascar; University Clinical Research Centre, Bamako, Mali; Leiden University Medical Centre, Netherlands; Johannes Gutenberg University Mainz, Germany.

This study was conducted at three Primary Health Care Centers (PHCCs) in Madagascar: Andina (20°30′58.8″S 47°09′05.2″E) and Tsiroanomandidy (18°46′21″S 46°02′57″E) in the centre, Ankazomborona (16°06′50″S 46°45′24″E) in the north western part of the island (Fig. 1). On the basis of the infrastructure and population size, Andina can be described as rural area, Ankazomborona and Tsiroanomandidy as peri-urban and urban areas, respectively [37], even though this classification cannot be aligned to the standard definition of the UN statistical commission due to the limited available data of the study sites [38].

Information sessions about the study were organized in the catchment areas of the included PHCCs. If interested, individuals were asked to attend PHCCs to assess their eligibility for the study (18 or older, not pregnant and willing to comply with protocol requirements). If eligible, an informed consent was signed in case of enrolment.

Data collection and management

Data collection took place between March 2020 and January 2021. Background characteristics of the participant were collected by means of a case report form (CRF). Completed CRFs were checked for missing entries manually by local study nurses and doctors following standard operating procedures. CRF data were fed into the database REDCap® (Vanderbilt University, Nashville, USA) via double data entry by two independent operators. Quality control of data processing and data validation was undertaken at regular intervals during the course of data entry.

Sample collection and management

For this study a sample of 9 ml of venous blood was collected from each participant. Blood samples were centrifuged at 1600 × g for 10 min and two aliquots of 1 ml each of serum was produced by qualified laboratory technicians. Samples were stored according to required quality standards at – 20 °C and transferred to long-term storage at – 80 °C in Madagascar. At the end of sample collection, one of the serum aliquots was shipped to Hamburg on dry ice and stored at – 80 °C until the analysis was performed.

Sample analysis

DNA was extracted with QIAamp MinElute ccfDNA Mini Kit from 1 ml serum according to the

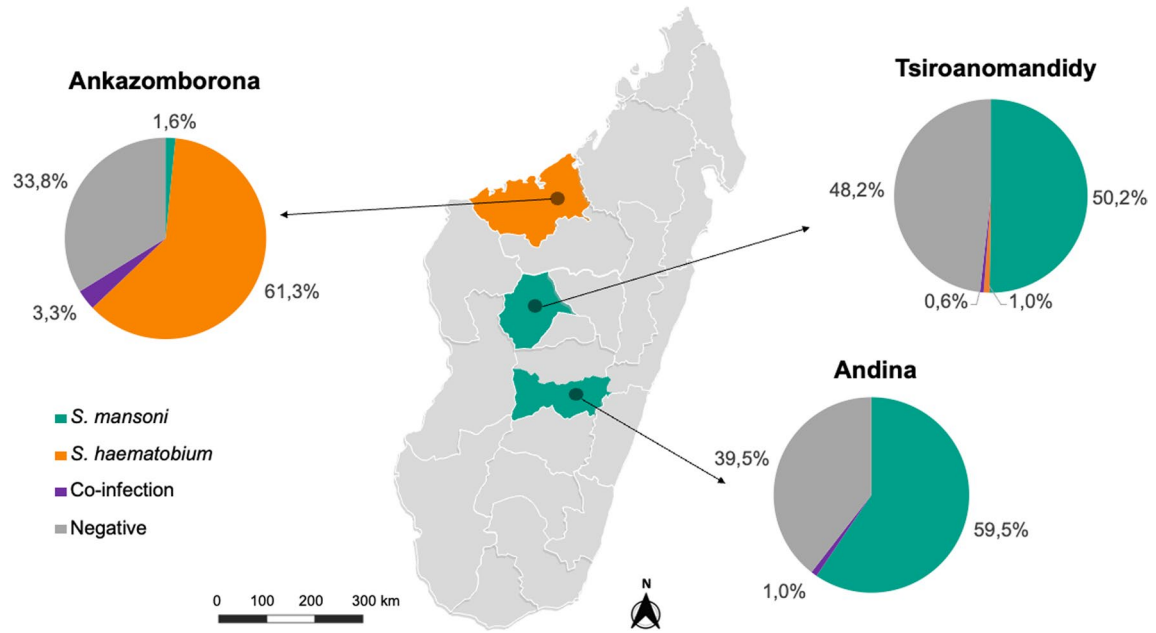

Fig. 1 Map of Madagascar showing the crude prevalence of *Schistosoma* species and co-infection status based on PCR at the study sites, $n = 1482$. Map was adapted using a template from https://yourfreetemplates.com

manufacturer's instructions (Qiagen, Hilden, Germany). Extracted DNA was stored at – 20 ℃.

The semi quantitative standardized polymerase-chain reaction (qPCR) analysis was based on the previously published protocol by Frickmann et al. [39] with described sensitivity of 94.9% and specificity of 98.4%. The primers used for the amplification were: *S. mansoni*—Forward Primer: 5′ CAA CCG TTC TAT GAA AAT CGT TGT 3′, *S. mansoni*—Reverse Primer: 5′ CCA CGC TCT CGC AAA TAA TCT 3′, *S. mansoni*—Probe: 'Fam-TCC GAA ACC ACT GGA CGG ATT TTT ATG AT-BHQ1′, *S. haematobium*—Forward Primer: 5′ GAT CTC ACC TAT CAG ACG AAA C 3′, *S. haematobium*—Reverse Primer: 5′ TCA CAA CGA TAC GAC CAA C 3′, *S. haematobium*—Probe: 5′ Joe-TGT TGG AAG ZGC CTG TTT CGC AA-BHQ1 3′ all synthesized by Biomers.net, Ulm, Germany. Primers and a probe were added for the detection of Phocid herpesvirus (PhHV) DNA as internal positive control (PhHV—Forward Primer: 5′ GGG CGA ATC ACA GAT TGA ATC 3′, PhHV—Reverse Primer: 5′ GCG GTT CCA AAC GTA CCA A 3′, PhHV—Probe: 5′ Cy5.5-TTT TTA TGT GTC CGC CAC CA-BBQ 3′).

The qPCRs were performed in a total reaction volume of 25 µl containing 12.5 µl of HotStarTaq Mastermix (Qiagen, Hilden, Germany), 1.75×10^{-8} mol $MgCl_2$, 1.25×10^{-13} mol of each *Schistosoma* primer, 6.25×10^{-14} mol of the *Schistosoma* probes, 1.0×10^{-12} mol of the PhHV primer, 1.25×10^{-12} mol of the PhHV probe, 1.425 µg of the PhHV DNA template, 4×10^{-5} mg bovine serum albumin and 5 µl DNA eluate. In each run two positive controls (*S. mansoni* and *S. haematobium* DNA) and a negative control (H_2O) were included. The qPCR was conducted using Corbett RotorGene 6000 (Qiagen, Redwood City, USA) with following steps: 15 min at 95 °C followed by 50 cycles of 15 s at 95 °C and 60 seconds at 60 °C with an initial touchdown from 65 to 60 °C in the first 11 cycles. The readout resulted from the RotorGene 6000 Software v.7.87 (Qiagen, Hilden, Germany). Results with a clean sigmoid curve within the PCR cycles were considered positive [39].

Statistical analysis

All analyses were conducted using R® v.4.1.2 (R Foundation for statistical computing, Vienna, Austria). Continuous variables were described using median and interquartile ranges (IQR). Categorical variables were presented using frequencies and percentages.

To estimate the prevalence of schistosome infection among the study population, relative frequencies of positive test results along with exact 95% confidence intervals (*CI*s) were determined.

For the risk factor analyses, the study population was divided into two distinct groups according to the areas of endemicity based on the species-specific PCR results. Test result distribution among individuals with various risk factors (study site, sex, age, education level, ever been treated with praziquantel, working as a farmer and being the main contributor to the family income) was described using frequencies and percentages. Univariable and multivariable logistic regression were performed to derive unadjusted and adjusted odds ratios (*OR*) and 95% *CI*s.

Ethical consideration

Ethical clearance was obtained from the National Ethics Committee of Madagascar (ref. no. N°23-MSANP/CERBM, 05/03/2018) and the Ethics Committee of the Hamburg State Medical Chamber in Germany (ref. no. PV7019-4419-BO-ff, 29/10/2019).

All participants were informed about the aims of the study and its procedures in the local language (Malagasy). Study participation was voluntary and informed consent for the participation was obtained from the individual participant by signature or, in case of illiteracy, through a thumbprint in the presence of an independent witness. In all cases, participants had the right to refuse participation and withdraw the informed consent at any time without giving reasons. No monetary incentives were released to participate in the study and exclusively travel costs were reimbursed, calculated on the basis of the distance of the participants' households from the PHCC.

Results

Study population

A total of 1482 adults were included in the study. Missing data are reported in the sections profession (0.8%) and praziquantel treatment (4.6%). All study sites were equally represented (ranging between 488 and 498 individuals across sites). The sex was balanced with highest proportion of females in Tsiroanomandidy (60.2%, Table 1), 54.5% females in Ankazomborona and 47.6% females in Andina.

Participants' age ranged from 18 to 84 years. Lowest median age of 28 years was described in participants from Ankazomborona. The majority of participants were aged between 18 and 29 years across all sites.

Most of the participants reported an education level of secondary school or higher in Tsiroanomandidy and in Ankazomborona. In Andina the majority had only completed primary school.

More than two thirds of the population has never been treated with praziquantel in Andina while it was less than a third at the other two study sites.

Table 1 Study population characteristics

Characteristics	Andina *n* (%)	Tsiroanomandidy *n* (%)	Ankazomborona *n* (%)
Total	496 (33.5)	498 (33.6)	488 (32.9)
Female sex	236 (47.6)	300 (60.2)	266 (54.5)
Age (years)[1]	38.5 (27.0–50.0)	36.0 (25.0–49.8)	28.0 (21.0–40.0)
Age group (years)[1]			
18–29	155 (31.2)	181 (36.3)	255 (52.3)
30–39	101 (20.4)	92 (18.5)	97 (19.9)
40–49	104 (21.0)	100 (20.1)	68 (13.9)
50 +	136 (27.4)	125 (25.1)	68 (13.9)
Education level			
Secondary school or higher	134 (27.0)	280 (56.2)	211 (43.2)
Primary school	313 (63.1)	160 (32.1)	152 (31.2)
Never gone to school	49 (9.9)	58 (11.7)	125 (25.6)
Never treated with praziquantel	353 (71.2)	142 (30.9)	118 (25.8)
Working as a farmer	471 (95.0)	314 (63.1)	370 (76.4)
Main contribution to family income			
Yes	338 (68.1)	311 (62.4)	257 (52.7)
Of whom female	140 (41.4)	152 (48.9)	101 (39.3)
No	158 (31.9)	187 (37.6)	231 (47.3)
Of whom female	96 (60.8)	148 (79.1)	165 (71.4)

Stratified by study sites ($n = 1482$)

[1] Median age and interquartile range

Farming was the most common occupation at all sites. However, the distribution was not equal: in Andina almost everyone was a farmer, while there were less in Ankazomborona and rarely in Tsiroanomandidy.

At all sites most of participants were the main contributor to the family income. In the group of the main contributors a higher percentage were males, while a higher percentage of females stated that they were not the main contributor.

Prevalence of schistosome infection in study area

Of importance, the *S. mansoni* infection showed dominant prevalence of 59.5% (95% *CI*: 55.0–63.8) in the rural area Andina and 50.2% (95% *CI*: 45.7–54.7) in the urban area Tsiroanomandidy in the central area of Madagascar and 1.6% (95% *CI*: 0.7–3.2) in peri-urban area Ankazomborona in the north-western part (Fig. 1). Mono-infections with *S. haematobium* were not found in Andina, while they were identified in 1.0% (95% *CI*: 0.3–2.3) of the participants in Tsiroanomandidy and 61.3% (95% *CI*: 56.8–65.6) in Ankazomborona. The prevalence of co-infections was generally low with 1.0% (95% *CI*: 0.3–2.3) in Andina, 0.6% (95% *CI*: 0.1–1.8) in Tsiroanomandidy and highest in Ankazomborona with 3.3% (95% *CI*: 1.9–5.3). Additional background information is listed in the Additional file 1: Table S1, specifying place of birth and residence of co-infected participants ($n = 24$). Endemicity of place of birth and place of home differed in six participants (25%), who were all participants in Ankazomborona.

Risk factors for schistosome infection

For the risk factor analysis co-infected participants ($n = 24$) and participants positive for the non-endemic species (*S. mansoni* area: $n = 5$, *S. haematobium* area: $n = 8$) were excluded yielding $n = 981$ participants from *S. mansoni* and $n = 464$ participants from *S. haematobium* endemic regions evaluable for risk factor assessments. Associations between risk factors and *S. mansoni* and *S. haematobium* infection status from logistic regression models are shown in Fig. 2. Adults attending the PHCC Tsiroanomandidy had lower odds of infection with *S. mansoni* when compared to adults attending the PHCC in Andina (adjusted *OR* = 0.45, 95% *CI*: 0.32–0.64). Higher infection rates of *S. mansoni* (adjusted *OR* = 1.16, 95% *CI*: 0.86–1.56) and *S. haematobium* (adjusted *OR* = 1.16, 95% *CI*: 0.74–1.83) were more likely to be observed in males than in females. Age groups older than 18–29 years, especially the 50 + age group, tended to have lower odds of infection with *S. mansoni* (adjusted *OR* = 0.49, 95% *CI*: 0.33–0.72) and *S. haematobium* (adjusted *OR* = 0.25, 95% *CI*: 0.13–0.48). Illiteracy increased the odds of infection with *S. mansoni* (adjusted *OR* = 1.73, 95% *CI*: 1.03–2.95) while infection rates with *S.*

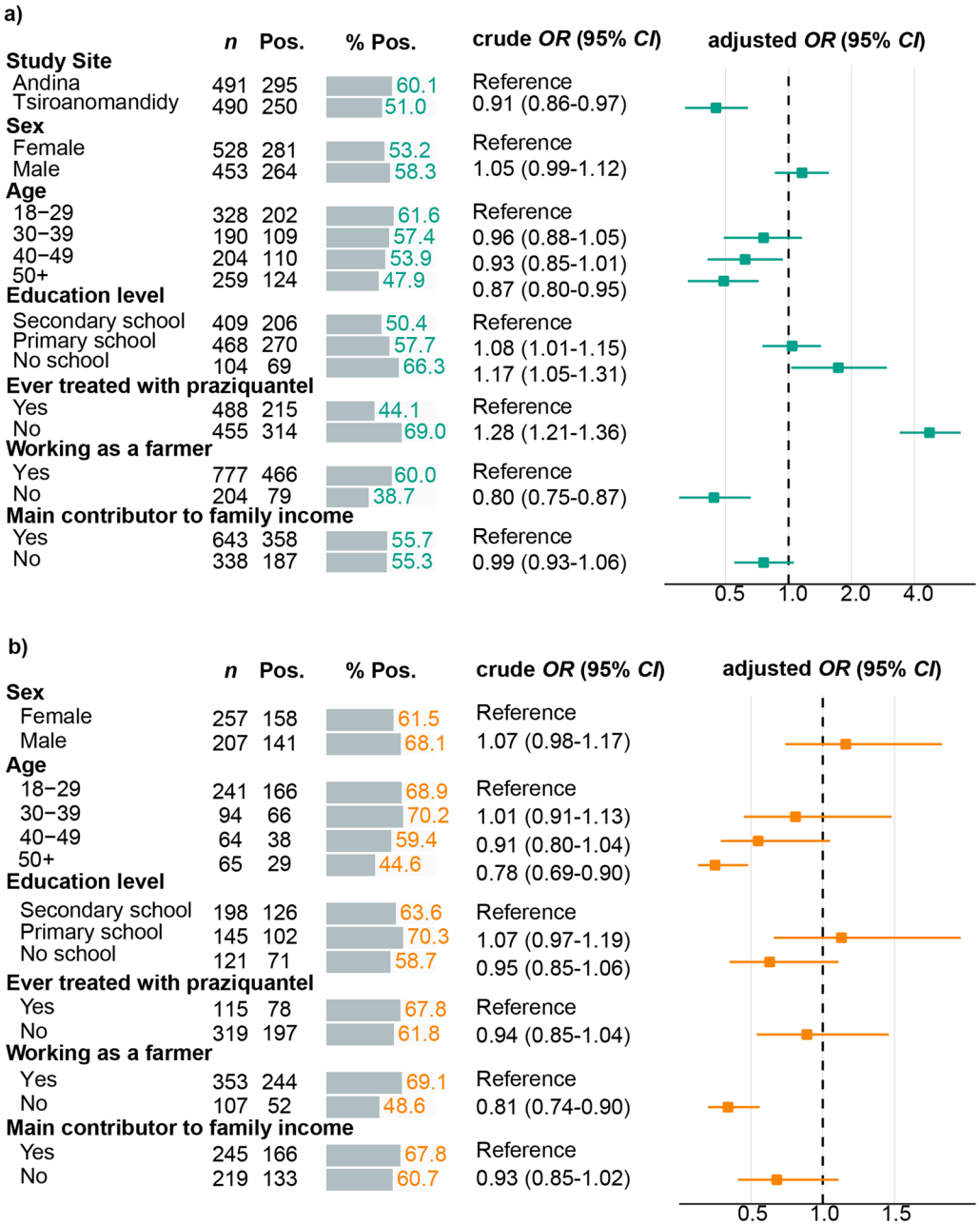

Fig. 2 Risk factor analysis for PCR positivity of participants enrolled at (**a**) *Schistosoma mansoni* ($n = 981$) and (**b**) *S. haematobium* ($n = 464$) endemic study sites. Positivity rates, univariable and multivariable logistic regression with effect estimates in terms of crude and adjusted *ORs* and 95% *CI*. Variables that were controlled for in the multivariable regression, included: study site (when applicable), sex, age groups, education level, ever treated with praziquantel, working as a farmer and being main contributor to the family income. *CI* confidence interval, *n* sample size, *OR* odds ratio, *PCR* polymerase chain reaction, *Pos.* positivity frequencies, *% Pos.* positivity percentages

haematobium varied across education levels being lowest in participants with no school education (58.7%). Odds of infection also varied among both species regarding the previous treatment of praziquantel. Participants, who have never been treated with praziquantel before, tended to have higher odds of infection with *S. mansoni* (adjusted $OR = 4.72$, 95% *CI*: 3.40–6.65), while chances of infection with *S. haematobium* were lower (adjusted $OR = 0.89$, 95% *CI*: 0.54–1.46). If not working as a farmer participants had lower odds of infection with *S. mansoni* (adjusted $OR = 0.44$, 95% *CI*: 0.30–0.66) and *S. haematobium* (adjusted $OR = 0.34$, 95% *CI*: 0.20–0.56). Similar

S. mansoni positivity rates were observed between being main contributor to the family income and not being main contributor to the family (adjusted *OR* = 0.76, 95% *CI*: 0.55–1.06). Odds of infection with *S. haematobium* were lower when not being main contributor to the family income (adjusted *OR* = 0.68, 95% *CI*: 0.41–1.11).

Discussion

This cross-sectional study reports findings of elevated prevalence of schistosome infections in adults with *S. mansoni* in central and *S. haematobium* in north-west of Madagascar. Our data show an alarming gap for the accomplishment of UHC in endemic countries like Madagascar as adults are at risk of infection with schistosomiasis, but excluded by structured control programs for the disease.

To our knowledge this is the first study describing prevalence of both endemic species in Malagasy adults with a highly sensitive and specific serum PCR. With prevalence of around 60% in a *S. mansoni* and a *S. haematobium* endemic area we found similar prevalence as previous studies on different age groups in the country, indicating that beside school-aged children, also adults carry a high burden of infection in Madagascar. The geographic distribution of schistosome species here described, is also aligned with the current literature [31, 40] and seems to be associated with the distribution of the different species of freshwater snails [41] in the country.

Based on our findings, our study areas can be classified by WHO definition as high prevalence (> 50%) areas with need for interventions [10]. However, we show that less than half of the infected study population was never treated with praziquantel suggesting that they could have been a carrier of the infection for longer with a higher likelihood of developing the chronic form of the disease and serving as reservoir for the community [16]. Interestingly, in the *S. mansoni* endemic population, never having been treated with praziquantel, represents a risk factor for adult infections. Since it is extensively described that recovering from treatment does not represent a protective factor for further infections, we can speculate that exposure to treatment and/or MDA campaigns can raise awareness for the disease and induce less risky behaviors towards the infection. However, our findings show that treatment with praziquantel did not lower the odds of infection in *S. haematobium* areas. This supports the concept that many risk factors depend on the geographical and cultural contexts which need to be taken into account when planning interventions.

Our study provides new insights into the distribution of schistosomiasis among Malagasy adults, which will be essential for the shift of schistosomiasis control programs from targeted to broader groups of intervention as key element for the elimination of schistosomiasis and the promotion of UHC. As an example, the frequency of infection in our study population significantly decreased with increasing age, meaning that in these areas, control strategies should also target adults especially within the young working population of Madagascar. It is concerning to notice that young adults for whom productivity is supposed to be highest, are highly infested with a parasite notably known to weaken individuals productivity, creating disabilities and perpetuating the vicious cycle of poverty [7, 25, 42, 43].

Further, we observed higher prevalence of schistosome spp. in the rural (Andina) and peri-urban (Ankazomborona) areas than in the urban area (Tsiroanomandidy) and higher odds of infection with *S. mansoni* in Andina compared to Tsiroanomandidy. This is aligned with country data showing that rural populations of Madagascar are six times more likely to live without clean drinking water and twice as likely to have no access to sanitation in comparison to urban areas, increasing the risk to have contact with infested water [44]. Also, we observed a lower level of education in the rural area: while 56% of the participants in Tsiroanomandidy (urban) and 43% of the participants in Ankazomborona (peri-urban) reported a secondary school or higher education, only 27% of the participants in Andina (rural) had a secondary school or higher education. In the risk factor analysis we saw that a low level of education was associated with a higher frequency of schistosome infection in the *S. mansoni* group, which was previously explained by a higher likelihood of health illiteracy [45]. However, we could not observe the same in the *S. haematobium* group.

Very interestingly, our data show how two main characteristics identified as risk factors in the *S. mansoni* area (no school education and never been treated with praziquantel before) could not be described in the *S. haematobium* area. This might be due to the different cultural contexts, but in line with Wiegand, et al. [46], it can also be suggested that measurements for the two species should differ in order to prevent a neglect of diverting transmission and risk factors of the schistosome spp.

Interestingly, we also detected co-infections with the two endemic species and mono-infections with the non-endemic species (Figure 1). Even though the number of co-infected individuals was not particularly high, our data suggests that further investigations towards the migration history might reveal further risk factors of coinfections in Madagascar. This shows the importance also in diagnostics to promote tools that can allow the detection of both species with the same sample in order not to miss the presence of non-endemic species, which can further delay the diagnosis and treatment of schistosomiasis and lead to more complicated chronic forms of

the disease especially in our global world, where mobility is becoming more frequent even in traditionally settled communities.

Previous control strategies by the WHO already recommend preventive treatment for adults with occupations, which bring them in steady contact with infested water, like farming, fishing and irrigation work [15] even though the alignment of national strategies is still delayed. Our data confirms the importance of occupational exposure as not working as a farmer, represented a strong protective factor for schistosome infection. As in Madagascar rice farming is the main occupation of the population [47], more tailored studies to deeply investigate the specific risk factors associated to farming are urgent in order to adapt infection control strategies. The higher prevalence of both species in men than in women could be attributed to the fact that in our study population men were more often the main contributors to the family income and thus engaging more in occupations like fishing or farming [48]. But in fact, in areas where farming or fishing is mostly done by women, higher prevalence of schistosomiasis was reported in women [42]. This shows that in shifting societies, occupational risk for schistosome infection should be addressed in a gender-neutral manner and accounting for the actual occupational risk of the specific communities.

This study has strengths and limitations. As a main strength, it assessed the schistosome infection status through a PCR methodology highly sensitive and specific allowing to distinguish the presence of two different schistosome species simultaneously [49–51]. Further, our study assessed the infection status of adults for the first time in rural, peri-urban and urban settings in Madagascar. The limitation of the applied methodology is that the test results may stay positive for a certain time following treatment [49, 52]. However, given that our sampling areas show a of high risk of transmission, we cannot exclude re-infections shortly after treatment. Moreover, the sampling approach through community workers did not guarantee the representativeness of the study population. Additional risk factors such as daily water activities, access to sanitation and hygiene behavior [53] could not have been explored in the frame of this study due to the structure of the investigation tool.

Conclusions

Our study provides evidence of a high prevalence of schistosomiasis in adult populations of Madagascar. Diagnosis and treatment of the disease are a clear unmet medical need hampering the goal of schistosomiasis elimination as public health problem in the country by 2030. As our data show that prevalence of schistosomiasis can differ by schistosome species, geographic location, age, sex and other factors it requires targeted context specific, holistic and integrated control strategies to reduce morbidity and work towards guaranteeing the essential human right of health in all individuals. A shift in schistosomiasis control strategies is urgent to reinforce fragile health systems, positively impacting the fight against other diseases and health seeking behaviors of populations left behind from the UHC goal.

Abbreviations

CI	Confidence interval
CRF	Case report form
DNA	Deoxyribonucleic acid
IQR	Interquartile range
MDA	Mass drug administration
NTD	Neglected tropical disease
OR	Odds ratio
PHCC	Primary health care centre
PhHV	Phocid Herpes virus
QALY	Quality-adjusted life-years
qPCR	Quantitative polymerase chain reaction
SDGs	Sustainable development goals
WASH	Water, sanitation and hygiene
WHO	World Health Organization
UHC	Universal health coverage
UN	United Nations

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40249-023-01094-z.

Additional file 1: Table S1. Mobility history of co-infected participants.

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Author contributions

DF and SKG contributed to the conceptualization of the manuscript. The main writers of the manuscript were SKG and DF. TR, RAR, ARR, ZTR, RMR, PRS, NR, RR, PK and DF contributed to the field implementation, data and sample collection. AZ and HvT performed the laboratory testing. AJ, PR and COD contributed to data management and cleaning. SKG performed data analysis with the support of PR and under the supervision of EL. NGS, DF, RR, RAR, GvD, ET and JM guaranteed the required funding for the study. All authors revised and approved the manuscript before submission. All authors read and approved the final manuscript.

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Availability of data and materials

Data and materials can be made available upon specific request.

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the National Ethics Committee of Madagascar (ref. no. N°23-MSANP/CERBM, 05/03/2018) and the Ethics Committee of the Hamburg State Medical Chamber in Germany (ref. no. PV7019-4419-BOff, 29/10/2019). All participants were informed about the aims of the study and its procedures in the local language (Malagasy). Study participation was voluntary and informed consent for the participation was obtained from the participant by signature or, in case of illiteracy, through a thumbprint in the presence of an independent witness.

Consent for publication

Not applicable.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary Table 1. Mobility history of co-infected participants. In orange: *S. haematobium* endemic, in green: *S. mansoni* endemic

Study Site	Place of birth	Place of home
Ankazomborona (north-western)	Fianarantsoa	Ambondromamy
	Ambararata fotsy	Ambonara
	Ambohimahasoa	Amboromalandy kely
	Ambositra	Ambonara
	Ankazomborona	Amboromalandy kely
	Ankazomborona	Madiromiongana
	Ankazomborona	Madirovalo
	Bekarara Ambony	Amboromalandy
	Fianarantsoa	Ambondromamy
	Fianarantsoa	Ambormalandy kely
	Fianarantsoa	Amboromalandy kely
	Madiromiongana	Madiromiongana
	Madiromiongana	Madiromiongana
	Maromanihy	Ambonara
	Marovoay	Madirovalo
	Tsaravotra Tsaratanana	Amboromalandy
Tsiroanomandidy (central)	Belohitsiribihina	Tsaratanàna
	Tsaratanàna	Tsaratanàna
	Tsiroanomandidy	Androtra
Andina (central)	Andina	Ampasina
	Andina	Ampasina
	Andina	Ampasina
	Andina	Ampasina
	Andina	Ampasina

II. PRESENTATION OF THE PUBLICATION

1. INTRODUCTION

1.1. The disease schistosomiasis

Schistosomiasis is one of the 20 Neglected Tropical Diseases (NTDs), which are mostly prevalent in settings of extreme poverty (Hotez and Kamath, 2009; WHO, 2023a), such as Madagascar (Barmania, 2015). Among all parasitic diseases schistosomiasis rates only second to malaria in terms of prevalence and health impact worldwide (Cioli et al., 2014). According to the World Health Organization (WHO), 230 million people in 78 countries are currently actively infected with schistosomes and more than 700 million people are living in endemic areas (WHO, 2022a). An infection with the worldwide most frequent schistosome species, *Schistosoma mansoni* and *Schistosoma haematobium*, can lead respectively to intestinal and urinary schistosomiasis (McManus et al., 2018). Humans get infected by skin penetrating cercaria when exposed to infested water during everyday activities, like domestic work, agriculture, fishing or bathing (WHO, 2021). Poor sanitation and hygiene practices favor open urinating and defecation, which introduce the parasite's eggs to freshwater bodies where the intermediate hosts, snails, reside (WHO, 2021) (**Figure 1**).

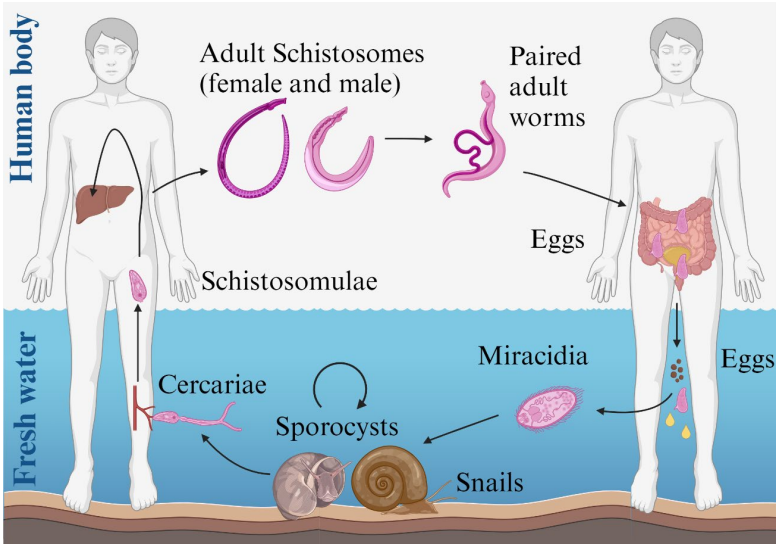

Figure 1. Schistosome life cycle: when released into fresh water, miracidia hatch from eggs and enter snails, where asexual reproduction takes place. Liberated cercariae penetrate human skin, detach tail and move to liver, where they develop to adult worms. Paired with other sex, they migrate to mesenteric veins (*S. mansoni*) or vesical vein plexus (*S. haematobium*) and lay eggs, which are excreted to fresh water by open urinating and defecation (Colley et al., 2014), created with BioRender.com.

The common drug used for treating the infection is praziquantel and is mostly distributed by vertical programs like Mass Drug Administration (MDA), an annual preventive chemotherapy, in school-aged children (Kokaliaris et al., 2022; WHO, 2022b, 2022c).

1.2. Problem definition

Even though adults living in areas with prevalence higher than 50%, and with occupations like fishing and farming are eligible to receive MDA (WHO, 2022a), the uptake among adults is described to be lower than in children (Faust et al., 2020; Gruninger et al., 2023; WHO, 2022b). Several barriers in diagnostic- and treatment-seeking of adults have been described, including the limited availability of praziquantel, the fear of social stigma, opening hours of health services overlapping with adults' working hours and associations of available treatment with out-of-pocket expenses (Dawkins et al., 2021; Evans et al., 2013; Faust et al., 2020; Gruninger et al., 2023). If infected adults remain untreated, they serve as infection reservoir for the community and risk the development of the severe chronic forms of the disease (Faust et al., 2020; Gruninger et al., 2023). Symptoms like anemia, undernutrition, diarrhea and chronic abdominal or pelvic pain can lead to chronic disability impairing the work capacity and life quality, measured in quality-adjusted life-years (QALY) (Fürst et al., 2012; Gruninger et al., 2023; King et al., 2005; Nascimento et al., 2018). As a result, vertical control programs seem to exacerbate health inequalities and hinder the achievement of Universal Health Coverage (UHC) (Cohn et al., 2019; Dean et al., 2019; Fusco et al., 2022; Rilkoff et al., 2013). UHC means that basic health care is available for everyone, everywhere and without out-of-pocket expenses (WHO, 2023b). Indeed, the control of NTDs, like schistosomiasis, has often been discussed as indicator towards UHC (Dean et al., 2019; Fitzpatrick and Engels, 2016; WHO, 2015). Countries, which succeed in implementing UHC, are also seen to improve other health-related targets and reinforce their health system (WHO, 2023b). The achievement of UHC and the control of NTDs is directly linked to reaching the sustainable development goal 3 (SDG) by 2030, which pledges to "ensure healthy lives and promote well-being for all at all ages" (United Nations, 2015). Responding to that goal the WHO released the NTD roadmap in 2021, targeting "the elimination of schistosomiasis as a public health problem" in all endemic countries, which is defined as "<1% proportion of heavy intensity schistosomiasis infections" (WHO, 2021).

1.3. Background on the study area

The study of this dissertation was conducted in Madagascar, a country with a poverty rate of over 80% (World Bank Open Data, 2023). Existence of *S. mansoni* in the East, South and in the central highlands and *S. haematobium* in in the West and Northern coastal part of the island are described (Ministère de la Santé Publique de Madagascar, 2016). Other health-issues co-exist in the country, as Madagascar reports a high burden of acute infectious diseases, like tuberculosis, plague and other chronic conditions, like malnutrition (Rasoamanamihaja et al., 2023). In 2021 schistosome spp. were endemic at all 106 implementation units of the WHO in Madagascar, 42 units reported a prevalence higher than 50%, including the district of our study site Ankazomborona (ESPEN, 2023). The overall prevalence of schistosomiasis in the country is estimated to be over 50% (Rollinson et al., 2013) and in 2022 almost 11 million of the almost 29 million inhabitants required treatment according to the WHO (WHO, 2022b). Previous studies in the country (shown in **Figure 2**) focused on school-aged-children, describing prevalence of *S. mansoni* ranging between 5% (Rasoamanamihaja et al., 2016) and 87.7% (Spencer et al., 2021) and of *S. haematobium* ranging between 30.5% (Rasoamanamihaja et al., 2016) and 64.5% (Robinson et al., 2021).

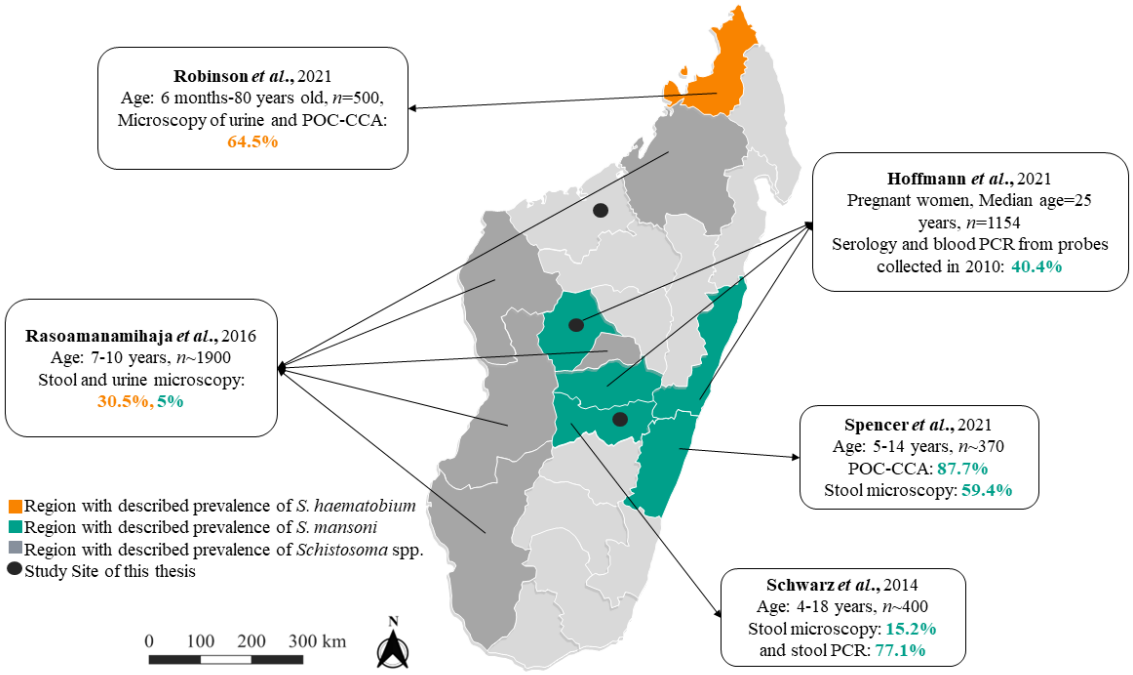

Figure 2. Map of Madagascar showing prevalence estimates from previous national studies mentioned in the original publication. Map was adapted using a template from https:// yourfreetemplates.com. *n* sample size, *OR* odds ratio, *PCR* polymerase chain reaction, *POC-CCA* Point of Care-Circulating Cathodic Antigen, *S. mansoni* Schistosoma mansoni, *S. haematobium* Schistosoma haematobium.

Studies including adults were limited to Robinson *et al*. including participants with age from 6 months to 80 years and Hoffmann *et al.* using conserved blood probes of pregnant women with median age of 25 years (Hoffmann et al., 2021; Robinson et al., 2021). Moreover, the common used diagnostic tools in the mentioned studies were Point of Care-Circulating Cathodic Antigen (POC-CCA) of urine, as well as microscopy of urine and stool, of which, when moving towards the elimination of the disease, low performances have been reported (Ajibola et al., 2018; Peralta and Cavalcanti, 2018). The Polymerase Chain Reaction (PCR) of schistosome Deoxyribonucleic acid (DNA) in human serum, urine, stool, water and snails has been found to have higher detection sensitivity and specificity, but is limited by high costs and that it requires special training of laboratory workers in low-resource settings (Ajibola et al., 2018; Frickmann et al., 2021).

1.4. Research questions and aims of the study

Based on scarce literature background, the aims of this study were to shed light on the prevalence of schistosomiasis among adults in the endemic country Madagascar with a highly specific and sensitive quantitative PCR (Frickmann et al., 2021). Further we aimed at evaluating associations between *S. mansoni* and *S. haematobium* infections in Malagasy adults and several risk factors to give a base for finding a way to broader public health interventions in the country in order to achieve UHC. Our approaches were led by following research questions:

(i) "What is the prevalence of *S. mansoni* and *S. haematobium* among adults in our study regions?"

(ii) "Which factors are related to the risk of infection with *S. mansoni* and *S. haematobium* in Malagasy adults and should be considered when broadening interventions ?"

We hypothesized that not only school-aged children, but also Malagasy adults are highly affected by schistosomiasis and that factors like age, occupation, education level and sex should be considered when it comes to planning broader schistosomiasis control strategies to reach the elimination of schistosomiasis and UHC.

2. MATERIALS AND METHODS

Three Primary Health Care Centers (PHCCs) in Madagascar were included in this study (Gruninger et al., 2023). Andina (rural) and Tsiroanomandidy (urban) are located in the center, Ankazomborona (peri-urban) is located in the north-western part of the island as shown in **Figure 2** (Gruninger et al., 2023; Madagascar en chiffres, 2022). The methodology of the study is displayed in **Figure 3**.

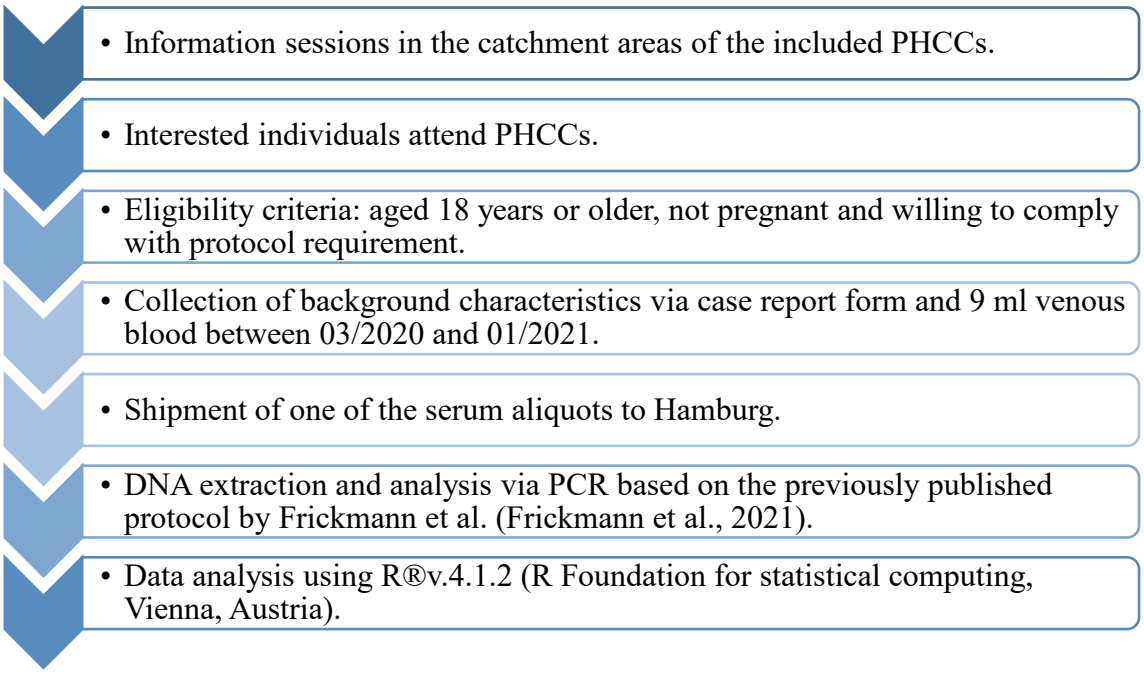

Figure 3. Flow-chart of data and sample collection and analysis process of the study (Gruninger et al., 2023). *DNA* Deoxyribonucleic acid, *PHCC* Primary Health Care Center, *PCR* polymerase chain reaction.

For the schistosomiasis prevalence estimations among the study population, relative frequencies of positive test results with 95% confidence intervals (*CI*s) were determined (Gruninger et al., 2023).

For the risk factor analysis, the study sites were divided into two subgroups according to their endemicity based on the species-specific test results (Gruninger et al., 2023). Co-infected and participants positive with the non-endemic species were excluded, so that *n*=982 participants from *S. mansoni* and *n*=464 participants from *S. haematobium* endemic regions were included in the univariable and multivariable logistic regression (Gruninger et al., 2023).

Ethical clearance was secured from the National Ethics Committee of Madagascar (ref. no. N°23-MSANP/CERBM, 05/03/2018) and the Ethics Committee of the Hamburg State Medical Chamber in Germany (ref. no. PV7019-4419-BO-ff, 29/10/2019) (Gruninger et al., 2023).

3. RESULTS

All results presented here are based on the original publication (Gruninger et al., 2023).

3.1. Study population

As displayed in **Table 1** of the original publication (Gruninger et al., 2023) 1482 adults were included with all study sites equally represented (488 to 498 individuals per site). 47.6% of the participants in Andina were female, 60.2% in Tsiroanomandidy and 54.5% in Ankazomborona. The age from the participants ranged from 18 to 84 years. With 31.2% in Andina, 36.3% in Tsiroanomandidy and 52.3% in Ankazomborona highest proportion of participants were between 18 and 29 years old. While 56.2% of the participants in Tsiroanomandidy and 43.2% in Ankazomborona reported an education level of secondary school or higher, in Andina 63.1% of the participation had only completed primary school. 71.2% of the participants in Andina had never been treated with praziquantel, while the proportion of participants never treated was 30.9% in Tsiroanomandidy and 25.8% in Ankazomborona. 95.0% of the participants in Andina, 63.1% in Tsiroanomandidy and 76.4% in Ankazomborona were working as farmer. 68.1% of the participants in Andina, 62.4% in Tsiroanomandidy and 52.7% in Ankazomborona were main contributors to the family income. While the percentage of females in the group of main contributors was 41.4% in Andina, 48.9% in Tsiroanomandidy and 39.3% in Ankazomborona, it was higher in the group of not being main contributor to the family income, with 60.8% in Andina, 79.1% in Tsiroanomandidy and 71.4% in Ankazomborona.

3.2. Prevalence estimates of schistosome infections in the study area

In the central area of Madagascar, the prevalence of *S. mansoni* infection was highest with 59.5% (95% *CI* [55.0;63.8]) in Andina and 50.2% (95% *CI* [45.7;54.7]) in Tsiroanomandidy. In Ankazomborona prevalence of *S. mansoni* was low with 1.6% (95% *CI* [0.7;3.2]). *S. haematobium* was identified in 61.3% (95% *CI* [56.8;65.6]) of participants in Ankazomborona in the northwestern, but only in 1.0% (95% *CI* [0.3;2.3]) of the participants in Tsiroanomandidy and in none of the participants in Andina. The highest prevalence of co-infections was found in Ankazomborona with 3.3% (95% *CI* [1.9;5.3]). Prevalence of co-infections was 1.0% (95% *CI* [0.3;2.3]) in Andina and 0.6% (95% *CI* [0.1;1.8]) in Tsiroanomandidy. The prevalence estimates are displayed in **Figure 4**.

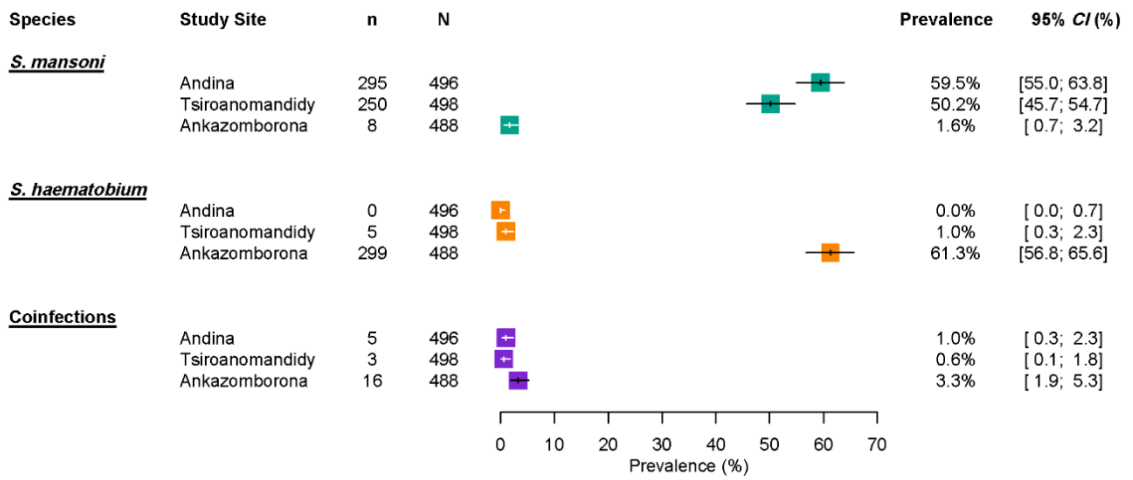

Figure 4. Forest plot showing the crude prevalence of Schistosoma species and co-infection status at study sites based on PCR results, n = 1482. *CI* confidence interval, *N* sample size, *n* positivity rate, *PCR* polymerase chain reaction, *S. mansoni* Schistosoma mansoni, *S. haematobium* Schistosoma haematobium.

3.3. Risk factors for schistosome infection

Our risk factor analysis, displayed in **Figure 2** of the original publication (Gruninger et al., 2023), showed that never having been treated with praziquantel increased the odds of infection with *S. mansoni* (adjusted *OR*: 4.72, 95% *CI* [3.40;6.65]), while odds of infection with *S. haematobium* decreased (adjusted *OR*: 0.89, 95% *CI* [0.54;1.46]).

Lower odds of infection with *S. mansoni* (adjusted *OR*: 0.49, 95% *CI* [0.33;0.72]) and *S. haematobium* (adjusted *OR*: 0.25, 95% *CI* [0.13;0.48]) were observed in age groups older than 18-29 years, especially the age group older than 50 years.

Participants in urban Tsiroanomandidy were less likely to be infected with *S. mansoni* when compared to participants in rural Andina (adjusted *OR*: 0.45, 95% *CI* [0.32;0.64]).

Illiteracy increased the odds of infection with *S. mansoni* (adjusted *OR*: 1.73, 95% *CI* [1.03;2.95]), but not with *S. haematobium* (adjusted *OR*: 0.63, 95% *CI* [0.35;1.11]).

Participants not working as a farmer were less likely to be infected with *S. mansoni* (adjusted *OR*: 0.44, 95% *CI* [0.30;0.66]) and *S. haematobium* (adjusted *OR*: 0.34, 95% *CI* [0.20;0.56]). We found higher positivity rates of *S. mansoni* (adjusted *OR*: 1.16, 95% *CI* [0.86;1.56]) and *S. haematobium* (adjusted *OR*: 1.16, 95% *CI* [0.74;1.83]) in males than in females. Odds of infection with *S. mansoni* were similar between being and not being main contributor to the family income (adjusted *OR*: 0.76, 95% *CI* [0.55;1.06]). Positivity rate of infection with *S. haematobium* was lower among the participants not being main contributor to the family income (adjusted *OR*: 0.68, 95% *CI* [0.41;1.11]).

4. DISCUSSION

In the study of this dissertation we found a prevalence of schistosome infections in adults of around 60% (Gruninger et al., 2023). *S. mansoni* was mostly prevalent in central Madagascar, while high prevalence of *S. haematobium* was detected in the north-west of the island (Gruninger et al., 2023). Alarmingly, our infection rates for both species in its endemic areas were higher than the national prevalence estimates (Rollinson et al., 2013) and prevalence among adults in other countries, like the Ivory Coast, where *S. mansoni* prevalence resulted in 23.2% (Bassa et al., 2022), and Tanzania, where *S. haematobium* prevalence was stated as 15.9% (Maseke et al., 2022). With this data we prove that also adults are at substantial risk of infection with schistosomes in endemic countries like Madagascar (Gruninger et al., 2023).

Although, our study areas exceeded the threshold for MDA (WHO, 2022c), more than 25% at each site was never treated with praziquantel before (Gruninger et al., 2023). Malagasy adults in our study regions seem systematically excluded by structured control programs, risking the accomplishment of UHC in the country, as well as SDG 3 and the NTD roadmap (Gruninger et al., 2023).

Further, the study of this dissertation provides new awareness of the distribution of schistosomiasis among adults in Madagascar, which will be important when broadening targeted interventions (Gruninger et al., 2023). First, we found a high association between younger age and infection with both Schistosome spp., implying that control strategies in these areas should particularly include Madagascar's young working population in order to reinforce the working power in the country (Bakuza et al., 2017; Bassa et al., 2022; Gruninger et al., 2023; McManus et al., 2018; WHO, 2022d). Moreover, even though prevalence seems to generally decrease in adulthood due to partially acquired immunity (Walz et al., 2015), prevalence of both species among the study participants with age older than 50 years were still over 40% (Gruninger et al., 2023).

Moreover, a lack of infrastructure, especially in rural areas, where over 60% of the Malagasy population lives, might be a reason for the higher prevalence of *S. mansoni* in rural Andina in comparison with urban Tsiroanomandidy (The World Bank, 2022). Health care centers in rural areas are often located a 2-3 hours walk away and a lack of access to sanitation seems twice as likely as in the city (Barmania, 2015; Gruninger et al., 2023; UNICEF, 2019). In the rural area Andina, we also observed lower levels of education (Gruninger et al., 2023; Raghupathi and Raghupathi, 2020). As a result, public health

interventions might need to consider the different demographic structures of the endemic areas.

Not working as a farmer was found to be a strong protective factor for schistosome infection in all study areas (Gruninger et al., 2023). As rice farming is one of the main occupations of the Malagasy population, control programs among farmers could have a great impact (The Commune Census of Madagascar in 2001, 2001).

Men in our study population were more likely to be infected, which could be explained by being the main contributor to the family income and therefore being more pronounced in occupations with higher risk of infection (Ayabina et al., 2021; Gruninger et al., 2023). However, gender equal distribution to the family income becomes more frequent and in control programs occupational risk should start being considered individually and gender neutral (Gruninger et al., 2023). **Figure 5** shows the results of the risk factor associations by species.

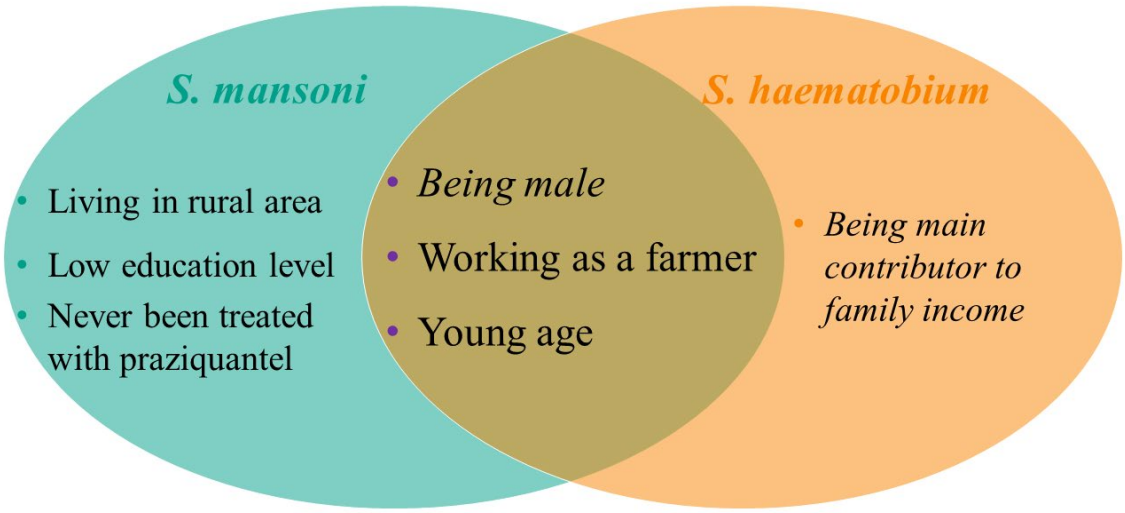

Figure 5. Venn-diagram displaying the associations with participants' characteristics and infection rate with each Schistosoma species and with both species. *Italic: OR with 95% CI crossing 0*. *CI* Confidence Interval, *OR* Odds Ratio, *S. mansoni* Schistosoma mansoni, *S. haematobium* Schistosoma haematobium.

The two main characteristics "no school education" and "never having been treated with praziquantel before" were shown as risk factors in the *S. mansoni* area but not in the *S. haematobium* area. This shows the importance to make a difference between both species in terms of control strategies (Gruninger et al., 2023; Wiegand et al., 2022).

The main strengths of this study are the use of the highly sensitive and specific quantitative PCR to assess the two species simultaneously (Cnops et al., 2013; Fuss et al., 2020; Obeng et al., 2008) and the division of the study areas in rural, peri-urban and urban

settings (Gruninger et al., 2023). The main limitation is the sampling approach through community workers, which did not guarantee the representativeness of the study population and the exploration of pre-selected risk factors (Grimes et al., 2014; Gruninger et al., 2023).

5. CONCLUSIONS

Schistosomiasis is an infectious disease of poverty; its control is often seen as indicator towards UHC. The data of this dissertation shows a schistosomiasis prevalence of over 60% in the adult populations of Madagascar, which is higher than previous national data showed (Gruninger et al., 2023). Our data reveals the relevant contribution of adults to schistosomiasis transmission and reports high prevalence in a group that is systematically excluded from interventions. Especially young adults are highly affected risking the economic productivity of the country (Gruninger et al., 2023). Farming, sex, education level and place of living also seemed to influence the chances of infection with Schistosome spp. in Malagasy adults (Gruninger et al., 2023). Keeping in mind the high prevalence and that a large number of participants has never been treated with praziquantel, our findings show a “clear unmet medical need”, which is impeding the goal of elimination of schistosomiasis in the country and UHC (Gruninger et al., 2023). Our data provides information to promote the shifting of schistosomiasis control programs towards broader interventions, including adults, to ensure that no one is left behind on the way to UHC.

6. LIST OF ABBREVIATIONS

CI: Confidence Interval

DNA: Deoxyribonucleic acid

MDA: Mass Drug Administration

NTD: Neglected Tropical Disease

OR: Odds Ratio

PCR: Polymerase Chain Reaction

PHCC: Primary Health Care Centre

POC-CCA: Point of Care-Circulating Cathodic Antigen

QALY: Quality-adjusted life-years

S. haematobium: Schistosoma haematobium

SDG: Sustainable Development Goal

S. mansoni: Schistosoma mansoni

UHC: Universal Health Coverage

WHO: World Health Organization

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8. ABSTRACT

Background: Eliminating schistosomiasis, a parasitic disease of poverty, as a public health problem is associated with the 2030 United Nations agenda for Sustainable Development Goals, including Universal Health Coverage (UHC). Current vertical control programs systematically neglect adults and impede reaching UHC. This dissertation aimed to analyze prevalence and distribution of risk factors for schistosomiasis among Malagasy adults to motivate the shift towards control strategies including adults.

Methods: This cross-sectional study was conducted between March 2020 and January 2021 at three primary health care centers in Andina, Tsiroanomandidy and Ankazomborona in Madagascar and included 1482 adult participants. Prevalence rate was determined by a semi-quantitative PCR assay from blood probes collected and risk factors for schistosomiasis were analyzed by univariable and multivariable logistic regression using the data from a case report form.

Results: Highest prevalence of *S. mansoni* was found in Andina with 59.5%, highest prevalence of *S. haematobium* was described in Ankazomborona with 61.3% and most co-infections with both species were also found in Ankazomborona with 3.3%. Protective factors for infection with both species were higher age and not working as a farmer. Higher prevalence of both species was observed among males. Living in a rural area, a low education level and no previous treatment with praziquantel increased the risk of infection with *S. mansoni*.

Conclusions: Our data show that adults in Madagascar are at high-risk for schistosomiasis. The exclusion of adults from control strategies for schistosomiasis in high endemic countries like Madagascar may hamper reaching the goal of elimination and represents a clear barrier for the achievement of UHC. Our findings suggest that re-addressing public health strategies for schistosomiasis towards broader approaches including adults will be needed to reach those goals.

Hintergrund: Das Ziel, die vernachlässigte Tropenkrankheit Schistosomiasis bis 2030 zu bekämpfen, steht im Einklang mit den Nachhaltigkeitszielen der Vereinten Nationen für 2030 und schließt auch das Prinzip der allgemeinen Gesundheitsabsicherung (englisch: Universal Health Coverage (UHC)) ein. Die derzeitigen Bekämpfungsstrategien gegen Schistosomiasis konzentrieren sich dabei allerdings auf Schulkinder und vernachlässigen systematisch Menschen im Erwachsenenalter. Das Ziel unserer Studie war, die Prävalenz und Verteilung von Risikofaktoren unter madagassischen Erwachsenen zu bestimmen und so breiter gefächerte Kontrollstrategien für Schistosomiasis zu unterstützen.
Methoden: Diese Querschnittsstudie wurde zwischen März 2020 und Januar 2021 in drei primären Gesundheitszentren in Andina, Tsiroanomandidy und Ankazomborona durchgeführt. Wir bestimmten die Prävalenz von Schistosomiasis in erwachsenen Madagassen und Madagassinnen mittels eines semiquantitativen PCR-Tests aus Blutproben von 1482 erwachsenen Teilnehmern und Teilnehmerinnen. Risikofaktoren wurden anhand univariabler und multivariabler logistischer Regression von Daten eines strukturierten Fragebogens analysiert.
Ergebnisse: Die höchste Prävalenz von *S. mansoni* lag bei 59,5% in Andina, von *S. haematobium* bei 61,3% in Ankazomborona und von Mischinfektionen bei 3,3% in ebenfalls in Ankazomborona. Nicht in der Landwirtschaft zu arbeiten und ein höheres Alter erwiesen sich als protektive Faktoren gegen eine Infektion mit beiden Spezies. Eine höhere Prävalenz von beiden Spezies wurde bei Männern beobachtet. In ländlicheren Gegenden zu wohnen, ein niedriges Bildungsniveau und noch nie mit Praziquantel behandelt worden zu sein erhöhten das Risiko sich mit *S. mansoni* zu infizieren.
Diskussion: Unsere Ergebnisse zeigen, dass Erwachsene eine Hochrisikogruppe für die Erkrankung mit Schistosomiasis sind. Der derzeitige Ausschluss von Erwachsenen von Kontrollprogrammen könnte dem Bekämpfen der Krankheit entgegenwirken und stellt ein klares Hindernis für das Erreichen des Nachhaltigkeitsziels 3 und UHC dar. Unsere Daten deuten darauf hin, dass die Kontrollstrategien für Schistosomiasis auch Erwachsene einschließen sollten, um UHC im Land zu erzielen.

III. LIST OF PUBLICATIONS

Gruninger S, Rasamoelina T, Rakotoarivelo R, Doumbia CO, Lorenz E, van Dam G, et al. Schistosomiasis control in adults: a call for action towards the goal of universal health coverage: Sarah Gruninger. European Journal of Public Health 2022;32:ckac130.031. https://doi.org/10.1093/eurpub/ckac130.031.

Gruninger SK, Rasamoelina T, Rakotoarivelo RA, Razafindrakoto AR, Rasolojaona ZT, Rakotozafy RM, et al. Prevalence and risk distribution of schistosomiasis among adults in Madagascar: a cross-sectional study. Infect Dis Poverty 2023;12:44. https://doi.org/10.1186/s40249-023-01094-z.

IV. AUTHOR CONTRIBUTION

The author of this thesis, Sarah Katharina Gruninger, contributed to the original publication of this thesis:

Title: **Prevalence and risk distribution of schistosomiasis among adults in Madagascar: a cross-sectional study**
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in the following parts:

Conceptualization of hypothesis,
Data cleaning, management, and analysis,
Main writing of the manuscript.

The contribution of co-authors was following:

Conceptualization and writing of manuscript:	Daniela Fusco
Implementation of the study in the field:	Tahinamandranto Rasamoelina, Rivo Andry Rakotoarivelo, Anjarasoa Ravo Razafindrakoto, Zaraniaina Tahiry Rasolojaona, Rodson Morin Rakotozafy, Philipp Klein and Daniela Fusco
Sample analysis:	Alexandre Zerbo and Heidrun von Thien
Data management and cleaning:	Anna Jaeger, Pia Rausche and Cheick Oumar Doumbia
Data analysis:	Pia Rausche, Eva Lorenz
Acquirement of funding of the study:	Norbert Georg Schwarz, Daniela Fusco, Raphael Rakotozandrindrainy, Govert van Dam, Egbert Tannich and Jürgen May

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VI. EIDESSTATTLICHE VERSICHERUNG

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe.
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Sarah Katharina Gruninger