Tropical Medicine and Health

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The prevalence of *Schistosoma mansoni* infection among adults with chronic non-communicable diseases in Malawi

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Abstract

Background: Schistosomiasis is a parasitic infectious disease caused by flatworms of the *Schistosoma* genus. The global burden of schistosomiasis is high. In Malawi, schistosomiasis is among the top 20 causes of outpatient department visits in health facilities. Schistosomiasis is among the most important but neglected causes of non-communicable diseases (NCD) peculiar to tropical endemic settings. While much is known about the contribution of *S. haematobium* to the NCD burden in Malawi, the role of *S. mansoni* remains largely unknown.

Methods: We conducted a cross-sectional study at Mangochi District Hospital. Adults over 18 years diagnosed with NCDs ($n=414$), admitted or attending weekly outpatient clinics were recruited between August 2021 and February 2022. Data were collected on sociodemographic characteristics, medical history, body weight, blood pressure, and fasting blood glucose. Stool and midstream urine were collected for Kato–Katz (KK) microscopy and urine point of care-circulating cathodic antigen (POC-CCA) tests, respectively. We computed prevalence of *S. mansoni* as number of positive KK and CCA tests, each divided by total submitted samples. Univariate and multivariable logistic regression were done to evaluate risk factors of NCDs and association between *S. mansoni* infection and NCDs.

Results: We recruited 414 participants, mean age 57 years (SD 16), 67% of whom were female. Prevalence of *S. mansoni* based on urine CCA was 15% (95% CI: 11–19) and 0% on KK microscopy. Hypertension was the most common condition with a prevalence of 85% (95% CI: 81–89), followed by diabetes mellitus with a prevalence of 42% (95% CI: 37–46) and heart disease with a prevalence of 3% (95% CI: 2–5). *S. mansoni* infection was not significantly associated with hypertension (OR: 1.2, 95% CI: 0.5–3.1), diabetes (OR: 0.6, 95% CI: 0.3–1.10) or heart disease (OR: 2.0, 95% CI: 0.4–10).

Conclusions: We observed moderate prevalence of *S. mansoni* infection among adults in the study per WHO classification of endemicity. This is within the range observed in children in Mangochi from 10 to 56.7%.

Keywords: *Schistosoma mansoni*, Non-communicable diseases, Urine POC-CCA test, Kato–Katz microscopy

Background

Schistosomiasis is a parasitic infectious disease caused by flatworms of the *Schistosoma* genus [1, 2]. Humans are infected by larval forms of the parasite called cercariae which are found in contaminated water sources [1, 2]. Once infected, the disease manifests in three progressive

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stages namely cercarial dermatitis (swimmer's itch), acute schistosomiasis (katayama fever) and chronic schistosomiasis [1, 3, 4]. There are six schistosome species known to cause disease in humans [5]. However, two species are prevalent in Malawi. *Schistosoma haematobium* causes urogenital schistosomiasis, and *Schistosoma mansoni* causes intestinal schistosomiasis [3, 6].

The global burden of schistosomiasis is high. Schistosomiasis transmission has been reported in 78 countries [5]. Every year, over 220 million people are infected with the various schistosome species [7]. There are over 280,000 deaths annually due to schistosomiasis [8]. It also causes disability on a massive scale accounting for over 29 million disability adjusted life years (DALYs) [8]. The greatest burden of disease is observed in Africa and South America among poor communities with limited or no access to clean water sources for cooking, washing and bathing [9]. Children under 14 years of age are also particularly vulnerable to infection [9].

In Malawi, schistosomiasis is among the top 20 causes of outpatient department visits in health facilities [10]. Over 40–50% of the population is at risk of infection [10]. *S. haematobium* is the most common parasite in Malawi with an average national prevalence of 50% [6]. While less common, *S. mansoni* infection is increasing in prevalence. This shift is most notable along the shores of Lake Malawi where the prevalence has gone from 0% before 2014 to 34.3% (95% CI: 27.9–41.3) among school children in Mangochi in 2017 [6, 11]. Follow-up studies done after this period have established the emergence of *S. mansoni* as an epidemic in Mangochi district with prevalence among school children ranging from 10 to 56.7% [12].

Schistosomiasis is among the most important but neglected causes of non-communicable diseases (NCD) peculiar to tropical endemic settings [13]. In Malawi, the STEPS survey identified risk factors of NCDs including tobacco smoking (25% in men vs 3% in women), excessive alcohol intake (30% in men vs 4% in women), overweight (28% in women vs 16% in men), physical inactivity (13% in women vs 6% in men) and raised cholesterol (11% in women vs 6% in men) [14]. However, these are common to both high and low–middle income countries. Chronic *S. haematobium* is associated with bladder cancer and cervical cancer, the 5th and 2nd most common cancers in Malawi [15, 16]. Both *S. haematobium* and *S. mansoni* cause hepatosplenic disease with portal hypertension [2]. Chronic *S. mansoni* infection also causes portal hypertension, pulmonary hypertension, cor pulmonale and eventual cardiac failure in 4–8% of those infected [17, 18].

While much is known about the contribution of *S. haematobium* to the NCD burden in Malawi, the role of *S. mansoni* remains largely unknown. Additionally, no local studies have been done to determine the prevalence of *S. mansoni* among adults who suffer from these NCDs. In this study, we investigated the role of *S. mansoni* infection in the NCD burden among adults at Mangochi District Hospital. Our aim was to estimate the prevalence of *S. mansoni* infection in adults with newly diagnosed (within 6 months) and chronic NCDs at Mangochi District Hospital, evaluate the risk factors of NCDs in this population and determine if there was an association between *S. mansoni* infection and NCD syndromes.

Methods

Study design and population

We conducted a cross-sectional study enrolling adults over 18 years with an existing or recent diagnosis of NCD attending the NCD clinic or admitted at Mangochi district hospital. The study was done over a 7-month period from August 2021 to February 2022. The enrolment criteria were: (1) all consenting adults; (2) age $\geq$ 18 years; (3) existing or recent diagnosis of NCD. We excluded everyone with critical illness defined as in a coma or requiring mechanical ventilation.

Study setting

The study was done in Mangochi, a lakeshore district at the southern tip of Lake Malawi. It has a population of 1, 148, 611 people, and 516, 976 are adults over 18 years old [19]. Mangochi district hospital is the largest health facility in the district and serves as the major referral point for health centres and other facilities. It has an NCD clinic that operates twice a week on Tuesdays (diabetes clinic) and Thursdays (hypertension clinic). Between 01 July 2019 and 01 July 2020, the clinic had a client population of 15, 903 patients. Recent studies in Mangochi district have demonstrated an emerging epidemic of *S. mansoni* infection amid the increasing prevalence of *S. haematobium* infections in this setting [12].

Sample size and subject selection

To the best of our knowledge, there was no previous epidemiological data on prevalence of *S. mansoni* in adults with NCDs. Therefore, we used a conservative estimate of 50%. Using a patient population of 15, 903, a sample size calculation with the single proportion formula (https://select-statistics.co.uk/calculators/sample-size-calculator-population-proportion/) showed that a sample of 376 was sufficient to estimate the prevalence of *S. mansoni* infection with 95% confidence and 5% margin of error. We estimated that there would be a refusal rate of 10%. Accounting for refusal, our final sample size was 414. We selected all participants who presented to the NCD clinic and the male or female wards at the hospital.

Data and specimen collection

After collecting informed consent, research assistants administered a structured questionnaire and collected data on sociodemographic factors including education, marital and employment status, risk factors for non-communicable diseases including smoking and alcohol consumption, medical history, and results of relevant laboratory investigations. We also collected data on body weight, blood pressure and fasting blood glucose parameters from hospital records. Then, participants were provided with a urine bottle and a stool collection bottle with a spoon to provide midstream urine and a stool sample. Those that could not provide samples on the same day provided them the following day. Same day sample collection occurred in the hospital. However, those who provided samples the following day collected them at home. All samples were transported to the laboratory within 12 h of collection.

Urine circulating cathodic antigen (CCA) test

S. mansoni was detected in urine using the Schisto POC-CCA test (Rapid Medical Diagnostics, Pretoria, South Africa). This rapid test detects Circulating Cathodic Antigen, one of the parasitic gut associated glycoproteins regurgitated by live adult worms in the human host. This antigen is primarily eliminated in urine and its presence is a marker for active infection. Sensitivity ranges from 70 to 100% and specificity in negative endemic populations is around 95%. For endemic studies, a single test closely demonstrates the true prevalence of infection. Two drops of urine were transferred to the circular well of a test cassette delivering a total volume of 100 µL. The result was read at 20 min. The presence of a control and test band was 'positive'. The presence of a control band and the absence of the test band was 'negative'. Participants who tested positive and reported back to the NCD clinic were prescribed praziquantel 40 mg/kg that they received at the district hospital pharmacy. Patients with known hypersensitivity to praziquantel were not treated.

Kato–Katz microscopy

To visualize *Schistosoma* ova in stool, faecal samples were pressed through a metal mesh (Sterlitech Corporation, Nylon screen, 100 mesh) to remove large particles. A portion of the sieved sample was then transferred to produce thick Kato–Katz smears on a slide. The smear was covered with a piece of cellophane soaked in a solution of glycerol and methylene blue. Light microscopy ($\times 10$ magnification and $\times 40$ magnification) was used to identify ova. Quantification of ova was not done.

Statistical analysis

Data obtained from the study were entered into ODK and the output was exported to Microsoft Excel spreadsheets. The spreadsheets were exported to STATA version 13 (StataCorp, 2013) and R version 4.1.1 (R Core Team (2021)) for analysis. We estimated the proportion of *S. mansoni* with binomial exact 95% confidence interval. Continuous variables were summarized using means $\pm$ standard deviations. Proportions were compared using two sample tests for comparing proportions and means were compared using the *t*-test. The association between two or more categorical variables was determined using the Chi-squared (χ^2) test. Univariate and multivariable logistic regression analysis were used to evaluate the risk factors of NCDs and the association between *S. mansoni* infection and NCD syndromes.

In the univariate logistic regression models, the outcome variables were binary: hypertension (yes/no), diabetes (yes/no) and heart disease (yes/no). The independent variables selected were *S. mansoni* infection, age, and sex, marital status, education status, and employment status, household income, smoking status, alcohol consumption and body weight. Risk factors with a p-value of < 0.05 on univariate analysis were selected for inclusion in the multivariable logistic regression model. The multivariable logistic regression models were checked using the Pearson χ^2 goodness-of-fit test or the Hosmer–Lemeshow goodness-of-fit test as appropriate. If the p-value for the goodness-of-fit test was < 0.05, we rejected the model. If the p-value was > 0.05, we failed to reject the model and concluded that the model fitted well. We reported results with 95% confidence intervals and p-values with significance level set at $p < 0.05$.

Ethical considerations

The protocol for the study was reviewed and approved by the College of Medicine Research Ethics Committee (COMREC P.10/20/3165). All participants provided written informed consent before participation in the study.

Results

A total of 414 adults were enrolled into the study. The mean age was 57 years (SD 16) and 67% were female. The male and female participants had mostly similar age, educational background, marital status, employment status and average household income. However, more men (78%) were currently married compared to women (51%) during the study period (difference of 27% (95% CI: 16–38). More men (45%) compared to women (29%) were also self-employed (difference of 16% (95% CI:

Table 1 Baseline sociodemographic characteristics of male and female participants

	Male	Female	Difference in mean/proportion (95% CI)	*p*-value
N (%)	137 (33%)	277 (67%)	34% (24–44)	< 0.001
Age (years)				
Mean (SD)	55 (18)	58 (14)	3 (− 6–0.1)	0.05
Education				
None	21 (15%)	67 (24%)	9% (− 27–9)	0.38
Less than primary	58 (42%)	140 (51%)	9% (− 24–6)	0.25
Primary school completed	21 (15%)	35 (13%)	2% (− 17–21)	0.83
Secondary school completed	24 (18%)	32 (12%)	6% (− 13–25)	0.53
College/university completed	8 (6%)	3 (1%)	5% (− 15–25)	0.73
Postgraduate degree	5 (4%)	–	4%	–
Marital status				
Never married	11 (8%)	7 (3%)	5% (− 15–25)	0.66
Currently married	107 (78%)	141 (51%)	27% (16–38)	< 0.001
Separated	3 (2%)	20 (7%)	5% (− 4–18)	0.74
Divorced	5 (4%)	26 (9%)	5% (− 25–15)	0.71
Widowed	11 (8%)	83 (30%)	22% (3–41)	0.12
Cohabiting	–	–		
Work status				
Government employee	11 (8%)	12 (4%)	4% (− 15–23)	0.68
Non-government	9 (7%)	7 (3%)	4% (− 17–25)	0.72
Self employed	61 (45%)	81 (29%)	16% (0.1–32)	0.05
Non-paid worker	8 (6%)	21 (8%)	2% (− 22–18)	0.85
Student	1 (1%)	–	–	–
Homemaker	3 (2%)	15 (5%)	3% (− 22–16)	0.82
Retired with benefits	13 (9%)	5 (2%)	7% (− 13–27)	0.60
Unemployed	31 (23%)	136 (49%)	26% (9–43)	< 0.01
Average household income (MK)				
Mean (SD)	87,016.15 (84,493.59)	69,117.52 (86,475.66)	17,898.64 (− 74–35 871)	0.05

0.1–32)). It was also noted that more women (49%) were unemployed compared to men (23%) during the study period [difference of 26% (95% CI: 9–43)] (Table 1).

A total of 339/414 (82%) participants submitted urine samples and 333/414 (80%) submitted stool samples. Prevalence of *S. mansoni* based on urine CCA was 15% (95% CI: 11–19) and 0% on KK microscopy. A greater proportion of women, 240/339 (71%) submitted urine samples than men 99/339 (29%), a statistically significant difference of 42% (95% CI: 31–53). The prevalence of *S. mansoni* in men and women was 8/50 (8%) and 42/50 (18%), respectively. However, this difference was not statistically significant [10% (95% CI: − 32–12)]. There were also no significant differences between participants who submitted stool and urine samples compared to those who did (Additional file 1: Table S1).

Hypertension was the most common condition among the study participants with a prevalence of 85% (95% CI: 81–89). This was followed by diabetes mellitus with a prevalence of 42% (95% CI: 37–46). Some participants, 28% (95% CI: 24–33) had both hypertension and diabetes mellitus. Heart disease with a prevalence of 3% (95% CI: 2–5) was not significantly different between men [4% (95% CI: 1–8)] and women [3% (95% CI: 1–5)].

There was low reported prevalence of smoking in men (9%) and women (2%). There was also low reported prevalence of past alcohol consumption in men (9%) and women (1%). There was no statistically significant difference in smoking and alcohol consumption between the two groups (Additional file 2: Table S2). Men and women had similar body weight [64 kg (SD 14) vs 64 kg (SD 18)]. However, height was not routinely measured to assess and compare mean body mass index. The mean systolic blood pressure in men was 150 mmHg (SD 34) and 156 mmHg (SD 33) in women (Table 2). The mean diastolic blood pressure in men was 84 mmHg (SD 17) and 88 mmHg (SD 17) in women. There was no statistically significant difference

Table 2 Body weight, blood pressure and fasting blood glucose parameters of male and female participants

	Male	Female	Difference in means (95% CI)	*p*-value
Body weight (kg)				
Mean (SD)	64 (14)	64 (18)	0.1 (− 4–3)	0.95
Blood pressure (mm/Hg)				
Systolic mean (SD)	150 (34)	156 (33)	6 (− 13–1)	0.10
Diastolic mean (SD)	84 (17)	88 (17)	4 (− 7–0.02)	0.05
Fasting blood sugar (mg/dl)				
Mean (SD)	226 (114)	250 (138)	25 (− 63–14)	0.21

in blood pressure between men and women. Men had a mean fasting blood glucose (FBS) of 226 mg/dl (SD 114) and women had mean FBS of 250 mg/dl (SD 138). However, these were not statistically significantly different.

In univariate and multivariable logistic regression analysis, the following variables were selected: *S. mansoni* infection, age, sex, education, marital status, employment status, average earnings, smoking, alcohol consumption and body weight. Age (OR: 1.1, 95% CI: 1.05–1.12), completing primary school education (OR: 0.2, 95% CI: 0.05–0.98), non-government work (OR: 7.2, 95% CI: 1.2–42), being self-employed (OR: 4.2, 95% CI: 1.2–15), being unemployed (OR: 4.7, 95% CI: 1.2–18), and body weight (OR: 1.04, 95% CI:1.01–1.07) were significantly associated with hypertension on univariate and multivariable analysis (Additional file 3: Table S3).

Age (OR: 0.97, 95% CI: 0.95–0.98), female sex (OR: 0.4, 95% CI: 0.2–0.7), smoking (OR: 6.6, 95% CI: 1.2–35), and body weight (OR: 1.02, 95% CI: 1.00–1.03) were significantly associated with diabetes on univariate and multivariable analysis (Additional file 4: Table S4). The multivariable logistic regression models to evaluate risk factors of hypertension (Pearson χ^2 goodness-of-fit p-value = 0.99; Hosmer–Lemeshow $\chi 2$ p-value = 0.53) and diabetes (Pearson χ^2 goodness-of-fit p-value = 0.06; Hosmer–Lemeshow χ^2 p-value = 0.38) were adequate and fit well with no evidence to reject the models. *S. mansoni* infection was not significantly associated with hypertension (OR: 1.2, 95% CI: 0.5–3.1), diabetes (OR: 0.6, 95% CI: 0.3–1.1) or heart disease (OR: 2.0, 95% CI: 0.4–10). Even after stratifying by sex to account for gender disparity in recruitment, *S. mansoni* infection was still not significantly associated with hypertension, diabetes or heart disease in men [(OR: 0.5, 95% CI: 0.1–2.4); (OR: 0.7, 95% CI: 0.2–2.9), respectively] or in women [(OR: 1.5, 95% CI: 0.4–5.2); (OR: 0.7, 95% CI: 0.3–1.5); (OR: 3.3, 95% CI: 0.5–20), respectively].

Discussion

This is the first study in Malawi to estimate the prevalence of *S. mansoni* infection in adults with NCDs. According to the WHO definition of endemicity for schistosomiasis, this is a moderate prevalence of *S. mansoni* infection in this population which is consistent with estimates in school going children in the district of 10–56.7% [12, 20]. This is also consistent with reports of an epidemic of both *S. mansoni* and *S. haematobium* in the district.

Increasing age and body weight, non-government work, self-employment and unemployment were associated with increased risk of hypertension. While increasing age and body weight are known risk factors [21–23], it is unclear how the various forms of employment affect hypertension. This could be related to effects of employment on lifestyle including stress, a known risk factor for hypertension [24]. Age and female sex were associated with reduced risk of diabetes. This is consistent with studies that demonstrate slight reduction in diabetes risk attributable to metabolic risk factors in younger patients (40– < 55) than older patients (≥ 75) [25]. Studies have also demonstrated that adult men have higher risk of type 2 diabetes than adult women [26, 27]. A previous study in Malawi also demonstrated higher prevalence of diabetes in men compared to women, though not statistically significant [28]. In this study, increasing body weight was also associated with increased risk of diabetes. The link between obesity and diabetes is well established and our finding is in line with this observation.

We found no statistically significant association between *S. mansoni* infection and NCD syndromes of hypertension, heart disease and diabetes. However, previous studies have linked infection with development of pulmonary hypertension [29]. Studies have also demonstrated the relationship between schistosomiasis and diabetes mellitus [30]. Chronic *S. mansoni* infection causes vascular remodelling in the pulmonary circulation which leads to pulmonary hypertension and eventual heart failure. However, the pathological changes in the heart often lead to reduced cardiac output and therefore low systemic blood pressure or hypotension as opposed to hypertension. There are also recent findings that suggest parasitic infections could protect against autoimmune and inflammatory conditions such as diabetes mellitus [29, 31–33]. In a Chinese study (n = 9539), adults over 40 years old with previous schistosome infection had lower prevalence of diabetes (14.9% vs 25.4%, p-value < 0.001) [30]. In the same study, adjusted logistic regression models showed that previous infection was protective of diabetes (OR: 0.51, 95% CI: 0.34–0.77) [30]. Other studies done in Southern Africa demonstrated that schistosome and other helminth infections reduced impaired fasting glucose

and improved pancreatic β-cell function [34]. The OR in our study (OR: 0.6, 95% CI: 0.3–1.1), would suggest a similar relationship, but this was not statistically significant.

In this study, *S. mansoni* infection was detected using POC-CCA but not KK microscopy. While surprising, this is not an unusual occurrence. When prevalence of *S. mansoni* is very high (≥ 50%), results from POC-CCA and KK microscopy are almost equivalent [35]. However, as prevalence declines below 50%, detection by POC-CCA becomes higher than KK microscopy by many degrees of magnitude [35]. In previous studies, it was observed that when prevalence of *S. mansoni* using POC-CCA was less than 30%, prevalence using KK microscopy was below 10% and even 0% in some cases [35].

A limitation of our study was that the NCD syndromes were not defined a priori. We recorded diagnoses of hypertension, diabetes and heart disease made at the clinic and did not apply our own definitions which risks misclassification of these outcomes. Secondly, physical measurements which we captured and recorded in the study such as weight, systolic blood pressure, diastolic blood pressure and fasting blood glucose were not done by the study staff. We relied on measurements done at the clinic. To the best of our knowledge, these measurements are not done using standardized instruments which risks measurement bias. Another limitation was the lack of height measurements which were not done routinely at the clinic or on the wards. Therefore, we did not report body mass index (BMI) as a possible risk factor, using body weight as a proxy instead. Furthermore, we did not prepare duplicate slides for KK microscopy. This would have increased the chances of finding eggs. Lastly, we did not collect data on recent use of praziquantel. Praziquantel-mediated killing of adult worms reduces the amount of eggs shed and chances of detection in stool.

Conclusions

There is a moderate prevalence of *S. mansoni* infection among adults with NCDs at Mangochi District Hospital. This reflects the moderate-to-high prevalence of infection observed in school going children in the district. However, there was no statistically significant association between *S. mansoni* infection and NCD syndromes. Due to the moderate prevalence of infection, we recommend continued screening and treatment of *S. mansoni* infection in this population. Larger follow-up studies to evaluate the association between *S. mansoni* infection and NCDs including hypertension, pulmonary hypertension, heart disease and diabetes should be done to assess this major public health problem.

Abbreviations

NCD: Non-communicable disease; ODK: Open data kit; POC-CCA: Point of care-circulating cathodic antigen; KK: Kato–Katz; FBS: Fasting blood sugar.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41182-022-00450-3.

Additional file 1: Comparison of participants who submitted and did not submit stool and urine samples.

Additional file 2: Behavioural risk factors and medical history of male and female participants.

Additional file 3: Regression analysis evaluating risk factors of hypertension.

Additional file 4: Regression analysis evaluating risk factors of diabetes mellitus.

Acknowledgements

We are grateful to the staff and patients at Mangochi district hospital who participated in our study. We thank Asante Makuta and Alfred Kunje for the grants and logistical support during the conduct of this study. The NCD BRITE consortium is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under grant number 5U24HL136791. The content in this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors report no relationships that could be construed as a conflict of interest.

Author contributions

WN designed the study. WN, CS, JN, GT collected data, stool and urine samples. EC and AM performed data entry. JK and KC performed laboratory tests on participant samples. WN performed statistical analysis. All authors read and approved the manuscript for publication.

Funding

This study was funded by the NCD-BRITE mentored research Grant for the period 2020–2022. The NCD BRITE consortium is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Grant number 5U24HL136791.

Availability of data and materials

The principal investigator will make data and materials available to interested parties on reasonable request.

Declarations

Ethics approval and consent to participate

The protocol for the study was reviewed and approved by the College of Medicine Research Ethics Committee (COMREC P.10/20/3165). All participants provided written informed consent before participation in the study.

Consent for publication

Not applicable.

Competing interests

All the authors report to competing interests.

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Received: 15 June 2022 Accepted: 12 August 2022
Published online: 19 August 2022

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