A cross-sectional study on urogenital schistosomiasis in children; haematuria and proteinuria as diagnostic indicators in an endemic rural area of Nigeria

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Abstract

Background: Rapid and accurate diagnosis is necessary for the management of schistosomiasis in endemic areas.
Objective: To assess the burden of urogenital schistosomiasis and the diagnostic efficiency of morbidity indicators of the disease in an endemic rural community of Nigeria.
Methods: A cross-sectional school-based study was conducted. Urine samples of 487 pupils were screened microscopically for *S. haematobium* and tested for haematuria and proteinuria using chemical reagent strips.
Results: The prevalence and intensity of infection were 57.1% and 45.0 eggs/10 mL urine respectively. Prevalence of infection in male (54.1%) and female (60.3%) individuals showed no significant variation (P>0.05). However, prevalence of infection was age dependent with those in age groups 3-5 and 12-14 years having the least and highest prevalence of infection respectively (P<0.05). Microhaematuria and proteinuria varied significantly with ages of the pupils with least (14.0, 40.0%) and highest (60.0, 80.0%) prevalence recorded in age groups 3-5 and 15-19 years respectively (P<0.05). Proteinuria showed higher sensitivity (80.3%) compared to microhaematuria (73.3%).
Conclusion: Schistosomiasis is highly endemic in the study area and the use of microhaematuria and proteinuria for mapping the infected population prior treatment could be adopted.
Key words: Schistosomaisis, haematuria, proteinuria, Nigeria
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Introduction

Schistosomiasis is a chronic disease with high public health importance as 207 million people have been estimated to be infected worldwide[1]. Most recent estimate reported 50.8 million infected individuals in aged ≤ 20 years in West Africa[2] (Schur *et al.,* 2011). Schistosomiasis has been widely reported in Nigeria[3-6].

The implementation of programmes to controlschistosomiasis requires up-to-date information regarding the prevalence and distribution of the diseases[7]. Rapid and indirect diagnostic methods have been suggested to aid quick mapping surveys in endemic regions[8].

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This becomes important as rapid detection of diseased individuals is necessary for efficient intervention through mass drug administration in the areas. Some of the notable indicators of infection especially due to *S. haematobium* for rapid assessment are haematuria, proteinuria and leukocyturia.

Operational research studies in Nigeria and other African countries have shown these indicators as good morbidity indicators of *S. haematobium* infection and have been successfully used to identify school children requiring treatment and subsequently monitor control[9,10]. However, the low sensitivities of these indicators to detect the diseased population especially in low endemic areas have raised some questions on the reliance of results obtained from such studies. An approach of combining two or more indicators has been developed to improve the diagnostic accuracy or efficiency[10].

The present school-based study reports the prevalence of urogenital schistosomiasis and reliability of haematuria and proteinuria as diagnostic indicators of the disease in a rural endemic area of Nigeria.

Materials and methods

Study setting

A cross-sectional school based study was conducted in Yewa North Central Primary School, Ijoun, Ogun State in the south-western part of Nigeria. Ijoun is a rural community with a heterogeneous population comprising the Yorubas, Fulanis, Igbos and few individuals from the Republic of Benin. The inhabitants depend on streams and rivers for their sources of water for domestic purposes. The snail intermediate hosts of *S. haematobium* have been discovered in the river bodies in the area[11].

Sample size and sampling procedures

Sample size was calculated using the method described by Naing et al.[12] A prevalence of 55% was used to compute the minimum sample size based on previous report on schistosomiasis in some other communities in the LGA[13]. The sample size arrived at was 380 with precision 0.05(5%) being the most suitable. The statistical power used was 80%. A total of 541 school pupils were recruited but 487 and 432 pupils provided urine samples for microscopic examination and reagent strips screening respectively. Class to class recruitment procedure was adopted during which the pupils through the help of the class teacher were given urine sample bottles and were monitored for urine collection. Samples were collected between March and April, 2010.

Data collection

Clean and sterile universal urine containers were given to each of the pupils to collect samples of urine. Urine, 10-20 mL, was collected at midday (10.00-14.00 hours) under the proper guide of the teachers and the research team. The urine containers were clearly labelled with the sample number assigned to each participant.

The freshly passed urine samples were inspected macroscopically for gross haematuria and then screened for microhaematuria and proteinuria using commercially available urine reagent strips (Medi-Test Combi 10, Standard Diagnostics Inc., Korea). The strip testing was performed in accordance with the manufacturer's instructions. The urinary protein content was recorded as negative (< 0.1g/L of urine), trace (<0.3g/L), 1+, 2+, 3+ or 4+. The symbols are intended to correlate as follows: +1 with 0.3 g/L, +2 with 1.0 g/L, +3 with 3.0 g/L and +4 with ≥5.0 g/L. The samples were transported in a dark container to the laboratory and processed within 24 hours after collection. Each sample was well-mixed and 10 mL was withdrawn using clean, sterile plastic syringes. This was then centrifuged at 5000 rpm for 5 minutes. The supernatant was decanted and the sediments were transferred to a clean slide and examined under a light microscope for eggs of *S. haematobium* using the x10 objective lens.

Intensity of infection was classified using Briand *et al.*'s modification of WHO recommendations[14]. Intensity of infection was thus categorized as no infection, light infection (1-9 egg/10mL of urine), moderate infection (10-49 eggs/10 mL of urine) and heavy infections (≥50 eggs/10 mL of urine). All the infected individuals were treated with single dose of 40 mg/kg of praziquantel.

The older pupils were asked their ages while in case of uncertainty and in younger pupils, the class teachers were engaged who confirmed their ages by consulting the class register containing each pupil bio-data. The age of each pupil was recorded against their names in the register created for the study.

Quality control

Urine samples collected were prevented from direct light penetration in order to avoid hatching of parasite eggs before microscopy examination. Parasite morphology and intensity was confirmed by another scientist during examination.

Ethical considerations

Ethical approval was obtained from the joint University of Ibadan/University College Hospital Ethical Review Board. Approval was also obtained from Ogun State Ministry of Health and the Ministry of Education. The community's leaders and the school's administrators were duly informed of the objectives and benefits of the study. The children parents were also invited to Parent Teacher Association (PTA) meeting during which they were briefed on the significance of the study. Written informed consent was obtained from them after a detailed explanation of the objectives of the study. Participant's personal information was treated private and was not divulged to third party. For example, sample bottles were identified only by a unique code allotted to them while every other information was recorded in the study's register.

Inclusion and exclusion criteria

All pupils with the exception of the very few ones who declined were recruited for the study.

Statistical analysis

Data were entered into an Excel spreadsheet, checked for entry errors and transferred into SPSS for Windows (version 15.0, SPSS Inc, Chicago, USA) for analysis. The sensitivity (number of individuals with a positive rapid test/individuals with a positive reference test) and specificity (number of individuals with a negative rapid test/individuals with a negative reference test) were calculated for rapid tests (chemical reagent strips) compared to the gold standard (microsscopy was used as the reference test). Chi-square tests were applied to compare relative proportions of infections between genders and ages of the pupils. When analyzing for the effect of age, pupils were divided into 5 groups: aged 3-5, 6-8, 9-11, 12-14, and ≥ 15 years. The intensity of infection measured by the parasite egg counts was logarithmically transformed into geometric mean. Student's t-test and ANOVA were used to determine significant differences in intensity of infection. P values < 0.05 were considered significant.

Results

The overall prevalence and intensity of infection due to *S. haematobium* were 57.1% and 45.0 eggs/10 mL urine (OR=1.8, CI=1.1-3.8) respectively. Prevalence of urogenital schistosomiasis varied significantly across age groups (P<0.05) with the least (27.5%) (OR=0.5, CI=0.3-1.0) and highest prevalence (68.4%) (OR=2.9, CI=2.0-4.2) recorded in age groups 3-5 and 12-14 years respectively (Table 1).

Table 1. Age and sex related infection pattern

Age group (years)	Sex	No. examined	No. infected (%)	Light infection (%)	Moderate infection (%)	Heavy infection (%)	OR(95%CI)
3-5	M	32	7(21.9)	3(42.9)	1(14.3)	3(42.9)	0.5(0.1-1.7)
	F	19	7(36.8)	2(28.6)	0(0)	5(71.4)	2.1(0.6-7.3)
	T	51	14(27.5)	5(35.7)	1(7.1)	8(57.1)	0.5(0.3-1.0)
6-8	M	65	33(50.8)	7(21.2)	14(42.2)	12(36.4)	1.4(0.7-2.8)
	F	58	25(43.1)	7(28.0)	10(40.0)	8(32.0)	0.7(0.4-1.5)
	T	123	58(47.2)	14(24.1)	24(41.4)	20(34.5)	1.2(0.8-1.8)
9-11	M	64	36(56.3)	7(19.4)	12(33.3)	17(47.2)	0.6(0.3-1.1)
	F	72	50(69.4)	8(16.0)	13(26.0)	29(58.0)	1.8(0.9-3.6)
	T	136	86(63.2)	15(17.4)	25(29.1)	46(53.5)	2.3(1.5-3.4)
12-14	M	81	52(64.2)	3(5.8)	20(38.5)	29(55.8)	0.7(0.3-1.3)
	F	71	52(73.2)	14(26.9)	11(21.1)	27(51.9)	1.5(0.8-3.0)
	T	152	104(68.4)	17(16.4)	31(29.8)	56(53.9)	2.9(2.0-4.2)
≥15	M	13	10(76.9)	1(10.0)	5(50.0)	4(40.0)	3.3(0.6-18.5)
	F	12	6(50.0)	1(16.7)	1(16.7)	4(66.7)	0.3(0.1-1.7)
	T	25	16(64.0)	2(12.5)	6(37.5)	8(50.0)	2.3(1.0-5.5)
Total	M	255	138(54.1)	21(15.2)	52(37.7)	65(47.1)	0.8(0.5-1.1)
	F	232	140(60.3)	32(22.9)	35(25.0)	73(52.1)	1.3(0.9-1.8)
	T	487	278(57.1)	53(19.1)	87(31.3)	138(49.6)	1.8(1.1-3.8)

Note: OR- odd ratio, CI- confidence interval

There was no gender difference in infection pattern (P>0.05), however, more female participants (60.3%) (OR=0.8, 0.5-1.1) were infected than the male participants (54.1%) (OR=1.3, CI=0.9-1.8). The overall prevalence of microhaematuria was 50.0% and age related prevalence of microhaematuria was similar to what was observed in infection due to *S. haematobium* with the least (14.0%) and highest (60.0%) prevalence recorded in age groups 3-5 and 12-14 years respectively (Table 2).

Table 2. Age and sex prevalence profiles of urogenital schistosomiasis morbidity indicators

Agegroup (years)	Sex	Macrohaematuria		Microhaematuria		Proteinuria
		No. examined	Prevalence (%)	No. examined	Prevalence (%)	Prevalence (%)
3-5	M	32	1(3.1)	31	4(12.9)	14(45.2)
	F	19	0(0.0)	19	3(15.8)	6(31.6)
	T	51	1(2.0)	50	7(14.0)	20(40.0)
6-8	M	65	11(16.9)	55	20(36.4)	33(60.0)
	F	58	12(20.7)	51	25(49.0)	21(41.2)
	T	123	23(18.7)	106	45(42.5)	54(50.9)
9-11	M	64	16(25.0)	51	28(54.9)	37(72.5)
	F	72	11(15.3)	55	34(61.8)	36(65.5)
	T	136	27(19.9)	106	62(58.5)	73(68.9)
12-14	M	81	16(19.8)	78	45(57.7)	65(83.3)
	F	71	8(11.3)	67	42(62.7)	49(73.1)
	T	152	24(15.8)	145	87(60.0)	114(78.6)
≥15	M	13	3(23.1)	13	7(53.9)	12(92.3)
	F	12	2(16.7)	12	8(66.7)	10(83.3)
	T	25	5(20.0)	25	15(60.0)	22(88.0)
Total	M	255	47(18.4)	228	104(45.6)	161(70.6)
	F	232	33(14.2)	204	112(54.9)	122(59.8)
	T	487	80(16.4)	432	216(50.0)	283(65.5)

Microhaematuria varied significantly across age groups ($P<0.05$) but showed no significant variation with gender ($P>0.05$). The overall prevalence of proteinuria is 65.5% with the least (40.0%) and highest (88.0%) prevalence recorded in age groups 3-5 and 15-19 years respectively. The difference in prevalence of proteinuria between age groups was statistically significant ($P<0.05$). Prevalence of proteinuria was significantly higher in male subjects (70.6%) than in the female subjects (59.8%) ($P<0.05$). The overall proportion of the population with proteinuria ranging from none (<0.1 g/L) to trace urinary quantity (<0.3 g/L) was 48.5% while 51.5% of the population had proteinuria ≥0.3 g/L. Most of the male subjects showed higher proportion of pathologic urinary proteinuria (56.3, 65.7, 100%) than their female counterparts (43.8, 34.3, 0.0%) in the 0.3, 3.0, 5.0 g/L categories respectively (Table 3).

Table 3. Severity of proteinuria in the study population (n=210)

Proteinuria Gradients (g/L)	Male Number (%)	Female Number (%)	Total (overall %)
<0.1(-ve)	10(31.3)	22(68.8)	32(15.2)
<0.3(Trace)	46(65.7)	24(34.3)	70(33.3)
0.3(1+)	36(56.3)	28(43.8)	64(30.5)
1.0(2+)	23(65.7)	12(34.3)	35(16.7)
3.0(3+)	1(100)	0(0.0)	1(0.5)
5.0(4+)	4(50.0)	4(50.0)	8(3.8)
Total (n)	120	90	210

The most sensitive (80.3%) *Schistosoma* morbidity indicator was proteinuria while macrohaematuria was the least sensitive (24.8%) indicator of infection due to *S. haematobium*. However, microhaematuria which recorded higher values in other diagnostic parameters compared to proteinuria showed overall highest diagnostic accuracy of 76.2% (Table 4).

Table 4. Diagnostic performance of indirect screening methods used for urogenital schistosomiasis

	Diagnostic Parameters					
Diagnostic Predictors	Sensitivity	Specificity	PPV[a]	NPV[b]	Accuracy	Reliability
Macrohaematuria	24.8	94.7	86.3	48.7	54.8	0.144
Microhaematuria	73.3	80.0	82.4	69.9	76.2	0.531
Proteinuria	80.3	53.4	68.9	67.8	68.5	0.337
Microscopy	100	100	100	100	100	1.000

Note a- positive predictive value, b- negative predictive value

Discussion

The results of this study confirm the active transmission of *S. haematobium* in the study area. The public health implication of the disease is high enough to attract appropriate interventions like mass drug administration and provision of safe water. The overall prevalence of urogenital schistosomiasis (57.1%) reported in this study is higher than Nigerian estimated mean prevalence 39.1%[2] and records from other African countries[15,16]. In moderate-to-high *Schistosoma* endemic regions, infection usually varies with age and gender. The heterogeneity in exposure influenced by behaviour, culture and social factors, the development of acquired immunity, as well as, physiological changes during puberty are factors that influence susceptibility to the parasite[17]. It is therefore of particular note that in the study area, this typical age-related profile of egg-positive cases appeared, being concordant with a typical endemic area. The age-related infection pattern is similar to other studies conducted in Nigeria[18,19] but clearly deviated from other studies that reported significant differences in sex-related prevalence[3]. The lack of association between infection and ages of the subjects could be due to equal dependent on natural water bodies in such low resource community with poor water development.

The high prevalence of microhaematuria and proteinuria is similar to a study conducted in Minna, Niger State, Nigeria[20]. These two morbidity indicators are recognized clinical features of *S. haematobium* infection[21]. Both symptoms are indicators of damage in the urinary tract and kidney[20]. Inconclusive evidence has suggested *S. haematobium* associated glomeruli pathology. When the glomeruli are damaged, protein and often red blood cells leak into the urine. Although, at the present, the precise origin and clinical significance of the proteinuria observed in *S. haematobium* infection remains unknown[22]. High prevalence of glomerulonephritis had been reported in areas of the tropic where urogenital schistosomiasis is also common, however

its relationship to *S. haematobium* remain unclear[23]. The occurrence of high proportion of pathologic urinary proteinuria (≥0.3 g/L) in the current study may suggest urogenital schistosomiasis involvement in inducing glomeruli pathology resulting in abnormal urinary protein excretion. This effect being more pronounced in the male subjects could be due to higher intensity of infection due to *S. haematobium* in the group compared to their female counterparts.

The degree of microhaematuria and proteinuria detectable by chemical reagent strip observed to correlate significantly with microscopy is also similar to the findings[18]. The association of these symptoms with urogenital schistosomiasis had been widely documented[24-26]. The high sensitivity for haematuria and proteinuria reported in this study conforms favourably with earlier reports[27-29]. Macrohaematuria was the most specific but least sensitive, although it has the benefit of not requiring reagent strips. Its gender disparity, however, needs to be considered if using this test, with females requiring additional test[30].

The inability to generalize result in other population groups since the participants constituted only school pupils and use of single urine sample for both microscopy and morbidity screening are the potential limitations of the study.

The present study shows that microhaematuria is the most accurate and reliable indirect diagnostic method. This is as a result of its high specificity for negative results and high positive predictive value for positive results. The high sensitivity values reflect the usefulness of these diagnostic indices as morbidity indicators of *S. haematobium* in an endemic area. It is also worth mentioning that a combination of proteinuria and microhaematuria may be more efficient in infection diagnosis than a single variable.

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