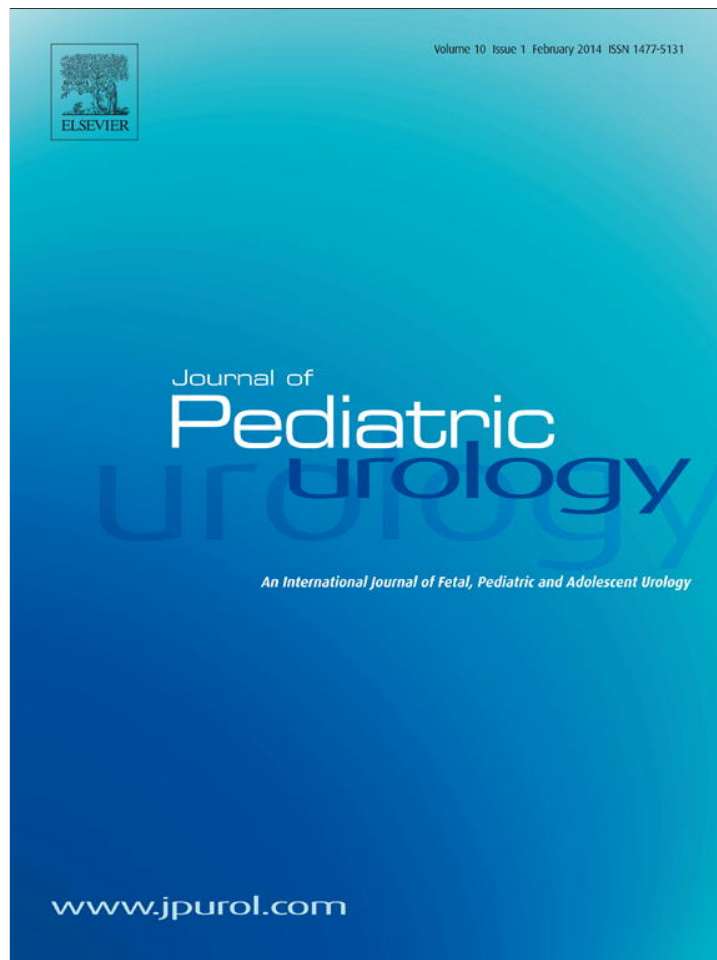


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# Urogenital schistosomiasis and urological assessment of hematuria in preschool-aged children in rural communities of Nigeria

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## KEYWORDS

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**Abstract** *Objective:* The study evaluates the prevalence of urogenital schistosomiasis and diagnostic performance of chemical reagent strips used for disease diagnosis in preschool-aged children ( $\leq 5$  years) in Nigeria rural communities.

*Patients and methods:* Urine samples from 419 children were observed microscopically for *Schistosoma haematobium* and screened for hematuria using standard urine chemical reagent strips.

*Results:* Prevalence and intensity of infection were 9.8% and 14.4 eggs/10 ml of urine, respectively. Prevalence of infection was similar in girls (10%) and boys (9.6%) ( $p > 0.05$ ). The intensity of infection was higher in boys (17.1 eggs/10 ml of urine) than in girls (12.8 eggs/10 ml of urine); however, this was not gender dependent ( $p > 0.05$ ). The occurrence of hematuria was not associated with gender ( $p > 0.05$ ), but was associated with prevalence of infection ( $p < 0.05$ ).

*Conclusion:* Infection with *S. haematobium* occurs early in life in the communities and although intensity of infection is low, it could have serious implications in disease transmission. Hematuria, although moderately sensitive to infection, is an important morbidity indicator of urogenital schistosomiasis in the study population.

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## Introduction

Schistosomiasis remains a major public health problem in many parts of the developing world [1] and being a

neglected tropical parasitic disease, the disease seems to have lost priority in the global health agenda. This is unfortunate as 50.8 million individuals aged  $\leq 20$  years in West Africa are infected with either *Schistosoma mansoni* or

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*Schistosoma haematobium*, or both species concurrently [2].

Occurrence of schistosomiasis in human populations has been widely reported in Nigeria [3–5]. These studies were, however, often targeted at school-aged children. In Nigeria and other parts of the world, preventive chemotherapy interventions with the anthelmintic praziquantel are principally targeted towards treatment of school-aged children (6–15 years old) and/or adults (>15 years old) in high-risk occupational groups. In some situations, treatments are targeted, often using school-based resources, towards those who harbor the greatest bulk of parasites [6].

Exclusion criteria against the treatment of preschool-aged children, that is children aged 5 years and below, was based on the belief that these children are not sufficiently exposed to infective water to experience high infection rates [6], which would lead to the clinical manifestation of disease, and the lack of safety data on administration of praziquantel in this age group [7]. Preschool children comprise between 10% and 20% of the 3.5 billion people living in schistosomiasis endemic areas [8]. Urogenital schistosomiasis among children in other parts of the world has been associated with poor nutritional status [9]. In Nigeria, these categories of children usually accompany their mothers to water contact sites and are very often left to play with or bathe in the river water. Thus preschool children can both be at risk of infection and a potential reservoir for the parasite in communities successfully targeted by mass anthelmintic treatment [10].

Rapid and indirect diagnostic methods have been suggested to aid quick mapping surveys in endemic regions [11]. 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 by *S. haematobium*, for rapid assessment are hematuria, proteinuria and leukocyturia. Hematuria has been the most widely studied indicator in endemic areas with high sensitivity to *S. haematobium*.

Until recently, studies on urogenital schistosomiasis among infants and preschool children were scarce in Nigeria. Urogenital schistosomiasis infections have been reported in preschool children in settlements in Adim, Cross River State and Ilewo-Orile, Ogun State, all in Nigeria [12,13]. These studies were often based on established information of high degree of human-water contact activities in these age groups. As such, the result of prevalence may not be adequate in planning an effective control program on a larger scale. The study therefore examined the prevalence of urogenital schistosomiasis among preschool children in Yewa North LGA, Ogun State to provide baseline information for mass drug administration in the area. The diagnostic accuracy of hematuria, an associated morbidity of infection, is also studied.

Yewa North LGA has the largest land area in the Ogun State, Nigeria and is located at latitude 7° 15' N and longitude 3° 3' E in a deciduous/derived savannah zone. The 2005 population projection of the State Demographic indicators showed that the population size was 232,236. The LGA has 11 wards: Ayetoro I, Ayetoro II, Ayetoro III, Igbo-gila, Ijoun, Sunwa, Imasai, Eggua, Joga/Iboro, Ohunbe and Ebute. It shares boundaries with Imeko-Afon LGA in the North, Yewa South LGA in the South, Republic of Benin in

the West and Abeokuta North and Ewekoro LGAs in the East. The people are mainly Yorubas speaking various dialects. There are many natural flowing rivers in the area, some of which include Yewa, Orori, Bareke, Iju and Iyaniwura rivers. Snail intermediate hosts of schistosomes have been sampled from the water bodies [14]. There is heavy dependence on these rivers for domestic purposes as a result of inadequate water supply in the area and various human-water contact activities like bathing, swimming, washing and fetching are common.

## Patients and methods

The cross-sectional descriptive study adopted a random sampling method to recruit preschool children. The subjects were drawn from eight wards randomly selected from the total of 11 wards in the LGA. The sample size was determined by the method of Daniel [15]. Children in their first year of life were considered as infants, while any child between the age of 1 and 5 years (i.e. between the 1st and the 5th birthday; mean age =  $4.2 \pm 1.1$  years) was considered a preschool child irrespective of his/her school enrolment status. Kindergarten pupils (age 3–5 years) from eight randomly selected primary schools and younger children recruited at the Primary Health Clinic Centers were invited to participate in the study. A preliminary pilot study was conducted to determine the prevalence or proportion of population infected. This included 30 infants and preschool children randomly selected from across the wards in the study area. The prevalence of urogenital schistosomiasis was 6.7% and precision used to calculate the sample size was 5% (0.05). A statistical power of 80% was used for the sample size determination.

The Joint Ethical Review Committee of the University of Ibadan/University College Hospital, Ibadan, Nigeria granted approval to this study. A pre-survey visit was made to the study area, during which time discussion was held with the community heads and the primary health care workers who assisted in mobilizing the people for the study. Participation of children was dependent on written consent from their parents. Children that were not resident in the study area and visitors were excluded from the study.

Pre-labeled screw-capped plastic containers for urine collection were given to 450 participants with their demographic information recorded against their numbers. The freshly passed mid-day urine samples (collected between 10 and 14 h) of 419 subjects were inspected macroscopically for macrohematuria and then screened for microhematuria using commercially available urine reagent strips (Medi-Test Combi 9<sup>®</sup>, Neumann-Neander-Str. 6-8. D-52355 Düren). The strip testing was performed in accordance with the manufacturer's instructions. The diagnostic performance of urine indicators of *S. haematobium* infection was determined. Each of the samples was well mixed and 10 ml drawn using clean, sterile plastic syringes into centrifuge tubes. Centrifugation was done at 5000 g for 5 min. The supernatant was removed using dropping pipettes and the sediments were viewed under a light microscope for the presence of terminal spined *S. haematobium* eggs. Intensity of infection was classified as light infection ( $\leq 50$  egg/10 ml of urine) and heavy infection ( $> 50$  eggs/10 ml of urine)

[16]. All children between age 4 and 5 years with positive urine samples were treated with praziquantel tablets (40 mg/kg) as recommended.

Data were entered into an Excel spreadsheet, checked for entry errors and transferred into SPSS for Windows (version 17.0, SPSS Inc, Chicago, USA) for analysis. Student's *t*-test was used to determine significant differences in the intensity of infection. Differences in proportions were tested by  $\chi^2$  tests. Contingency ( $\chi^2$ ) was performed to determine associations between variables. Pearson's correlation analysis was used to test the relationship between intensity of infection by *S. haematobium* and microhematuria. The diagnostic performance of reagent strips was assessed by calculating sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

## Results

Prevalence of infection was similar in the two sexes, with 10.0% and 9.6% prevalence in girls and boys, respectively ( $p > 0.05$ ). The geometric mean intensity of infection was higher in boys (15.4 eggs/10 ml of urine) than in girls (12.5 eggs/10 ml of urine) (Table 1); however, variation in the intensity of infection in relation to sex was not significant ( $p > 0.05$ ). No infection was recorded among the infants (3 months–1 year). The proportions of light and heavy infections in preschool-aged children were 78% and 22%, respectively.

There was a significant difference in the prevalence of urogenital schistosomiasis among preschool-aged children across the wards ( $\chi^2 = 19.32$ ,  $df = 5$ ,  $p < 0.05$ ). There was, however, no significant difference in the geometric mean intensity of infection with *S. haematobium* among the preschool-aged children in the different wards ( $p > 0.05$ ). Eggua ward had the highest prevalence of infection (19.1%), whereas no infection was recorded in Sunwa ward. The geometric mean intensity of infection was highest in Ayetoro ward with 42.6 eggs/10 ml of urine (Table 2).

The prevalence of macrohematuria in preschool-aged boys was 0.5%, whereas no visible hematuria was observed in preschool-aged girls. The prevalences of microhematuria as detected by the reagent strip in boys and girls were 7.3 and 8.0%, respectively (Table 3). The occurrence of macrohematuria and microhematuria was not associated with sexes of the children ( $p > 0.05$ ), but was associated with

**Table 1** Sex prevalence of urogenital schistosomiasis among preschool children in Yewa North LGA, Ogun State, Nigeria.

Gender	No. examined	No. infected	Prevalence (%)	GMI/10 ml urine
Male	218	21	9.6	15.4
Female	201	20	10.0	12.5
Total	419	41	9.8	14.4
<i>p</i>				0.60
OR				4.29
(95%CI)				(0.45–8.13)

OR: odds ratio; CI: confidence interval; GMI: geometric mean intensity.

**Table 2** Prevalence and intensity of urogenital schistosomiasis in preschool-aged children by wards in the LGA.

Wards	No. examined	No. positive	Prevalence (%)	GMI/10 ml urine
Ijoun	105	18	17.1	11.2
Sunwa	27	0	0.0	0.0
Imasai	35	1	2.9	19.0
Ayetoro (3)	91	3	3.3	42.6
Ijoga/iboro	77	3	3.9	9.4
Eggua	84	16	19.1	14.8
Total	419	41	9.8	14.4
<i>p</i>			<0.05	>0.05

$p > 0.05$  = no significant difference.

$p < 0.05$  = significant difference.

GMI: geometric mean intensity.

prevalence of infection ( $p < 0.05$ ). A very low proportion (0.3%) of the children showed gross hematuria, whereas microhematuria increased with age, with the age group 4–5 years having the highest proportion (7.6%).

The sensitivity (detection of *S. haematobium*-positive cases) and specificity (detection of negative cases) of macrohematuria and microhematuria are shown in Table 4. Screening for macrohematuria alone enabled accurate detection of 2.4% of *S. haematobium*-positive cases and 100% of negative cases, and the PPV, which is important in determining cost-effectiveness, was also 100% (Table 4). Microhematuria was more sensitive with 59.5%, and was considerably less specific than macrohematuria. However, the NPV of microhematuria (96.1%) was higher than that of macrohematuria (81.2%). Diagnosis of urogenital schistosomiasis using microhematuria was most accurate.

Combination of the two morbidity indicators of infection by *S. haematobium* significantly improved the sensitivity of macrohematuria from 2.4% to 29.1%. However, the sensitivity of microhematuria when used alone as a diagnostic indicator was higher than when combined with macrohematuria. Generally, the combination of the two morbidity indicators of the disease did not improve the diagnostic efficiency of reagent strips to detect *S. haematobium*-positive subjects. The intensity of infection (egg counts) showed significant positive correlation with microhematuria ( $r = 0.39$ ) ( $p < 0.01$ ).

## Discussion

Determination of schistosomiasis in preschool children is necessary because Nigeria is highly endemic for the disease [17–19], yet most previous studies focused on older school-aged groups and adults.

Urogenital schistosomiasis is endemic in Yewa North LGA and this study has shown that infection can be acquired early in life as soon as children start to come in contact with infective water. Generally, the prevalence and intensity of infection (1–14 eggs/10 ml urine) among preschool children were low. The low level of infection observed in this study can lead to benign and chronic infections, which can compromise healthy growth of preschool children in the study area, particularly when they

**Table 3** Association between gender and prevalence of hematuria in preschool-aged children in Yewa North LGA, Ogun State.

Gender	No. examined	Hematuria				OR (95% CI)
		Macrohematuria		Microhematuria		
		No. positive	Prevalence (%)	No. positive	Prevalence (%)	
Male	218	1	0.5	16	7.3	1.0 (0.5–2.0)
Female	201	0	0.0	16	8.0	1.0 (0.5–2.1)
Total	419	1	0.2	32	7.6	
<i>p</i>			0.30		0.97	

OR: odds ratio; CI: confidence interval.

are excluded from targeted preventive chemotherapy. It has been suggested that untreated infections acquired in early childhood may contribute to worsening the long-term clinical picture of disease in the individual [20].

There was no infection among the infants in this study. This may be because they were engaged in little or no active water contact activities in natural water bodies. Infants were often seen strapped to the back of their mothers while the mothers were engaged in washing or water fetching. However, the preschool children, even those who could not swim, were often left to play or bathe in the water. When the infants were bathed with water collected from natural sources or in the water bodies directly, the time spent in the water is incomparable with that of the preschool or older children. Lack of accurate diagnosis could also be responsible for the lack of infection by *S. haematobium* in the infants.

Communities with highest prevalence of urogenital schistosomiasis in preschool children in this study, are probably those in which the highest degree of human-water contact activities take place. These communities are known to lack potable water supplies, thus restricting them to the natural water bodies. In addition, in one of the most endemic communities (Ijoun), water from their wells is often of no use as there have been complaints about its hardness, hence challenge to wash with soap. The highest prevalence of infection recorded in Eggua ward could also be because of the total dependence of the people on river water that serves as transmission focus of infection. The report on the occurrence of highest intensity of infection in Ayetoro in the present study is somewhat surprising as it falls among the least endemic communities in Yewa North LGA. Being the headquarters of the LGA, the community witnesses relatively good development in terms of water supply. However, the high intensity was because of high egg loads of few individuals. On interrogation, these individuals

were cases of 'imported' infections into Ayetoro community. This has implications for control, as mobility of infected individuals between wards or communities can contribute significantly to increased risk of infection and re-infection in this area.

The similarity in the prevalence of infection recorded in girls and boys was in contrast to other similar studies in Nigeria, which reported higher prevalence in male subjects [4,13]. This may be an indication that both genders are equally exposed to infection through water contact. Higher intensity of infection in boys reported in this study could be a result of higher duration of human-water contact activities by the boys. The prevalence of urogenital schistosomiasis reported in the present study is lower than the values reported in other studies in Nigeria [4,13] and other regions of the world [10,21,22]. This could be primarily because of larger areas covered by this study, which also included areas with low endemicity of schistosomiasis. Other secondary reasons could include factors such as immunity, water contact practices and density of infected snail intermediate hosts in the water bodies [13].

Reliable and rapid diagnosis is central to the mapping of schistosomiasis [23]. Testing urine with reagent strips for blood is a simple, indirect method of identifying individuals infected by *S. haematobium*, and who require treatment [24,25]. The sensitivity of microhematuria to detect infected individuals in our study was lower than many previously reported values in Nigeria and other parts of *Schistosoma*-endemic regions of Africa [26–28]. Conversely, the specificity in the present report showed an opposite trend when compared with other reports. The discrepancy observed in the sensitivity value of microhematuria in our study with other works could be a result of regional differences and varying quality of reagent strips from different manufacturers [29]. A very low worm burden in the study population could also be a contributing factor.

**Table 4** Diagnostic performance of indicators of urogenital schistosomiasis in preschool-aged children in Yewa North, LGA.

Diagnostic parameters	Diagnostic predictors			Microscopy (%)
	Macrohematuria (%)	Microhematuria (%)	Macro + Micro (%)	
Sensitivity	2.4	59.5	29.1	100
Specificity	100	98.2	98.7	100
PPV	100	75.9	76.7	100
NPV	81.2	96.1	90.4	100
Accuracy	81.3	94.7	90.1	100

PPV: positive predictive value; NPV: negative predictive value.



It is, however, impossible to record such a very low sensitivity in highly endemic populations such as school children and young adults.

The 100% PPV for macrohematuria in this study shows its ability to detect all true positive individuals in an infected population. However, the limited number of children with macrohematuria makes it difficult to reach a definite conclusion. Macrohematuria also best diagnosed all uninfected individuals as a specificity of 100% was determined. This seems to be an advantage over other studies that enrolled only school children or the adults. Few other studies have reported very high PPV ( $\geq 90\%$ ) and specificity ( $\geq 98\%$ ) [27]. The 100% values reported for the two diagnostic parameters in our study could be an indication of low cases of hemoglobinuria in younger children [30], thus leading to absence of false-positive results with macrohematuria. The result of the combination of the two morbidity indicators of the disease not significantly improving the diagnostic efficiency of reagent strips to detect *S. haematobium*-positive subjects was similar to the Cooppan et al. [31] report on combination of hematuria with proteinuria. One limitation to the use of hematuria is that it is semi-quantitative and has a limited concentration detection range [23]. Also, the true prevalence status might have not been presented as the study made use of school-based resources and children recruited at the health centers. The children of parents with very low economic status but who are diseased may be underrepresented. Examination of a single urine specimen for both microscopy and screening of indicators of infection might have not portrayed the true prevalence status.

Result from this study showed that preschool children also stand a risk of infection by schistosomes when they come into contact with infective water. Their exclusion from preventive chemotherapy is therefore unjustifiable as many studies have shown the safety of praziquantel administration in this group. Microhematuria, although moderately sensitive to *S. haematobium* detection, is the best diagnostic indicator of infection. Macrohematuria sensitivity can be improved when used in combination with microhematuria as diagnostic indicators of urogenital schistosomiasis. Other available methods of rapid diagnosis of urogenital schistosomiasis confirmed to be more sensitive than microscopy include the soluble egg antigen enzyme-linked immunosorbent assay (SEA-ELISA) and the monoclonal antibody (MoAb)-based dipstick method. However, the cost-effectiveness of these methods compared with chemical reagent strip test can pose some limitations to their application in the disease surveillance in endemic areas. Further studies on the possible link between maternal and infant schistosomiasis in the study area are being considered.

### Conflict of interest

None.

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