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Original Article

Diagnostic Accuracy of Urine Test Strip and Morbidity Indicators of Urogenital Schistosomiasis in Kwara State, Nigeria

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Abstract

Background: The efficient management of schistosomiasis depends on the rapid and accurate diagnosis of infection. Rapid diagnostic tests are essential for identifying morbidity markers of urogenital schistosomiasis.

Methods: A total of 1,341 urine samples collected from school-age pupils in Kwara State were screened for *Schistosoma haematobium* eggs using the syringe filtration method. Haematuria and proteinuria were assessed using commercial urine reagent strips (Medi-Test Combur-9).

Results: Overall, 277 participants were infected, of which children >15 yr accounted for 37.5% of the disease prevalence. Only light and moderate infection was observed. Microhaematuria varied significantly with egg intensity ($P < 0.05$), but no association was found between hematuria severity and age. The overall prevalence of macrohaematuria was 1.3%, while microhaematuria and proteinuria were 53.9% and 19%, respectively. Macrohaematuria was found in 88.9% of *S. haematobium*-positive children while 13% of positive children tested negative for microhaematuria. Microhaematuria showed higher sensitivity (70.8%) compared to other biomarkers, while macrohaematuria had higher specificity (99.8%).

Conclusion: In the absence of other morbidity markers, microhaematuria appears to be a good proxy for urogenital schistosomiasis in our setting.

Introduction

Urogenital schistosomiasis, a parasitic disease caused by *Schistosoma haematobium* is a significant public health problem in many parts of sub-Saharan Africa.

In Nigeria, it is the most prevalent form, contributing to high morbidity and mortality rates (1). The disease burden is notable especially in



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rural areas where residents rely on surface waters.

The pathology of *S. haematobium* infection begins when the parasite inhabits the venous plexus surrounding the urinary bladder. The disease affects the urinary and genital tracts, leading to a range of clinical symptoms. Morbidity arises as a result of the host's immune response to the eggs laid by the parasite. The accumulated eggs in venules obstruct blood flow and can rupture blood vessels, allowing both eggs and blood to enter the bladder, thereby causing hematuria. Eggs trapped in the submucosa of the bladder provoke inflammatory response and granulomatous reactions, contributing to further tissue damage (2). Chronic infections may lead to fibrosis of the bladder and ureters, and in advanced stages, complications such as bladder cancer, renal failure, and genital schistosomiasis in both males and females may occur (3, 4).

Disease diagnosis is traditionally based on detection of viable eggs in urine using methods like filtration and concentration techniques (sedimentation and centrifugation). While urine microscopy remains the gold standard, it has notable limitations. It is labor-intensive, time-consuming, and requires specialized expertise to differentiate *S. haematobium* ova from other species. Moreover, it has reduced sensitivity in detecting low-intensity infections, leading to false-negative results (5-8). Despite these limitations, the WHO recommends urine microscopy and urine dipstick assays for hematuria as essential tools for field-based mapping and control of schistosomiasis.

Accurate diagnostic tools are critical to the success of control programs, surveillance efforts, and school-based interventions, particularly in endemic regions. Rapid diagnostic tests are used for on-the-spot detection of urogenital schistosomiasis aiding the early detection of cases and preventing long-term complications associated with chronic disease. (9). The urine dipstick test is favored due to its low cost, simplicity, and accuracy in detecting microhematuria (10, 11). Once microhematuria is identified

through the dipstick, confirmation of infection is performed using urine filtration and microscopy to detect and quantify eggs (12).

Morbidity indicators such as hematuria, proteinuria, and leukocyturia are frequently employed for the rapid screening of urogenital schistosomiasis (13, 14). However, their reliability is questionable in regions with low endemicity, where they fail to detect the disease accurately. Additionally, they cannot distinguish between schistosome-induced hematuria and hematuria resulting from other medical conditions, like urinary tract infections (UTIs). These false positives can reduce the diagnostic accuracy of the dipstick test, highlighting the need for additional diagnostic methods or confirmatory tests. A more comprehensive diagnostic approach is recommended to enhance specificity and prevent misdiagnosis, especially in regions with overlapping endemic conditions (15).

Several studies have documented the efficacy of urine dipstick in the diagnosis of urogenital schistosomiasis in field settings (13, 16, 17, 18). Similarly, varying sensitivity and specificity for morbidity markers have been reported in surrounding regions such as Ondo (19), Oyo (20), Osun and Ogun States (21). Microhaematuria has been described as highly sensitive and specific in Southwest region (19, 22), while a combination of haematuria+leucocyturia+nitrituria was highly sensitive and specific in diagnosing infection in North Central Nigeria (15).

Although the diagnostic performance of urine dipstick in detecting urogenital schistosomiasis at point-of-care was assessed in some parts of Kwara State where microhaematuria was observed to be highly sensitive and specific (22), researches comparing the performance of reagent urinalysis dipsticks against the urine filtration method in different transmission settings remain insufficient.

Therefore, we aimed to determine the diagnostic accuracy of urine reagent strips compared with the urine filtration method in detecting urogenital schistosomiasis and to

evaluate morbidity indicators among school-aged children in Kwara State, Nigeria.

Materials and Methods

Study Setting

A cross-sectional school-based study was carried out in 2023 in Kwara State, located in Nigeria's North-Central region. The State is divided into three senatorial districts: Kwara North, Kwara Central, and Kwara South and is geographically situated between latitude 9°38'54.6642" and longitude 5°7'41.6496". The randomly selected study locations were of heterogeneous population with the Nupe and Yoruba ethnic groups being the most dominant. The region faces challenges related to infrastructure, with healthcare facilities, electricity, and pipe-borne water being insufficient in many areas. Additionally, the majority of residents rely on surface water sources for their domestic and agricultural needs.

Ethical Consideration

Ethical approval for this study was granted by the Kwara State Ministry of Health Research and Ethics Committee (Ref. No.: ERC/MOH/2023/01/085). Community leaders and school administrators were thoroughly briefed on the study's goals and potential benefits. Additionally, parents and guardians were informed about the study through the Parent-Teacher Association (PTA). Consent forms were duly signed by the parents/caregivers before children were enrolled.

Study population

Following initial visits to randomly chosen schools, children aged 4 to 20 yr were selected from the study areas. Overall, 1341 children participated in the study.

Inclusion and exclusion criteria

Only children whose parents or guardians had provided signed consent and resided in the area for at least 6 months before the study

began were included. Exclusion criteria included children whose parents did not provide consent, those not lived in the community for the required 6-month period, and menstruating females, due to risk of false-positive hematuria.

Sample Collection

Participants were provided with a clean, sterile, pre-labeled universal container for urine collection between 10 a.m. and 1 p.m. Samples were first examined macroscopically for visible hematuria and then tested for microhematuria and proteinuria using urine reagent strips. Afterward, the samples were preserved with 1-2 drops of 10% formalin and transported to the Parasitology Laboratory at the Zoology Department, University of Ilorin.

Determination of microhaematuria and proteinuria

Urine reagent strip (Medi-test Combur-9; Analytic on Biotechnologies, Lichtenfels, Germany) was immersed in the urine sample for approximately one second, after which excess urine was removed by gently sliding the strip along the edge of the container. Results were read after one minute, with the color change on the strip compared to the manufacturer's diagnostic color chart. Microhaematuria was scored based on the number of erythrocytes per microlitre of urine: negative, 5-10 Ery/uL, 50 Ery/uL, and 250 Ery/uL. Proteinuria was scored as negative, 30 mg/dL, 100 mg/dL, and 500 mg/dL, in line with the manufacturer's guidelines.

Urine filtration technique

The filtration method was employed to detect *S. haematobium* eggs in urine. In brief, 10 mL of urine was drawn using a clean plastic syringe and filtered through a qualitative paper filter with an 8µm pore size. The filter was stained with 10% Lugol's iodine and examined under a 10x objective of a light microscope. The eggs, which stained orange, were counted and intensity classified as light (1-49 eggs/10 mL),

moderate (50-499 eggs/10 mL), and heavy (>500 eggs/10 mL) (23).

Data Analysis

All data were entered into SPSS ver. 24 (IBM Corp., Armonk, NY, USA). Descriptive statistics was used to obtain the frequency of participants with macrohaematuria, microhaematuria, and proteinuria. The severity of microhaematuria with respect to egg intensity and age groups among the *S. haematobium* infected study respondents was tested using Fisher's exact. To evaluate the diagnostic performance of test strips, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy was calculated. The sensitivity of the reagent dipstick test was determined by calculating the proportion of true positives correctly identified when compared to the standard method (urine filtration). The specificity was calculated as the proportion of true negatives correctly identified against the reference standard. PPV represents the likelihood that the disease is present when the test

result is positive, while NPV indicates the likelihood that the disease is absent when the test result is negative. All charts were generated using Microsoft Excel, *P*-values <0.05 were considered statistically significant.

Results

Kwara South had the highest number of respondents with macrohaematuria (2.7%), followed by Kwara North (0.9%). Microhaematuria and proteinuria were more evident in Kwara Central (62.3%) and Kwara South (26.4%) (Table 1). Macrohaematuria was observed in all age-groups except for respondents ≤5 and >15 yr of age. Age group ≤5 yr had a higher prevalence of microhaematuria while proteinuria was more common in age group 11-15 yr. The overall prevalence of microhaematuria and proteinuria was 53.9% and 19% respectively (Table 2). Macrohaematuria was observed in more males (1.8%) than females (0.9%).

Table 1: Prevalence of macrohaematuria, microhaematuria, and proteinuria, stratified by sex and senatorial district of the study respondents

Senatorial district	Sex	Macrohaematuria		Microhaematuria		Proteinuria	
		No examined	Prevalence (%)	No examined	Prevalence (%)	No examined	Prevalence (%)
Kwara North	M	148	0(0)	148	65(43.9)	148	22(14.9)
	F	174	3(1.7)	174	91(52.3)	174	35(20.1)
	T	322	3(0.9)	322	156(48.4)	322	57(17.7)
Kwara Central	M	263	2(0.8)	263	169(64.3)	263	38(14.4)
	F	268	0(0)	268	162(60.4)	268	31(11.6)
	T	531	2(0.4)	531	331(62.3)	531	69(13)
Kwara South	M	247	10(4)	247	122(49.4)	247	71(28.7)
	F	241	3(1.2)	241	109(45.2)	241	58(24.1)
	T	488	13(2.7)	488	231(47.3)	488	129(26.4)
Total	M	658	12(1.8)	658	356(54.1)	658	131(19.9)
	F	683	6(0.9)	683	362(53)	683	124(18.2)
	T	1341	18(1.3)	1341	718(53.5)	1341	255(19)

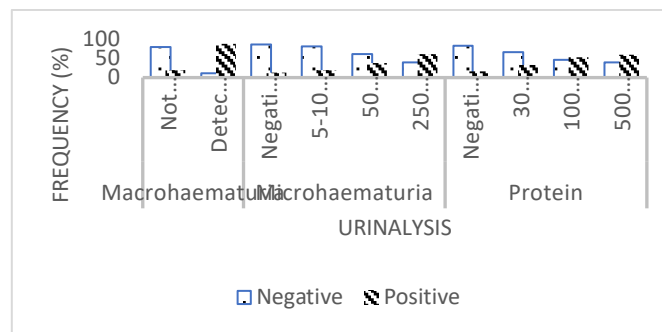
*M-Male, F-Female, T-Total

Table 2: The distribution of macrohaematuria, microhaematuria, and proteinuria with respect to the age and sex of the study respondents

Age group (yr)	Sex	Macrohematuria		Microhaematuria		Proteinuria	
		No exam-ined	Preva-lence (%)	No exam-ined	Preva-lence (%)	No exam-ined	Preva-lence (%)
≤5	M	41	0(0)	41	24(58.5)	41	4(9.8)
	F	31	0(0)	31	19(61.3)	31	4(12.9)
	T	72	0(0)	72	43(59.7)	72	8(11.1)
6-10	M	291	6(2.1)	291	165(56.7)	291	51(17.5)
	F	300	4(1.3)	300	154(51.3)	300	54(18)
	T	591	10(1.7)	591	319(54)	591	105(17.8)
11-15	M	301	6(2)	301	153(50.8)	301	73(24.3)
	F	337	2(0.6)	337	185(54.9)	337	63(18.7)
	T	638	8(1.3)	638	338(53)	638	136(21.3)
>15	M	25	0(0)	25	14(56)	25	3(12)
	F	15	0(0)	15	4(26.7)	15	3(20)
	T	40	0(0)	40	18(45)	40	6(15)
Total	M	658	12(1.8)	658	356(54.1)	658	131(19.9)
	F	683	6(0.9)	683	362(53)	683	124(18.2)
	T	1341	18(1.3)	1341	718(53.5)	1341	255(19)

The distribution of macro-haematuria, micro-haematuria, and proteinuria among *S. haematobium* infected and uninfected respondents is shown in Fig. 1. Macro-haematuria was detected in 88.9% of infected pupils. However, only 11.1% of pupils who were negative for *S. haematobium* showed visible signs of haematuria. Eighty-seven percent of uninfected pupils

tested negative for microhaematuria. Only 13% of pupils tested negative for microhaematuria despite being infected. Up to 250 Erythrocytes per microlitre (Ery/uL) of urine was observed in 60.7% of infected pupils, while only 18.9% had as low as 5-10 Ery/uL of urine. Sixty percent of infected pupils had up to 500 milligrams per deciliter (mg/dL) of protein in urine.

**Fig. 1:** Distribution of macrohaematuria, microhaematuria, and proteinuria among *Schistosoma haematobium*-infected and uninfected study respondents

Only light and moderate infections were observed in the study population (Table 3). Microhaematuria varied significantly with egg

intensity while there is no significant association between the severity of hematuria and the age of the study respondents.

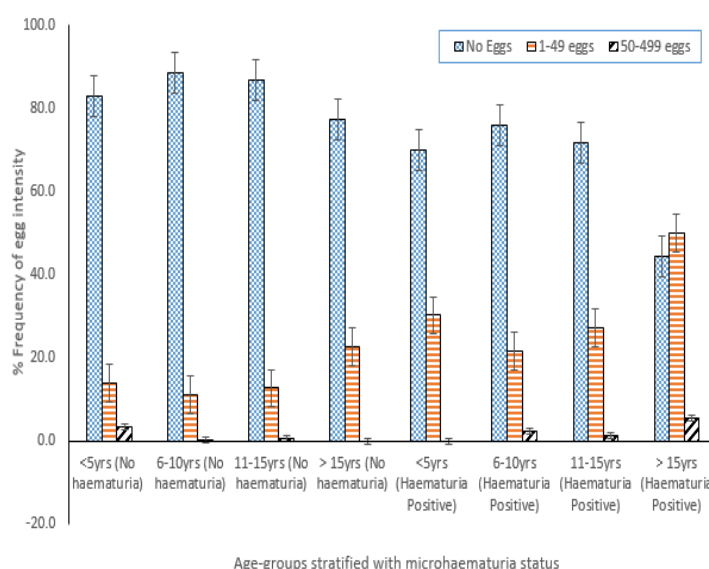
Table 3: Severity of microhaematuria in relation to egg intensity and age groups of *Schistosoma haematobium*-infected study respondents.

Variables	Microhematuria				P-value
	Negative	5-10 Ery/uL	50 Ery/uL	250 Ery/uL	
Egg inten-	77(29.6)	98(37.7)	30(11.5)	55(21.2)	0.007
sity	4(23.5)	2(11.8)	1(5.9)	10(58.8)	
1-49					
50-499					
Age(yr)	5(27.8)	5(27.8)	5(27.8)	3(16.7)	0.640
≤5	31(28.7)	35(32.4)	13(12)	29(26.9)	
6-10	40(29.4)	54(39.7)	12(8.8)	30(22.1)	
11-15	5(33.3)	6(40)	1(6.7)	3(20)	
>15					

*1-49 eggs - Light infection; 50-499 eggs - Moderate infection

The level of microhaematuria stratified with egg intensity and age groups is shown in Fig. 2. In all the age-groups, except for >15 yr, microhaematuria was higher in participants with no eggs in urine compared to those with

light and moderate infection. In all participants, microhaematuria was highest among those with moderate infection in the age group >15 yr.

**Fig. 2:** Level of microhaematuria stratified by egg intensity and age groups

Microhaematuria showed a higher sensitivity (70.8%) compared to proteinuria (32.9%) and macrohaematuria (5.9%). Conversely, macrohaematuria had a higher specificity (99.8%)

compared to proteinuria (84.6%) and microhaematuria (50.9%) (Table 4).

Table 4: Diagnostic performance of indirect screening methods use for the screening of urogenital schistosomiasis

	TP	FP	FN	TN	SENSITIVITY	SPECIFICITY	PPV	NPV
Micro-haema-turia	196	522	81	542	70.76	50.94	27.30	87.00
Pro-tei-nuria	91	164	186	900	32.85	84.59	35.69	82.87
Macro-hema-turia	16	2	261	1062	5.78	99.81	88.89	80.27

*True positive (TP), False positive (FP), False negative (FN), True negative (TN), Positive predictive value (PPV), Negative predictive value (NPV)

Discussion

The overall prevalence of macrohaematuria observed in this study is quite lower compared to reports of other authors (24, 25). Kwara South had the highest number of respondents with macrohaematuria (2.7%). During this study, variability in the frequency of chemotherapy was observed with selected areas in Kwara South having either nil or long history of drug intervention. Only light and moderate infection was recorded in this study. This could have informed the low prevalence of macrohaematuria observed, as it is often positively correlated with moderate-heavy infections. Moreover, a high correlation between infection intensities and elevated morbidity levels has been observed (26). The absence of heavy infection could be as a result of intensified mass drug administration, especially in Kwara North. In the past, authors have reported heavy infections among respondents in this study area (27, 28) and other regions (16, 29). However, similar observation was made in the assessment of urogenital schistosomiasis among school children in Southwest Nigeria (30).

Several pupils (11.1%) who were negative for *S. haematobium* showed visible signs of haematuria. This could be that eggs were missed during routine microscopy. The WHO opined that the sensitivity of urine testing can be improved “by repeated sampling and/or sampling of a

larger volume of urine”, but such methods are considered “not practical” (31). In addition, macrohaematuria with no concomitant egg in urine could be induced by other disease conditions.

Children of age group ≤ 5 yr had a higher prevalence of microhaematuria. Although, this age bracket accounted for 25% of disease prevalence, an increasing burden of urinary schistosomiasis has been observed in them (32-34). Some participants tested positive for microhaematuria despite having zero egg in urine. The prevalence of microhaematuria rarely dips to zero even after treatment with praziquantel, either because bladder lesions and associated microhaematuria persists longer than the actual excretion of eggs into the bladder (35), or due to the differential sensitivity or performance of reagent strips in their ability to detect microhaematuria (14).

More than half (53.5%) of the study population had microhaematuria. Several authors have made similar observations in their studies (36, 37). A high grade microhaematuria of up to 250 Ery/uL of urine was observed more in participants with moderate infection than those with light infection (58.8%, 22.1% respectively), $P < 0.05$. This could be as a result of egg build up in the capillary beds of the urinary bladder as the disease progresses.

The reliability of any test is hinged on its ability to correctly identify individuals who actually

have the disease (sensitivity), and also correctly identify those who do not have the disease (specificity). In this study, microhematuria appear to be a fairly good morbidity indicator for urogenital schistosomiasis due to its relatively high sensitivity, however, it suffers low specificity. In regions with low prevalence, microhematuria is considered an unreliable marker for identifying urogenital schistosomiasis (38). However, several studies have shown a high sensitivity and specificity for urine reagent strips (13, 22, 39).

Ideally, a test should have a high sensitivity and specificity. However, none of the morbidity markers assessed in this study matches this criterion. Moreover, a trade-off between sensitivity and specificity was observed. Although microhaematuria showed a high sensitivity (70.8%), a very high number of false positives (low specificity) was observed. Similarly, for proteinuria and macrohaematuria which showed very high specificities (84.6% and 99.8% respectively), a high number of false negatives (low sensitivity) was observed for these indicators. This buttresses previous observations that the combination of two or more morbidity indicators will improve diagnostic accuracy and reliability of reagent strips in the detection of *S. haematobium*. Observations from North Central Nigeria indicated that haematuria + leucocyturia + nitritia were the most sensitive morbidity markers for *S. haematobium* infection with sensitivity and specificity of 56.7% and 92.0% (15). Similarly, when proteinuria and hematuria are used in combination, they provide a more accurate assessment of morbidity compared to when they are used individually (14).

A high number of participants (82.9%) negative for *S. haematobium* infection were also negative for proteinuria. Proteinuria has been found to have a strong correlation with urogenital schistosomiasis, as the eggs of *S. haematobium* are metabolically active and release over a thousand proteins to aid their passage through tissues (40). However, other health conditions can also lead to proteinuria. Elevated urine protein levels in *S. haematobium* infections have

been associated with conditions such as nephritis, nephrotic syndrome, and bladder pathology. Nevertheless, bilharzial proteinuria does not necessarily indicate renal dysfunction (41).

Conclusion

Accurate diagnosis and timely treatment of urogenital schistosomiasis are essential to prevent long-term morbidity. This study highlights the utility of reagent strips as a cost-effective, rapid, and user-friendly adjunct for disease detection, with microhaematuria showing high sensitivity and serving as a reliable proxy in the studied population. Combining microhaematuria with other biomarkers, such as proteinuria, enhances the diagnostic accuracy and better captures disease morbidity. The potential inaccuracies of dipsticks in low-prevalence areas must be considered. Therefore, diagnostic decisions should be supported by microscopic examination of urine. These findings are significant for disease control, particularly in school-based screening programs and public health initiatives. Integrating simple diagnostic tools like reagent strips into existing WHO programs can improve early detection and contribute to the global effort to eliminate urogenital schistosomiasis.

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Conflict of interest

The authors declare that there is no conflict of interest.

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