

## Original Research Article

# Clinical usefulness of urinary symptoms and urinalysis in diagnosis of *Schistosoma haematobium* infection in an endemic area in Southern Nigeria: descriptive study

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**Received:** 08 March 2024

**Revised:** 31 March 2024

**Accepted:** 03 April 2024

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## ABSTRACT

**Background:** *Schistosoma haematobium* infection occurs worldwide with the largest number of cases seen in sub-Saharan Africa. Most of the infections are acquired during childhood and are linked to urogenital diseases which contributes significantly to morbidity and mortality. A study on the use of urinary symptoms, signs and urinalysis in the diagnosis of *S. haematobium* infection might aid in providing early, prompt and rapid intervention that will limit associated complications.

**Methods:** The study was a descriptive cross-sectional of 421 children aged 6-12 years in Ohaukwu LGA, Ebonyi State, recruited from four public primary schools using multistage sampling method. Urinary symptoms and signs were obtained using a questionnaire; urine samples were collected for urinalysis and urine microscopy. Simple proportions and odds ratio (CI) were used to analyze the data. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for various symptoms and signs. The data was analyzed with IBM-SPSS 20. Significance was set at  $p < 0.05$ .

**Results:** The prevalence of *S. haematobium* infection among school children in Ohaukwu LGA was 30.17%. Visible blood in urine 71.77% and dysuria 70.16% were the predominant symptoms while liver tenderness 8.87% was the most common sign. The sensitivity vs specificity of visible blood in urine and microscopic haematuria were 71.77% vs 94.43% and 100.00% vs 97.21% respectively.

**Conclusions:** Microscopic haematuria alone was highly sensitive and specific and can be a reliable alternative to the gold standard in making diagnosis of *S. haematobium* infection in children living in this endemic region.

**Keywords:** Urinary, Schistosomiasis, Symptoms, Signs, Diagnosis

## INTRODUCTION

Schistosomiasis is a common intravascular infection caused by parasitic *Schistosoma* trematode worm.<sup>1</sup> It is a major neglected tropical disease considered as the third

most devastating tropical disease in the world, after malaria and intestinal helminthiasis, with more than 200,000 people dying from it each year.<sup>2,3</sup> It occurs in 78 countries, with 240 million infected people and close to 700 million at risk individuals.<sup>4,5</sup> It is a disease of poverty

with 85% of all schistosomiasis cases occurring in Sub-Saharan Africa, especially in communities without access to safe drinking water and adequate sanitation.<sup>6</sup> Despite the introduction of the schistosomiasis control initiative by the world health organization (WHO) since 2002, only sporadic control activities have taken place in Sub-Saharan Africa.<sup>4,6</sup> Consequently, current schistosomiasis disease burden remains high and could exceed 70 million disability-adjusted life-years (DALYs).<sup>6</sup> Nigeria has the greatest number of cases of schistosomiasis worldwide with an estimated 29 million people infected (among which 16 million are children) and 101 million people at risk of infection. The disease occurs in all 36 states of Nigeria and the federal capital territory.<sup>3,5,7,8</sup>

Urogenital schistosomiasis usually presents with haematuria a few weeks after infection and is the first sign of established disease.<sup>1,2</sup> Dysuria and haematuria can occur in early and late disease.<sup>1,6</sup> Late manifestations include proteinuria, bladder calcification and ureteric obstruction, secondary bacterial infection in the urinary tract which can lead to renal failure, in addition, it can also lead to morphologic changes in the bladder.<sup>1,6</sup> To control the negative effects of *S. haematobium* infection, early diagnosis and prompt treatment are required.

The use of urine microscopy, which is the gold standard in the diagnosis of *S. haematobium* infection, requires specialized skills, equipment and regular electricity.<sup>9</sup> These resources might not be readily available in most primary and secondary health care facilities in Nigeria. Also, microscopy gives a low yield in areas of low intensity of infection.<sup>9</sup> Therefore, an alternative means of diagnosis which is less resource intensive and requires a lower degree of specialization is needed. Hence, this study aimed to evaluate the accuracy, sensitivity and specificity of urinary symptoms, signs and urinalysis in making a diagnosis of *S. haematobium* infection.

## METHODS

### *Study area and population*

This study was conducted in primary schools in Ohaukwu local government area (LGA) of Ebonyi State, South-Eastern part of Nigeria.<sup>16</sup> Ohaukwu LGA has a population of about 196,337 people.<sup>10</sup> The study population comprised of primary school pupils aged 6-12 years selected from government approved public school within the study area. The study was carried out from May to July 2018. Four primary schools were selected for the study following a multistage sampling method, namely: central primary school Ezzamgbo, Okporo forest primary school Effium, central primary school Ngbo and Ndiaguigubebe primary school Ngbo.

### *Study design and protocol*

This was a descriptive cross-sectional study. Ethical approval committee of the federal medical centre (FMC)

Owerri. A protocol approval and permission were then gotten Ebonyi State universal basic education board, Abakaliki and the headmaster /headmistresses of the selected schools. Children aged 6-12 attending the selected public primary schools within the study area, whose parents /guardians consented to their participation in the study and who had lived in Ohaukwu LGA for at least twelve weeks were recruited. Children with intake of anti-schistosomal drug and arthemeter compound within three months prior to the commencement of the study and children with urogenital or perineal trauma in the previous four weeks were excluded from the study. Also, the females whose menstruation occurred within seven days prior to day of recruitment were excluded from the study.

### *Sample size determination*

Using the prevalence of 46.1% from *S. haematobium* in a study done among school age children in Ebonyi, South-Eastern Nigeria, minimum the sample size was estimated as 421 pupils using the formula below.<sup>11,12</sup>

$$N = Z^2P(1-P)/ D^2$$

Multistage random sampling technique was used to select the schools and the subjects. Four schools were randomly chosen while the number of pupils to be recruited per school and per class were proportionally calculated using the formulae below;

Population of the target school × calculated sample size/Total population of 4 schools

Population of the class × calculated number of pupils in the selected school/population of the target school

The subjects were then selected from each class by a simple random sampling method using the class register. Selected pupils were given the consent form and the questionnaire to take home to their parents/caregivers to fill, and measurements were taken when they returned a completely filled questionnaire.

### *Urinalysis*

The participants were given a wide mouthed screw-capped 40ml code-matched container each to collect at least 20ml of urine in the school urinary after running across the school field for 5 minutes as exercise.<sup>13,14</sup> This was carried out between 10.00 am and 2.00 pm when the highest egg count is usually obtained.<sup>14,15</sup> Urinalysis with dipstick of the urine sample was done using Medi-Test Combi 9<sup>®</sup> test strips (MACHEREY-NAGEL Gmb H and Co. KG, Germany). Blood and protein concentration were semi-quantitatively determined by briefly dipping each strip into freshly voided stirred urine sample making sure that the test areas were fully immersed. The colour changes were read after one minute in a good light by

comparing with the colour scale on the container and result were recorded on a code-matched questionnaire.

### Urine microscopy

The same urine sample used for urinalysis was transported to the hospital microbiology laboratory for urine microscopy after adding a drop of 10% formalin to prevent the eggs from hatching. Urine microscopy was done using Nytrell Millipore filters.<sup>15</sup> Ten millilitres of the urine was withdrawn using 10 ml syringe. The urine was then injected through a 12-millimetres (mm) diameter Swinnex® filter support containing 13 mm Nytrell T1 20 HD filter with a mesh size of 20 micron. Once the urine was completely expelled from the syringe, time was allowed for the urine to filter. The filter support was then opened and the filter was removed with the forceps and placed to face upwards on a glass slide and a drop of saline was added to prevent drying. The glass slide was examined under a binocular light microscope to identify the presence of *Schistosoma* eggs. Presence or absence of *Schistosoma* eggs was then recorded.

### Data analysis

Data was analysed using statistical package for social sciences (IBM SPSS) version 20. Data was presented in the form of tables, mean and standard deviation. Odds ratio and CI was used to analyse associations. The appropriate analysis tool was used to determine sensitivity, specificity, as well as, positive and negative predictive values of the symptoms, and signs, haematuria and proteinuria individually and in combinations. Significance was set at  $p < 0.05$ .

## RESULTS

Table 1 shows the demographics of the study participants. Four hundred and twenty one (421) participants were recruited, 240 (57.00%) males and 181 (43%) females. The majority of them 288 (68.41%) were in age range of 10-12 years. In addition, 394 (93.59%) were from the lower social class while none of the study participants were from the upper social economic class.

**Table 1: Socio-demographics characteristics of the study participants.**

Variables	N (%)
<b>Gender</b>	
Male	240 (57.00)
Female	181 (43.00)
<b>Age group (in years)</b>	
6-9	133 (31.59)
10-12	288 (68.41)
<b>Social class</b>	
Upper	0
Middle	27 (6.41)
Lower	394 (93.59)
<b>Class grouping</b>	
1-3	183 (43.50)
4-6	238 (56.50)

Visible blood in urine and dysuria were the most common urinary symptoms in microscopy positive participants. Symptoms significantly occurred in microscopy positive participants when compared to microscopy negative participants ( $p=0.001$ ). Liver tenderness was the predominant sign in microscopy positive participant (11, 8.87%) while the suprapubic tenderness was the least sign observed (4, 3.23%). Majority of the microscopy positive subjects had more than one symptom. Children who were positive for schistosomiasis were significantly more likely to have liver tenderness by approximately 14 times. Majority of the microscopy positive subjects had more than one symptom.

All the microscopy positive children (100%) had microhematuria by reagent test, while 88.19% had proteinuria by reagent test. This difference was statistically significant ( $p=0.001$ ). Also 112 of the ova positive children had proteinuria compared with two of the ova negatives ( $p < 0.001$ ).

All the urinary symptoms (haematuria and dysuria) tested had higher specificity than sensitivity, A combination of visible blood in urine, microhaematuria and proteinuria for diagnosis was highly sensitive and highly specific.

**Table 2: Comparison of various symptoms and signs between microscopy positive and negative participants.**

Symptoms	Microscopy positive, (n=127) (%)	Microscopy negative, (n=294) (%)	X <sup>2</sup>	P value	
Visible blood in urine	91 (71.77)	16 (5.57)	8.36	0.001*	
Urine frequency	50 (39.52)	16 (5.57)	5.84	0.001*	
Dysuria	89 (70.16)	32 (10.80)	7.64	0.001*	
Lower abdominal pain	77 (60.48)	36 (12.20)	6.63	0.001*	
Sign	Microscopy positive, n=127 (%)	Microscopy negative, n=294 (%)	Total	OR (95%CI)	P value
Liver tenderness	11 (8.87)	2 (0.70)	13 (3.09)	13.8 (3.02-63.6)	0.001*
Suprapubic tenderness	4 (3.23)	2 (0.70)	6 (1.43)	4.80 (0.86-26.28)	0.060
Renal tenderness	8 (6.45)	4 (1.40)	12	4.88 (1.44-16.52)	0.009*

\*Statistically significant, OR=Odds ratio.

**Table 3: Comparison of prevalence of micro-haematuria and proteinuria among microscopy positive and negative participants.**

Reagent findings	Microscopy positive, n (%)	Microscopy negative, n (%)	P value
<b>Microhaematuria</b>	127 (100.00)	8 (2.72)	0.001*
<b>Proteinuria</b>	112 (88.19)	2 (0.68)	0.001*

\*Statistically significant.

**Table 4: Validity of combination of symptoms, signs and urine tests in diagnosis of schistosomiasis.**

Variables	SEN (%)	SPE (%)	PPV (%)	NPV (%)
<b>Visible blood in urine (VBU)</b>	71.77	94.43	84.76	88.56
<b>Dysuria</b>	70.16	89.20	73.73	87.37
<b>VBU + dysuria</b>	59.68	96.52	88.10	84.71
<b>VBU + dysuria + frequency</b>	23.39	98.26	85.29	74.80
<b>VBU + dysuria + frequency + abdominal pain</b>	19.35	98.95	88.89	73.96
<b>Dysuria + frequency</b>	31.45	96.52	79.59	76.52
<b>Dysuria + frequency + abdominal pain</b>	25.81	98.61	88.89	75.47
<b>Frequency + abdominal pain</b>	32.26	96.86	81.63	76.80
<b>VBU + liver tenderness</b>	13.71	98.61	80.95	72.56
<b>Hematuria by reagent strip alone</b>	100.00	97.21	93.94	100.00
<b>Proteinuria by reagent strip alone</b>	87.90	99.30	98.20	95.00
<b>VBU + liver tenderness + hematuria</b>	13.71	100.00	100.00	72.84
<b>VBU + liver tenderness + proteinuria</b>	13.71	100.00	100.00	72.84
<b>VBU + micro-hematuria</b>	71.77	99.30	97.80	89.06
<b>VBU + proteinuria</b>	65.32	100.00	100.00	86.97
<b>Proteinuria + microhematuria</b>	87.90	99.30	98.20	95.00
<b>VBU+ microhematuria + proteinuria</b>	85.82	98.97	97.32	95.10

SEN=sensitivity; SPE=specificity; PPV=positive predictive value; NPV=negative predictive value; VBU=visible blood in urine.

## DISCUSSION

The gold standard for the diagnosis of *S. haematobium* infection is urine microscopy, which can be cumbersome and time-consuming.<sup>1,9,16</sup> The current study assessed the performance of urinary symptoms, signs and urinalysis as a diagnostic tool for *S. haematobium* infection. Visible blood in urine (participant reported) and dysuria were the predominant symptoms observed while urinary frequency was the least common. Visible blood in urine is thought to be due to the inflammation of the bladder wall microvasculature during the passage of ova through the bladder mucosa, while dysuria and abdominal pain could arise from the ulceration of the bladder wall.<sup>17,18</sup> Urinary frequency on the other hand, occurs as a result of increased excitation of vesical membrane.<sup>17</sup> The reason why visible blood in urine and dysuria were reported more in this study could be that seeing blood in urine and having pain during micturition were discomfoting and scaring to both parents and the children. On the hand urinary frequency was the least symptoms. This is possibly due to the fact that urinary frequency is not seen as any threat to the children and they may not keep count. Visible blood in urine has been documented by several researchers as the most predominant symptom in children with *S. haematobium* infection.<sup>18,19</sup> This study observed that liver tenderness was predominant sign while suprapubic pain was least sign. Liver tenderness is caused by enlargement of the liver which is a sign of advanced

disease. This may be a pointer that in this endemic region some children may be in advanced stage of *S. haematobium* infection. This underlines the need for prompt and early detection. Urinary schistosomiasis should be suspected in this area and in similar regions where children presently have hepatomegaly and tenderness.

The overall prevalence of microscopic haematuria (32.07%) in this study was higher than proteinuria (27.08%). Microscopic haematuria usually results from the granulomatous host response to deposition of the schistosome eggs in the bladder wall tissue as well as its localization in the vesical plexus. Microscopic haematuria is usually the first feature of infection explaining therefore it's high prevalence. On the other hand, the urinary protein indicates that the lesions in the bladder and ureters have advanced to possibly cause glomerular pathology. This finding is consistent with that observed by Lengeler et al and several other studies.<sup>20-22</sup> In contrast, Morenikeji et al reported a higher prevalence of proteinuria (65.5%) when compared with microscopic haematuria (50%).<sup>23</sup> They suggested that the heavy intensity of infection in their study area could have resulted in increased glomerular injury leading to excess urinary protein excretion.<sup>23</sup> This is supported by Barsoum et al who indicated that in the presence of *S haematobium* ova, there may be deposition of immune complexes in the

glomerular mesangium causing local inflammation and thus protein leak from the glomeruli.<sup>24</sup>

Importantly, this study also showed that microscopic haematuria occurred in all children positive for *S. haematobium* ova by urine microscopy whereas proteinuria was found only in 88% of them. This is similar to finding of Okeke et al and Ogbonna et al both in Enugu State of Nigeria and several other studies.<sup>18,19,25,26</sup> Therefore, microscopic haematuria by reagent strip could be reliable and rapid diagnostic tool and may be used in mapping of urogenital schistosomiasis in endemic areas.

Furthermore, when sensitivity and specificity, of some parameters in diagnosis of *S. haematobium* infection were tested in this study, visible blood in urine alone showed high sensitivity (71.77%) and higher specificity (94.43%) while microhaematuria alone showed the highest sensitivity (100%) and very high specificity (97.21%) for the diagnosis of *S. haematobium* infection. Also, visible blood in urine combined with microhaematuria and proteinuria showed high sensitivity (85.82%) and a much higher specificity (98.97%) This indicates that microhaematuria alone could identify up to 100% of those who truly have the disease and 97.21% of those who did not have the disease, while visible blood in urine combined with microscopic haematuria and proteinuria would identify up to 85% true positives and 97.21% of true negatives. However, Salawu et al reported a high specificity of 98.7% and a much lower sensitivity of 29.1%.<sup>27</sup> when both macro and micro haematuria were used in the diagnosis of *S. haematobium* infection. Observed variation in sensitivities of microhaematuria could be due to regional differences and the nature of study population. In their study, participants were mainly pre-school children who were known to have very low worm burden due to little or no exposure to contaminated water.<sup>25</sup> Although, combination of visible blood in urine, microscopic haematuria and proteinuria is highly indicative of a diagnosis of *S. haematobium* infection, microscopic haematuria alone showed the highest sensitivity and specificity, hence, can be employed in diagnosis *S. haematobium* infection in this resource poor endemic area similar environments.

### Limitations

This study was cross-sectional in nature, it was difficult to assess the day-to-day variation of egg excretion or haematuria which may have influenced diagnostic performance. The lack of access to the private schools in the study, also limited assessment of the prevalence of *S. haematobium* infection in children who attend private primary schools the study area.

### CONCLUSION

The use of microscopic haematuria alone in diagnosis of *S. haematobium* infection was highly sensitive and highly

specific in this population. Visible blood in urine and dysuria were the predominant symptoms of urinary Schistosomiasis in the study participants. During school enrolment, the use of microhaematuria can be a reliable alternative to urine microscopy in screening for *S. haematobium* infection in this and similar endemic regions. This would enhance control activities including intermittent mass drug administration and community screening programs.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Nwaoha CA, Nwolisa EC, Ikejiaku UP, Amamilo IB, Ekanem EE. Clinical usefulness of urinary symptoms and urinalysis in diagnosis of Schistosoma haematobium infection in an endemic area in Southern Nigeria: descriptive study. *Int J Contemp Pediatr* 2024;11:507-12.