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EVALUATING THE EFFECTIVENESS OF POSITIVE URINALYSIS IN THE DIAGNOSIS SCHISTOSOMA HAEMATOBIUM INFECTION IN CHILDREN IN ABUJA
Adaora Adeline Okechukwu. (FMCPaed), Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada. P.M.B 228, Gwagwalada, Federal Capital Territory, Abuja, Nigeria,
Agnes-Jane Ifeanyichukwu Dike. (FWACP),Department of Paediatrics, Federal Medical Centre, Makurdi, Hospital Road, Makurdi. P.M.B 102004. Makurdi, Benue State.

Corresponding author: Adaora Adeline Okechukwu: Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada. PMB 228, Gwagwalada, Federal Capital Territory, Abuja, Nigeria,
Email: nebokest@yahoo.com

EVALUATING THE EFFECTIVENESS OF POSITIVE URINALYSIS IN THE DIAGNOSIS SCHISTOSOMA HAEMATOBIUM INFECTION IN CHILDREN IN ABUJA

A. A. Okechukwu, and A. I. Dike

ABSTRACT

***Objective*: To determine the prevalence of urogenital schistosomiasis among children with positive urinalysis, and the diagnostic efficacy of such in the diagnosis of urinary schistosomiasis.**
***Design*: A cross sectional school-based study.**
***Setting*: The study was among apparently healthy, school children from public primary schools in Gwagwalada Area Council, of Federal Capital Territory, Abuja, Nigeria.**
***Subjects*: Urinalysis was carried out among 861 healthy primary school pupils. The egg of Schistosoma haematobium was sought in the urine sample of 145 subjects with positive urinalysis using light microscope. Their bio data, and social class were assigned to the subjects.**
***Results*: One hundred and forty-five (16.8%) subjects had positive urinalysis. The prevalence of Schistosoma haematobium infection among such subjects was 36(24.8%). More of the infected were females (52.8%), those between 9-10years (36.1%), those from rural schools (86.1%), and those from low social class (58.3%). The most sensitive urinalysis morbidity indicator for Schistosoma haematobium infection in this study was combination of haematuria+leucocyturia+nitrituria with sensitivity, specificity, positive predictive value, accuracy and reliability of 56.7%, 92.0%, 60.7%, 90.6%, 85.6%, and 0.743, followed by haematuria+leucocyturia. The least were leucocyturia, and nitrituria with sensitivity, positive predictive values of 0.0% each, and reliability of 0.482 and 0.307 respectively. The only risk factor for Schistosoma Haematobium infection in this study was source of water supply, OR=3.71, 95% CI 0.93-16.02, p=0.009.**

Conclusion: **The prevalence of urinary schistosomiasis among primary school pupils with positive urinalysis was high. Presence of haematuria+leucocyturia+nitrituria or haematuria+leucocyturia can be a useful rapid diagnostic morbidity indicator for urinary schistosomiasis.**

INTRODUCTION

Schistosomiasis is one of the neglected tropical diseases (NTD), and most important water-borne infestation with devastating effects on those affected.[1] According to WHO, it is second to malaria as the most important socio-economic deadly NTD, affecting more than 243 million people worldwide, with over 93% cases in sub-Saharan Africa, and Nigeria having the highest burden across the globe.[2,3] Schistosoma Haematobium (SH) belong to the species of flat worms affecting mostly the rural dwellers, children, and disadvantaged urban population.[3] The infection is acquired through contact with cercariae-polluted water during washing of clothes, swimming, and bathing in infested water. Symptoms may be acute or chronic, and usually present with microscopic or macroscopic haematuria, proteinuria, leucocyturia, dysuria, recurrent urinary tract infection (UTI), and genital ulcers.[4] Distribution of this disease is focal, commonly in rural areas where natural fresh water is used for domestic water supply, recreational activities, and agricultural production. Extreme poverty, lack of knowledge of the risks, inadequacy of public health facilities, unsanitary conditions are factors contributing to the risk and transmission of infection.[5] Nigeria has the highest burden of this disease with prevalence rates ranging from 10.3% to 57.1%.[5-8]

Rapid and indirect diagnostic methods have been suggested to aid in the quick mapping survey for SH infection in endemic areas.[9] Some of these notable indirect indicators are haematuria/microhaematuria, proteinuria, and leucocyturia.[10] Studies in Africa have shown such indirect method to be effective in identifying children with SH infection.[11,12] However, their low sensitivity (SS) and specificity (SP) have raised some questions on its reliance. The clinical usefulness of any diagnostic test is determined by its accuracy in identifying disease condition in question. Accuracy measures SS, SP, positive and negative predictive values (PPV, NPV) by calculating these indices using egg microscopy as gold standard.[12,13] The predictive value of these tests however varies with changing prevalence and intensity of disease.[12,14] Parasitological diagnoses of SH can be difficult among persons with chronic infections because of passage of small quantity of eggs in the urine. Clinicians therefore resorted to other methods for diagnosis such as rectal biopsy, presence of antigens, antibody, indirect methods such as haematuria/microheamaturia, proteinuria, detection of specific DNA Dra1 fragments, and ultrasound scanning of the urinary tract.[15] These other methods have their own challenges such as the invasive nature of rectal biopsy which may not be ethically right for just diagnosis. However, the diagnostic performance of some of the other techniques are variable, and difficult to set a "gold" standard in areas with variable SH prevalence.[15]

Combining two or more of these indirect morbidity indicators may improve diagnostic accuracy/reliability of SH. We therefore conducted this study to establish not only the

prevalence of SH infection among healthy primary school children with urinary abnormalities in Gwagwalada, Abuja, but also to assess the accuracy and reliability of using such abnormalities in the diagnosis of SH infection.

SUBJECTS AND METHODS

The study was carried out in Gwagwalada area council (GAC), of Federal Capital Territory (FCT), Abuja, Nigeria, which has 10 wards, and Guinea Savannah as the predominant vegetation. There is six months of rainy season (May to October) and six months of dry season (November to April) with temperature varying between 12^{0}C to 40^{0}C.[16] Over one million people reside in the area council which has urban, semi-urban, and rural settlements. A major stream with pockets of ponds can be seen within the area. The area council is inhabited mainly by farmers, civil servants, traders, skilled and unskilled artisans. GAC has 80 government primary schools, 60 in the rural areas and 20 in the urban areas.

The study was cross sectional, school-based study conducted over a 6month period of September 2017 to March 2018, in apparently healthy, school children, aged 6-12years from 24 selected public urban and rural primary schools in GAC. A five (5) staged multi-random sampling was used in the selection of the subjects. The 1st stage was selection of schools from the 80 public primary schools using a simple random sampling method. With the ratio of 1:3 urban to rural primary schools in the area council, 6 urban schools, and 18 rural schools were randomly selected. The 2nd to the 5th stages were apportioning, and selection of the subjects from the selected schools. Using sample size of 1008 subjects calculated from prevalence of urinary abnormality of 9.6% from a Nigeria study,[17] 252 and 756 subjects were apportioned for the selected urban and rural schools with a total of 42 subjects picked from every selected school. A flow diagram of the subject selection was shown in Fig 1.

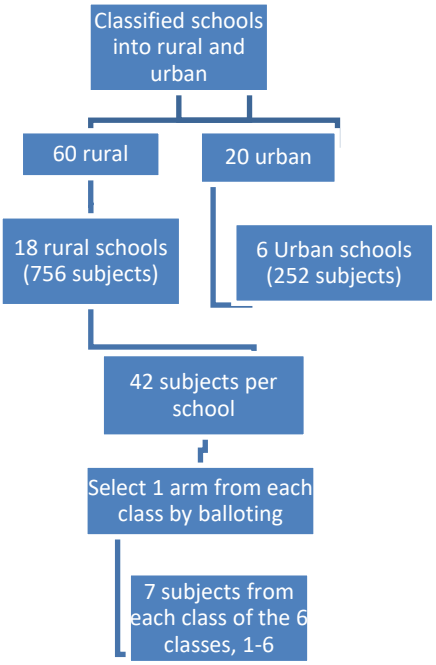

Fig 1: Flow diagram showing selection of the study population

Inclusion criteria for the study were healthy children who agreed to be part of the study, and whose parents/caregiver also signed informed consent form. Excluded were children with evidence of kidney disease such as nephrotic syndrome, those with history of passage of bloody urine, girls who were menstruating, and those whose parents or caregivers did not want to be part of the study. Questionnaires on the bio-data, and the procedure for urine sample collection was explained to the children. Collected early morning urine samples were analysed using the Combo strips (DFI co. Ltd.). Urinary protein was recorded as negative, trace, 1+, 2+, 3+ or 4+. Haematuria, leucocyturia, and nitrituria were also recorded as positive or negative in the assay.

Another urine was collected between 10.00 am-14.00 pm for subjects with positive urinalysis and transported in a dark container to the laboratory for microscopic view for egg of SH within 24 hours of collection. Each sample was centrifuged at 5000 rpm for 5 minutes, the supernatant decanted, the sediments transferred to a clean slide and examined under a light microscope for eggs of SH using x10 objective lens. Intensity of infection was thus categorized as no infection, light infection 1+, 2++, and heavy infections, 3+++. All the infected individuals were treated with single dose of 40 mg/kg of praziquantel. The flow diagram of the subject selection for egg of S. Haematobium was shown in Fig 2.

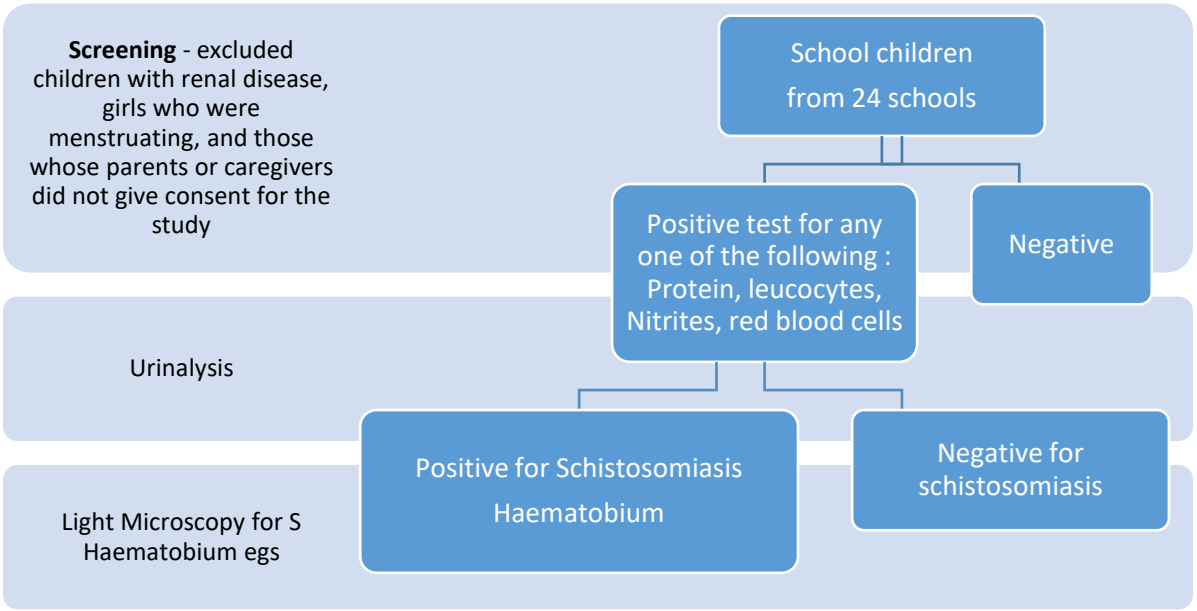

Fig 2: Flow chart showing selection of the study population for Egg of S. Haematobium.

Bio-data collected included: type of house, type/source of water supply, ethnic group, religion, level of education of both parents/ caregiver, their type of occupation, history of any renal disease. Socio-economic class (SEC) was assigned to every subject using Oyedei *et al*[18] classification which was based on father's occupation and mother's level of education

Ethics Clearance was obtained from the UATH Ethics Committee, the F.CT. Research

Committee, F.C.T. department of policy and implementation education Secretariat, F.C.T Universal Basic Education Board, and Heads of the selected schools.

Data analysis was done using statistical package for Social Sciences (SPSS) version 22, and Stata version 14. Frequency table was calculated, and chi-square used to compare categorical variables, while logistic regression was used to test the covariates with significant values. P value of <0.05 was considered statistically significant. Reliability test was used to calculate of the sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and accuracy of the positive urinalysis.

RESULTS

Table 1 is the socio-demographic characteristics of the study population. Of the 861 samples analysed, more were females (53.9%), more had negative urinalysis (83.2%), more were between the ages of 9-10years (36.4%), and more schools were in the rural communities (75%). Majority were Moslem (57.7%), most were from the lower social class (46.2%), and 66.9% uses pipe born water. For the category with positive urinalysis which constitute 16.8% of the subjects, there were also more females (60.0%), more (38.6%) between the ages of 11-12 years, more were Moslems (76.6%), more from rural schools (80.6%), more (47.5%) from the low social class, and more (51.7%) that uses pipe born water. There was no statistical significant difference between the mean age of subjects with positive and negative urinalysis, 9.66±2.06 years Vs 9.45±2.12 years (x^2=0.956, p=0.35), and some other variables: sex, urinalysis result, age range, and location of schools. There was however statistically significant difference between subjects with positive and negative urinalysis for religion (x^2=27.51, p=0.001), ethnic group (x^2=14.0, p=0.003), type of housing (x^2=6.036, p=0.049), source of water supply (x^2=25.57, p=0.001), and social class (x^2=24.48, p=0.001).

Table 1

Socio-Demographic Characteristics of the Study Population

Variables	**Total Population N (%) N=861**	**Negative urinalysis N (%) N = 716**	**Positive urinalysis N (%) N=145**	**Chi-square statistic**	**P Value**
Sex					
Male	397 (46.1)	339 (47.3%)	58 (40.0)	2.62	0.106
Female	464 (53.9)	377 (52.7%	87 (60.0)		
Urinalysis					
Positive	145 (16.8)	109(15.2)	36 (24.8)	0.067	0.796
Negative	716 (83.2)	607(84.8)	109 (75.2)		
Age range (years)					
6 – 8	277 (32.2)	233(32.6)	44 (30.3)	4.37	0.113
9 – 10	313 (36.3)	268(37.4)	45 (31.0)		
11 – 12	271 (31.5)	215(30.0)	56 (38.6)		
Mean					
Age (years)	*9.49±2.11	*9.45±2.12	*9.66±2.06	0.956	0.34

Location of school					
Urban	215 (25)	187(26.1)	28 (19.3)		
Rural	646 (75)	529(73.9)	117 (80.6)	2.982	0.084
Religion					
Christian	339 (39.4)	310(43.3)	29 (20.0)		
Moslem	497 (57.7)	386(53.9)	111 (76.6)	27.51	0.001
ATR	25 (2.9)	20(2.8)	5 (3.4)		
Ethnic group					
Ibo	73 (8.5)	67(9-.4)	6 (4.1)		
Yoruba	93(10.8)	84(11.7)	9 (6.2)	14.0	0.003
Hausa	203 (23.6)	155(21.6)	48 (33.1)		
Others	492 (57.1)	410(57.3)	82 (56.6)		
Type of house					
One/two rooms	284 (33.0)	238(32.2)	46 (31.7)	6.036	0.049
Flat	359 (41.7)	308(43.0)	51 (35.2)		
Others	218 (25.3)	170(23.7)	48 (33.1)		
Source of water Supply					
Stream	109 (12.7)	78(10.8)	31 (21.3)	25.57	0.001
Ponds	153 (17.8)	115(16.1)	38 (26.2)		
Pipe borne water	599 (66.9)	524(73.1)	75 (51.7)		
Social Class					
Upper	218 (25.3)	197(27.5)	21 (14.5)	24.48	0.001
Middle	245 (28.5)	190(26.5)	55(38.0)		
Lower	398 (46.2)	329(46.0)	69 (47.5)		

Fig 3 and 4 showed the pie chart for subjects with positive urinalysis, and those positive urinalyses with ova of SH. For the first category of subjects (Fig 3, positive urinalysis) single urine abnormality showed haematuria of (32.0%), proteinuria of (21.0%), leucocyturia 11.0%), and nitrituria (8.0%). Positive urinary abnormalities in combination were proteinuria+haematuria (11.0%), haematuria+leucocyturia+nitrituria (10.0%), haematuria+leucocyturia (4.0%), and haematuria+nitrituria in (3.0%). The second category (Fig 4, positive urinalysis with ova of SH), ova was seen in 47.2% of combination of haematuria+leucocyturia+nitrituria, was also documented in 25.0% with haematuria+leucocyturia, in 8.0% of haematuria+nitrituria, 8.0% of proteinuria+haematuria, 6% of proteinuria, and 6.0% of haematuria. Positive urinalysis with no eggs of SH were leucocyturia (0.0%), and nitrituria (0.0%).

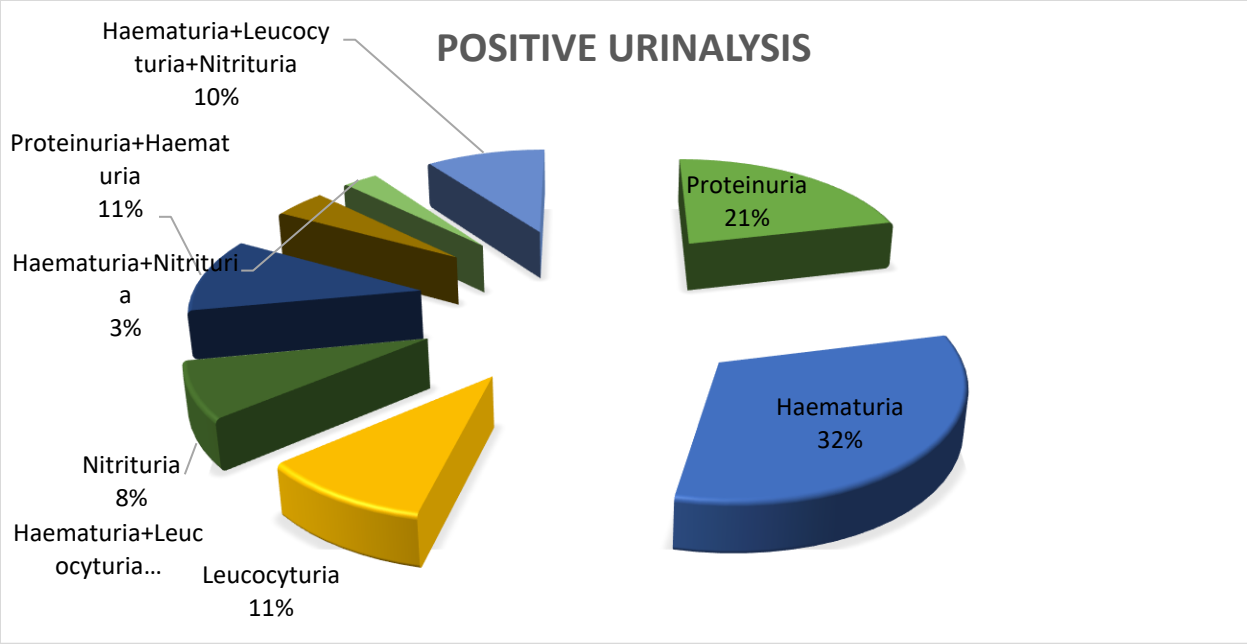

Fig 3: Pie Chart of Subjects with Positive Urinalysis

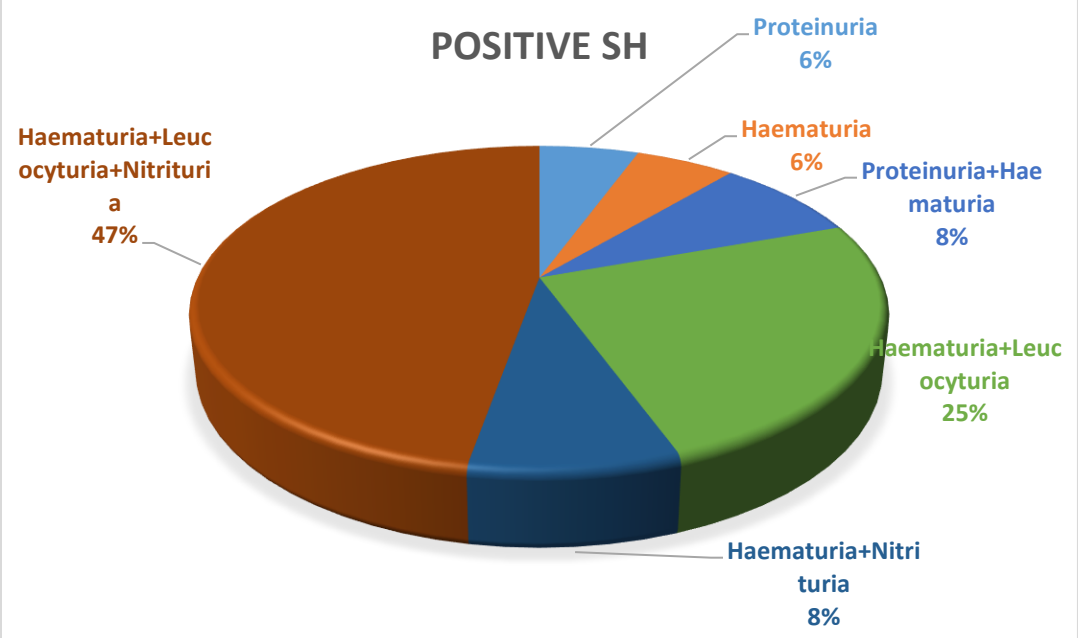

Fig 4: Pie Chart of Urinary S. Haematobium in Subjects with Positive Urinalysis

Table 2 shows factors associated with positive and negative SH in subjects with positive urinalysis. Among these 145 subjects, 36 (24.8%) had ova of SH in their urine. There were more females (52.8%), more (36.1%) between the ages of 9-10 years, more (86.1%) from rural areas, more (58.3%) Muslims, and more (58.3%) from other ethnic groups aside from the major tribes of Igbo, Hausa and Yoruba. Majority (41.7%) were living in flats, many (44.4%) were using pipe borne water, while (58.3%) were also from low social class.

For the other group without ova of SH, there were more females too (59.6%), more (45.0%) between the ages of 9-10 years, more (77.1%) from rural communities, more (53.2%) Muslim,
most (84.4%) were also using pipe born water, and most (45.9%) were also from the low social class. The only factor that was statistically significant in both bivariate and multivariate analysis was source of water supply (OR: 3.9, CI 0.97-16.3, and 15.8 (CI 5.48-45.6), p=0.001) for bivariate analysis, and (OR: 3.71(0.93-16.02), p=0.009) for the multivariate analysis.

Table 2

Factors Associated with Positive and Negative S Haematobium in Subjects with Positive Urinalysis

Characteristics	S Haematobium +ve N (%) N=36	No S Haematobium N=109	Uni/bivariate analysis OR (95% CI)	P Value	Multivariate analysis OR (95% CI)	P Value
Sex						
Male	17 (47.2)	44(40.4)				
Female	19 (52.8)	65(59.6)	1.65(0.77-3.5)	0.192		
Age						
6-8	12(33.3)	29(26.6)				
9-10	13(36.1)	49(45.0)	1.56(0.63-3.88)	0.616		
11-12	11(30.6)	31(28.4)	1.17(0.44-3.07)			
Mean Age	9.28±2.17	9.5±1.79		0.534		
Location of school						
Urban	5(13.9)	25(22.9)				
Rural	31(86.1)	84(77.1)	0.54(0.19-1.53)	0.245		
Religion						
Christian	14(38.9)	50(45.9)				
Moslem	21(58.3)	58(53.2)	0.77(0.36-1.67)	0.212		
ATR	1(2.8)	1(0.9)				
Ethnic group						
Ibo	3(8.3)	21(19.3)				
Yoruba	4(11.1)	11(10.1)	0.39(0.08-2.05)	0.36		
Hausa	8(22.2)	15(13.8)	0.27(0.06-1.13)			
Others	21(58.3)	62(56.9)	0.42(0.17-1.53)			
Type of house						
One/two rooms	12(33.3)	30(27.5)				
Flat	15(41.7)	50(45.9)	1.33(0.54-3.26)	0.137		
other	9(25.0)	29(26.6)	1.29(0.47-3.53)			
Source of water supply						
Stream	11(30.6)	4(3.7)				
Ponds	9(25.0)	13(11.9)	3.9(0.97-16.3)	0.001	3.71(0.93-16.02)	0.009
Pipe borne	16(44.4)	92(84.4)	15.8(5.48-45.6)			
Social class						
Upper	4(13.9)	17(15.6)				

Middle	13 (27.8)	42(38.5)	0.76(0.22-2.68)	0.709		
Low	19(58.3)	50(45.9)	0.62(0.18-2.07)			

ATR: African traditional religion

Table 3 showed performance of urinary abnormalities in the diagnosis of SH. The most sensitive SH morbidity indicator was combination of haematuria + leukocyturia + nitrituria, with SS, SP, PPV, NPV, accuracy and reliability of 56.7%, 92.0%, 60.7%, 90.6%, 85.6%, and 0.743 respectively. This was followed by haematuria+leucocyturia with SS, SP, PPV, NPV, accuracy and reliability of 33.3%, 87.6%, 37.0%, 85.7%, 77.8%, and 0.605. The least were leucocyturia and nitrituria with SS, and PPV of 0.0% each, and reliability of 0.482, and 0.307 respectively.

Table 3

Performance of Urinary Abnormalities in the Diagnosis of SH

	Diagnostic Parameters					
Diagnostic Predictors	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**Reliability**
Proteinuria	23.1	80.3	15.8	80.7	76.9	0.433
Haematuria	43.3	94.9	15.2	81.9	78.4	0.491
Leucocyturia	0.0	96.4	0.0	81.5	79.0	0.482
Nitrituria	0.0	61.3	0.0	73.7%	53.3	0.307
Proteinuria +Haematuria	25.8	83.6	39.3	85.5	76.5	0.575
Haematuria+Leucocyturia	33.3	87.6	37.0	85.7	77.8	0.605
Haematuria+Nitrituria	10.0	92.0	37.5	83.0	80.8	0.532
Proteinuria+Haematuria+Leucocyturia	66.7	96.4	60.7	90.6	85.6	0.743
Microscopy	100	100	100	100	100	1.000

PPV: Positive predictive value, NPV: Negative predictive value, SH: Schistosoma Haematobium

DISCUSSION

The prevalence of SH among primary school pupils with abnormal urinalysis in this study was 24.8%. This was comparable to 26.02%,[6] from Ebonyi state, Nigeria, and national pool prevalence of 34.7%.[19] It was however much lower than 57.1%,[20] 48.0%,[21] and 53.5%[22] from other states in Nigeria, and Cameroun. The lower prevalence rate in this study might be due to the methodological differences in the study design. While this study focused on finding egg of SH in urinalysis with abnormal findings, other prevalence studies cut across those with and without urinary abnormalities. In the pathophysiology of SH infection in human, there is significant difference in morphology, clinical, laboratory, and mode of treatment between the active (egg deposition phase) and inactive (after cessation of ovi-position) disease.[18] Nearly half of the complications of SH infestation occur during the inactive phase of the disease.[23] This phase which represents the phase of pathological/ granulomatous inflammatory damages in the urogenital organs represent the phase when fewer numbers of eggs will be seen in the urine, and when there will be likely changes in urinalysis. This could possibly explain the lower prevalence of SH eggs in the subjects with urinalysis abnormalities when compared to those from other studies that cuts across those with and without urinary abnormalities.

The high urinary abnormalities of 16.8% in this study when compared to others with higher rates,[24,25] may be due to the endemicity of kidney related diseases in the various vicinity. Combinations of proteinuria+haematuria+leucocyturia (47.2%), and haematuria+leucocyturia (25.0%) had the highest morbidity indicators for egg of SH in this study. These are not only well recognized laboratory features of SH infection, but also indicators of damage to the urinary tract.[20] When glomeruli are damaged, protein and often red blood cells leak into the urine, however most haematuria in SH infection are largely non-glomerular, though glomerular form with dysmorphic red blood cells can also be seen. Leucocyturia is also one of urinary variable that signifies not only infection of the urinary tract but also inflammatory processes. The combination of two or three of such abnormalities in the urine is strongly in support of inflammation and glomerular damage. Our finding of proteinuria of (5.6%), and haematuria of (5.6%) in subjects with positive SH eggs was in contrast with report by Morenikeji *et al*[20]. In their study, they documented proteinuria of 80.3%, and microhaematuria of 76.2% as the most sensitive urinary indicator for SH morbidity. Proteinuria they observed had a SS of 95.7% and SP of 67.2%, while microhaematuria recorded 64.8% SS, 89.6% SP. The present study recorded lower SS of (23.1%) for proteinuria, and (43.3%) for haematuria, but much higher SP of 80.3%, and 94.9% respectively. Proteinuria alone was not seen as a morbidity indicator in this study probably because most proteinuria documented (83.3%) was 1+ signifying less pathological damage. Morenikeji and co-workers[20] however recommended combination of morbidity indices (proteinuria and microhaematuria) than using single indicator for better accuracy in the diagnosis. This was also observed in this study where combination indicators (proteinuria+haematuria+leucocyturia) was found to have the highest accuracy (85.6%), and reliability (0.743) than the other single indirect methods. This is as a result of its highest SP for negative results 90.6%, and highest PPV 60.7% for positive results than the other combinations. Its highest accuracy and reliability underscore its usefulness as diagnostic morbidity indicator of SH diagnosis in an endemic area. Kotb et al[24] had a contrary view and noted combination of grades of haematuria and proteinuria not to have any significant increase either in SS or SP for SH, but rather recommended haematuria to be a valuable technique for screening rural Egyptian school children for
urinary Schistosomiasis.

In moderate-to-high SH endemic regions, infection usually varies with age and gender due to heterogeneity in exposure influenced by behavioural, cultural, and social practices, acquired immunity, and physiological changes during puberty. In the present study, age was found not to be significantly associate with SH infection. This finding was equally reported in other studies[5,16] probably from equal exposed of all ages to the source of SH infection, and equal dependent on natural water for domestic activities in low resource community. Our study also showed prevalence of SH infection to be non-statistically commoner in females compared to males, 52.8% Vs 47.2%, CI 1.65 (0.77-3.5), p=0.192, a finding that was in consistent with some reports.[16, 17] This could probably because of much involvement of female folks in domestic activities requiring frequent visits to the stream/ponds for fetching water or washing of clothes. School location was also found not to be significantly associated with SH infection in this study, probably because of non-proximity of the

schools to the stream/ponds, which will decrease the likely hood of the pupils frequenting them for swimming or other recreational activities. Other variables found not to have significantly associated with SH infections in this study were religion, ethnicity, type of housing, and social class. Some studies[5,6] have however linked low social class to SH infection. This they attributed to poverty, lack of knowledge of the risks in acquiring SH infection, inadequacy of public health facilities, and unsanitary conditions common with low social class population.

Source of water supply was the only statistically significant risk factor for SH infection in this study, (OR=3.71, 95% CI 0.93-16.02, p=0.009). Dawet *et al*,[9] and Ndamukong *et al*,[17] noted use of stream/pond as source of water supply to be significant association with SH infection in their study and attributed such to openness and contamination of the stream by infected individuals. South Africa study equally documented 4.4% decline in intensity of SH re-infection with every percentage increase in piped born water.[8]

CONCLUSION

Prevalence of SH among school children with urinary abnormalities was high in this study. Combination of haematuria+leucocyturia+nitrituria, and haematuria+leucocyturia can be used to predict those that may require further urinary evaluation for SH infection. Functional pipe borne water should be made available to those at the rural communities.

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