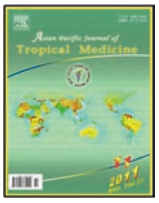
Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage:www.elsevier.com/locate/apjtm



Document heading doi: 10.1016/S1995-7645(11)60233-2

Performance of microhaematuria and proteinuria as measured by urine reagent strips in estimating intensity and prevalence of *Schistosoma haematobium* infection in Nigeria

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ARTICLE INFO

Article history:
Received 2 July 2011
Received in revised form 15 July 2011
Accepted 15 August 2011
Available online 20 December 2011

Keywords:
Microhaematuria
Proteinuria
False positive
Benue State
Nigeria

ABSTRACT

Objective: To assess if microhaematuria and proteinuria as measured by reagent strips could estimate intensity of *Schistosoma haematobium* (*S. haematobium*) infection in endemic areas and evaluate their screening performance among children in Benue State, Nigeria. **Methods:** A total of 1 124 urine samples were collected, screened for microhaematuria and proteinuria using reagent strips (Combi 9) and results were compared to filtration technique, the gold standard method. **Results:** A significant correlation was observed between microhaematuria (*rho*= 0.66, $P<0.01$), proteinuria (*rho* = 0.71, $P<0.01$) and intensity of *S. haematobium* eggs. Proteinuria had sensitivity of 95.7% and specificity of 67.2%, while microhaematuria had sensitivity of 64.8% and specificity of 89.6%. The proportion of false positive diagnoses was higher in proteinuria (19.2%) than microhaematuria (6.0%). **Conclusions:** The findings suggest that use of urine reagent strips could potentially estimate intensity of *S. haematobium* infection and their performance to screen urinary schistosomiasis agreed with previous observations.

1. Introduction

Urinary schistosomiasis is a major debilitating disease caused by *Schistosoma haematobium* (*S. haematobium*) and characterized by the presence of blood in urine. Other symptoms are proteinuria, dysuria, bladder carcinoma, bladder stones, calcification of bladder wall and sometimes renal failure.

The distribution of schistosomiasis has changed over time with some countries in South America, Asia, the Caribbean and the Middle East bringing down the prevalences of the disease through a concerted public health effort[1]. In sub-Saharan Africa, prevalence levels have increased and vary from one country to another; this is mostly because of water resources development, roads and dams projects, irrigation of land for agricultural purposes, inactive control programme and mostly neglect from the part of governments to implement control programmes in endemic areas.

Nigeria is one of the highly endemic countries where the disease has been unsystematically reported and status in large areas remain unknown[2].

Screening using rapid, indirect tests has been proposed as a procedure to simplify mapping surveys[3]. Haematuria (blood in urine) has been proposed as a valid indication of current infection in *S. haematobium* endemic populations[2,4-6].

Testing urine with reagent strips for microhaematuria and proteinuria is such a simple and indirect diagnostic technique that could estimate the prevalence of urinary schistosomiasis in school children of endemic communities. Operational research studies in Africa showed that screening using reagent strips is an effective method to identify school children requiring treatment and subsequently monitor control[7-9]. Several research studies reported high sensitivity and specificity of reagent strips compared to urine filtration, the most conclusive diagnostic for urinary schistosomiasis, which is expensive, cumbersome and too technical for lay use[2,7]. However, this study was undertaken to assess if microhaematuria and proteinuria detected with reagent strips could estimate

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intensity of *S. haematobium* infection in endemic areas and evaluate their diagnostic performance in screening urinary schistosomiasis among children in Benue State, Nigeria.

2. Materials and methods

2.1. Study area

The study was conducted from November 2008 to September 2009 in Buruku and Katsina-Ala local government areas (LGAs) of Benue State, Nigeria which are known for their endemicity for urinary schistosomiasis[10,11]. Before the commencement of the study, permission was sought from directors of health and local government education authorities of both areas. The climate of the areas is tropical with two seasons, the dry season which starts from October to March and the rainy from April to October. Agricultural activities like crop farming and rearing of animals are the mainstay of the inhabitants.

2.2. Sample collection and examination

A total of 1 124 urine samples were collected from pre and school children (primary and secondary) aged 3-27 years between 10:00 and 14:00 hrs using universal bottles. Urine were rapidly tested on the field using Medi Test combi 9 (Macherey-Nagel GmbH & Co.KG, Germany) reagent strips for the determination of microhaematuria and proteinuria. Microhaematuria and proteinuria were measured as erythrocytes/ μL and mg/dL of albumin respectively. The degree of microhaematuria and proteinuria concentrations were as follows: 0 (negative), Ca.5-10 (+), Ca.50 (++) and Ca.250 (+++) and 0 (negative), Ca.30 (+), Ca.100 (++) and Ca.500 (+++) respectively.

Immediately after testing with the reagent strips, 1 mL of ordinary household bleach was added to each collected urine sample to preserve any ova present and then taken to the laboratory within 2 hrs for parasitological examination. 10 mL of urine was taken and filtered through a 12 μm polycarbonate membrane in a filter holder. With the help of a forceps, the filter was removed from the filter holder and placed on a slide. A drop of Lugol's iodine was added and the slide examined under microscope using ×10 and ×40 objective lenses. The number of eggs was counted per 10 mL of urine and intensities of infection were classified as 1-10 eggs, 11-49 eggs and > 50eggs for light, moderate and heavy infections respectively.

2.3. Statistical analysis

Collated data were double entered in Microsoft excel and analysed in PASW (Predictive Analysis software) version 18.0. Associations between variables were tested using Spearman correlation (*rho*) at $P< 0.01$ significance level.

The diagnostic performance of microhaematuria and proteinuria was assessed by calculating sensitivity, specificity, positive predictive value and negative predictive value using the following formulae.

$$\text{Sensitivity} = \frac{a}{a+b}$$ with a=True positive, b = False negative

$$\text{Specificity} = \frac{c}{c+d}$$ with c = True negative, d = False positive

$$\text{Positive predictive value (PPV)} = \frac{a}{a+d}$$

$$\text{Negative predictive value (NPV)} = \frac{c}{c+b}$$

3. Results

Table 1 shows the relationship between microhaematuria and intensity of *S. haematobium* eggs. of the 151 subjects having microhaematuria at Ca.5-10 (+), light infection had the highest rate 62 (41.1 %); while moderate and heavy infection had 39 (25.8 %) and 12 (7.9 %) respectively. Of the 72 screened for microhaematuria at Ca.50 (++), moderate infection had the highest rate with 42 (58.3%) while light and heavy infection had 5(6.9 %) and 6 (8.3%) respectively. Of the 147 subjects screened for microhaematuria at Ca.250, heavy infection had the highest rate with 69 (46.9 %). It was observed that various degree of microhaematuria concentrations, +, ++ and +++ corresponded to highest rate of light, moderate and heavy intensity of eggs respectively. A significant relationship was found between microhaematuria at different concentration and intensity of infection (*rho* = 0.66, $P<0.01$).

The comparison between microhaematuria as indicator of urinary schistosomiasis and the true disease status as determined by filtration technique showed that microhaematuria was detected in 370 (32.9 %), among these 302 (26.9 %) had both microhaematuria and presence of eggs (true positive) and 68(6.0 %) had microhaematuria with no presence of eggs (false negative). Of the 754 (67.1%) subjects screened that did not have microhaematuria in their urine, 164 (14.6 %) had *S. haematobium* eggs (false positive) and 590 (52.5 %) were devoid of eggs (true negative).

Table 2 shows the relationship between proteinuria and intensity of *S. haematobium* eggs among children in Katsina-Ala and Buruku LGAs of Benue State. It was observed that of the 317 screened having proteinuria at Ca.30 (+), light infection recorded the highest rate with 118 (37.2 %), while moderate infection recorded the highest rate with 84 (37.3 %) out of the 225 screened for proteinuria at Ca.100 (++). Heavy and moderate infection intensities recorded 52(43.3 %) and 54 (45.0%) respectively out of the 120 screened for proteinuria at Ca.500 (+++). It was observed that various degree of proteinuria concentrations, +, ++ and +++ corresponded to highest rate of light, moderate and heavy intensity of eggs respectively although moderate infection was found having an edge over heavy infection at

Ca.500. A significant spearman correlation (*rho*= 0.71, *P*< 0.01) was found between different degrees of proteinuria concentrations and intensity of S. haematobium eggs.

The comparison between proteinuria as indicator of urinary schistosomiasis and the true disease status as determined by filtration technique showed that proteinuria was observed in 662 (58.9%) children, 446(39.7%) had both proteinuria and *S. haematobium* eggs (true positive), while 216(19.2 %) had proteinuria with absence of *S. haematobium* eggs (false positive). Of the 442 screened having no proteinuria in their urine, 20(1.8 %) had S. haematobium eggs, while 442(39.3%) were devoid of *S. haematobium* eggs (true negative).

The ability of microhaematuria and proteinuria to accurately identify all those with the disease (sensitivity) was 64.8% and 95.7% respectively, while their ability to correctly sort out all those without the disease (specificity) was 89.6 % and 67.2 % respectively. Microhaematuria had higher positive predictive value (PPV) (81.6 %) than proteinuria (67.7%), but had lower Negative Predictive Value (NPV) 78.2% against 95.6%.

Table 1
Relationship between microhaematuria and intensity of *S. haematobium* eggs among pre and school children in Katsina-Ala and Buruku LGAs of Benue State.

Microhaematuria(ery/ μ L)	Negative	Intensity of eggs per 10 mL of urine			Total
		(1–10 eggs)	(11–49 eggs)	(> 50 eggs)	
Negative	590(78.2)	118(15.6)	45(6.0)	1(0.1)	754
Ca.5–10	38(25.2)	62(41.1)	39(25.8)	12(7.9)	151
Ca.50	19(26.4)	5(6.9)	42(58.3)	6(8.3)	72
Ca.250	11(7.5)	12(8.2)	55(37.4)	69(46.9)	147
Total	658(58.5)	197(17.5)	181(16.1)	88(7.8)	1124

1–10 eggs/10 mL of urine = light infection; 11–49 eggs/10 mL of urine = Moderate infection; >50 eggs/10 mL of urine = Heavy infection

Table 2
Relationship between proteinuria and intensity of *S. haematobium* eggs among pre and school children in Katsina-Ala and Buruku LGAs of Benue State.

Proteinuria (mg/dL)	Negative	Intensity of eggs per 10 mL of urine			Total
		(1–10 eggs)	(11–49 eggs)	(> 50 eggs)	
Negative	442(95.7)	13(2.8)	7(1.5)	0(0.0)	462
Ca.30	155(48.9)	118(37.2)	36(11.4)	8(2.5)	317
Ca.100	56(24.9)	57(25.3)	84(37.3)	28(12.4)	225
Ca.500	5(4.2)	9(7.5)	54(45.0)	52(43.3)	120
Total	658(58.5)	197(17.5)	181(16.1)	88(7.8)	1124

4. Discussion

The present study demonstrates that the use of microhaematuria and proteinuria to estimate the intensity of urinary schistosomiasis has potential utility in discriminating intensity of infection among infected individuals in endemic areas.

The significant relationships observed between microhaematuria, proteinuria and filtration technique clearly demonstrate that the presence or absence of microhaematuria or proteinuria in urine is function of *S. haematobium* eggs excretion in urine. However, the false positive results of microhaematuria and proteinuria observed entails the daily variation of *S. haematobium* eggs excretion in infected individuals. The absence of microhaematuria and proteinuria in infected individuals (false negative) could be the result of new infection in which tissues of the urinary bladder and kidney have not been damaged yet.

The evaluation of only microhaematuria as indicator of urinary schistosomiasis shows sensitivity of 64.8 % and specificity of 89.6 %. This is closely related to findings of Ugbomoiko *et al*[9]. who reported sensivity of 68.3 % and specificity of 83.2 % among school children of two endemic areas in southwestern, Nigeria. However, the sensitivity of microhaematuria in this study is higher than that of Anosike *et al*[2]. who obtained sensitivity of 41.0 % but with a similar specificity (82.0 %) in a study conducted in Bende LGA of Abia State, Nigeria. Sensitivity and specificity of microhaematuria in this study are lower than that reported among zanzibari school children in Tanzania with sensitivity of 77.0% and specificity of 97.0 %[8]. However, variation in sensitivity and specificity of microhaematuria during *S. haematobium* infection has been reported in several studies conducted in different African settings. They have been reported to vary from 41.0 % to 93 % and from 67 % to 99 % for sensitivity and specificity respectively[2,4,6,8,9,12].

The diagnostic performance of proteinuria as indicator of urinary schistosomiasis showed sensitivity of 95.7 % and specificity of 67.2% which are higher than findings of Brouwer *et al*.[13,14] who obtained 65.0% and 60.0% respectively among Zimbabwean school children. Ugbomoiko *et al*.[9] reported lower sensitivity (67.7 %) and higher specificity (79.6 %) among school children in southwestern Nigeria than the present study. Proteinuria is seen as a sign of bladder damage occurring principally in severe infections. The high sensitivity (95.7%) of proteinuria observed in this study cannot be conclusive about *S. haematobium* infection; this is because of the relatively

high rate of false positive result (19.2%) than that of microhaematuria (6.0 %). However, this false positive result could be due to other urinary tract infections.

The use of urine reagent strips has been proposed as an indirect method in identifying *S. haematobium* infected children, hence a useful tool to rapidly map the prevalence of urinary schistosomiasis in endemic areas.

The present study also shows that using microhaematuria and proteinuria as detected by reagent strips easily estimate intensity of infection; this is because they showed ability to discriminate between children at different level of infection intensity. Moreover, it was found that microhaematuria and proteinuria with higher positivity level detected infection of higher intensity (moderate and heavy).

Microhaematuria performed better in detecting moderate and heavy infection in the children than proteinuria. However, this corroborates findings of Anosike *et al.*[2] and Ahmed[15] who found similar results among Nigerian and Yemeni children.

The positive predictive value (probability of infected children with *S. haematobium* eggs among those having microhaematuria or proteinuria) was higher in children having microhaematuria (81.6 %) than proteinuria (67.7 %). This indicates that almost all children with microhaematuria were indeed infected with *S. haematobium* eggs.

In conclusion, using microhaematuria and proteinuria as detected by reagent strips is practical-cheap, fast and easy to use in estimating intensity and prevalence of *S. haematobium* infection. This can be used in Primary Health Care (PHC) setting with limited resources to screen and monitor *S. haematobium* infection in endemic areas.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

Our sincere appreciation goes to all the children that participated in the study, their parents/guardians, teachers, head teachers and principals whose collaboration and understanding made the study feasible. We are indebted to Messrs J, Meme and C, Ansough, staff of the epidemiological units, Health Departments of Katsina-Ala and Buruku LGAs respectively for their help in translating English to local language during sample collection. We finally thank the Local Government chairmen of Katsina-Ala and Buruku Areas and their respective education authorities for granting permission before commencement of the research. This paper constitutes part of a PhD research of the first author to the Biological Sciences Programme, Abubakar Tafawa Balewa University, Bauchi, Bauchi State, Nigeria.

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