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Microhaematuria as a diagnostic marker of *Schistosoma haematobium* in an outpatient clinical setting: results from a cross-sectional study in rural Ghana

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Abstract

The utility of microhaematuria (as measured by urine reagent strips) as a surrogate marker for *Schistosoma haematobium* infection is not established in patients with urogenital symptoms presenting to clinical settings, although previous studies have demonstrated its utility in screening asymptomatic individuals in large community or school-based settings. In this cross-sectional study of 201 patients, multivariate analysis demonstrated microhaematuria as an independent predictor of *S. haematobium* infection (OR, 4.29; 95% CI, 1.6–11.9) in individuals presenting with urogenital symptoms to an outpatient medical department (OPD) at a rural Ghanaian medical center. Microhaematuria is predictive of *S. haematobium* infections in clinical settings in endemic regions.

Keywords

Schistosomiasis, diagnosis, microhaematuria, reagent strip

Introduction

Schistosomiasis is one of the most prevalent neglected tropical infections in the developing world, and poses great health risks to people living in rural areas of developing countries, with sub-Saharan Africa disproportionately affected.[1] Microhaematuria has been considered as a useful diagnostic marker for suspected *Schistosoma haematobium* infection in epidemiologic settings, and is typically quantified via urine reagent strips.[2,3] In these large school- or community-based surveys of asymptomatic individuals, the sensitivity of microhaematuria with urine reagent strips for *S. haematobium* diagnosis is in the range of 70–100% and the specificity is approximately 60–80%.[4–6] Little is known about the diagnostic utility of urine reagent strips for *S. haematobium* diagnosis in individuals with urogenital symptoms presenting to clinical settings, such as outpatient medical departments (OPD). The purposes of this study was to: (1) establish and quantify the prevalence of *S. haematobium* infection in patients living in an endemic region who presented with urogenital symptoms to an outpatient department; and (2) to elucidate the role of microhaematuria for the diagnosis of *S. haematobium* in an OPD setting.

Methods

This cross-sectional study was carried out at the Kete-Krachi district hospital in the Volta region of Ghana. The town of Kete Krachi has an estimated population of 11,788 people. Between November 2012 and May 2013,

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we tested 201 patients who presented to the OPD of our facility with a primary complaint of genital pain, lower urinary tract symptoms (e.g. hesitancy, frequency or a sensation of incomplete voiding) or microhaematuria for urinary schistosomiasis. Male and female participants of all ages were included. The study was approved by the Institutional Review Board of the University of Cape Coast (IRB/UCC) and the authorities of the Krachi District Hospital. Informed consent was obtained from each participant who was recruited into the study.

Urine samples were evaluated by urine reagent strips (CYBOW^{TM} DFI Co Ltd, Gimhae-City, Republic of Korea) to detect haemoglobin, protein and leukocytes in a semi-quantitative manner. Ten millilitres of that same urine specimen was shaken and then centrifuged at 5000 rpm for 5 min. The deposit was examined via a light microscope using 10× and 40× objective lenses for *S. haematobium* ova. *S. haematobium* infections were categorised as either low intensity or heavy intensity as per World Health Organization criteria.[7] Urine cultures or molecular tests for sexually transmitted infections were not available at this setting. Data were entered into Microsoft Excel (Microsoft, Redmond, WA, USA) and analysed with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Sensitivity, specificity, and positive and negative predictive values for microhaematuria as detected by urine regent strip were calculated. Multivariate logistic regression evaluated microhaematuria, urine protein, urine leukocytes, age and sex to identify independent risk factors associated with urinary schistosomiasis.

Results

A total of 213 individuals met eligibility criteria for the study. Twelve did not consent and were excluded, leaving a total of 201 participants who were enrolled. Of those enrolled, 56 (27.9%) were infected with *S. haematobium* as diagnosed by urine microscopy. The distribution of infection among male participants of 31 (15.5%) and 25 (12.4%) among female participants were comparable (Table 1).

In an OPD setting, microhaematuria has sensitivity and specificity for *S. haematobium* of 91.1% and 32.4%, respectively, with a positive predictive value of 34.2% and negative predictive value of 90.4%. Multivariate logistic regression analysis revealed microhaematuria as an independent predictor of infection (OR, 4.29; 95% CI, 1.6–11.9).

Table 1. Prevalence and intensity of infection of *S. haematobium* among study participants presenting to an outpatient medical department with lower urogenital symptoms, stratified by age and sex.

Variables	Examined (*n*)	Infected (*n*)	Prevalence (%)	Intensity of *S. haematobium* infection	
				Light* *n* (%)	Heavy† *n* (%)
Gender					
Male	116	31	15.5	25 (12.4)	6 (3.0)
Female	85	25	12.4	24 (11.9)	1 (0.5)
Total	**201**	**56**	**27.9**	**49 (24.4)**	**7 (3.5)**
Age range (years)					
3–15	62	21	10.4	16 (8.0)	5 (2.5)
16–28	89	28	13.9	27 (13.4)	1 (0.5)
29–41	22	2	0.9	2 (1.0)	0 (0.0)
42–54	17	5	2.5	4 (2.0)	1 (0.5)
>55	11	0	0	0 (0.0)	0 (0.0)
Total	**201**	**56**	**27.9**	**49 (24.4)**	**7 (3.5)**

S. haematobium ova per 10 mL urine 1–49.
†*S. haematobium* ova per 10 mL urine ≥50.

Discussion

Accurately diagnosing schistosomiasis is essential at the individual patient level and in regional control programs.[8] Unfortunately, traditional light microscopy, the gold standard for diagnosis, lacks in sensitivity, especially in the case of light infections.[9–12] These challenges necessitate the development of more reliable diagnostic methods that are cost-effective and simple to use, such as urine reagent strips.[10,11] Our study is unique as we demonstrate the utility of microhaematuria detected by urine regent strips as a surrogate marker for *S. haematobium* infection in individuals presenting with lower urinary tract symptoms to an outpatient medical facility. Prior studies only evaluated this association in public health surveys of schools or communities. Importantly, individuals evaluated in school and community-based surveys were either asymptomatic or had symptomatic lower urinary tract disease at a sub-clinical level. In such settings, microhaematuria demonstrates wide ranges in sensitivity (approximately 70–100%) and specificity (approximately 60–80%) for *S. haematobium* infection.[4–6,13] In an outpatient medical setting we demonstrate higher sensitivity (91.1%) but lower specificity (32.4%) for microhaematuria, as measured by urine regent strips.[5,6,14] Given the high sensitivity and negative predictive value, patients with microhaematuria should either undergo urine microscopy to confirm *S. haematobium* diagnosis or be empirically treated for this infection if such facilities are not available.

It is important to evaluate the role of microhaematuria as a predictor of *S. haematobium* in clinical setting as patients evaluated here are likely quite different from prior studies where individuals were examined in cross-sectional school- or community-based surveys.

Individuals presenting to an outpatient department are unwell enough to seek medical care, and such individuals may be absent during cross-sectional public health surveys, which very likely represent a much healthier cohort. Second, the cohort presenting for medical care all had urogenital symptoms in an *S. haematobium*-endemic setting, and hence may have a higher prevalence of infection compared to the general public. The prevalence of infection in this study was almost 30%; however, it is unclear what the current regional prevalence of this infection is at the moment.

Weaknesses of this study include the inability of our centre to perform urine culture or test for sexually transmitted infections. Many patients are treated empirically based on subsequent history and physical examination. These are all potential aetiologies of urinary tract symptoms in addition to *S. haematobium* infection. Another weakness of our study is that we may be underestimating the prevalence of infection in our cohort due to the collection of only one urine sample.[15] While multiple samples would likely increase diagnostic sensitivity, it is unfortunately very challenging to obtain serial specimens in an outpatient medical setting.

Given the utility of microhaematuria to predict *S. haematobium* infection in clinical settings of an endemic region, a urinalysis is an inexpensive first line test to perform on patients with urogenital symptoms. All positive urine reagent tests for microhaematuria should be examined by light microscopy for the presence of *S. haematobium* ova, or treated empirically with praziquantel. Ideally these diagnostic tests could be coupled with urine culture to detect urinary tract infections, and when appropriate, molecular testing for sexually transmitted infections for a comprehensive diagnostic approach.

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Declaration of conflicting interests

All the authors have seen the manuscript and approve it for submission. The authors have no competing interest in the publication of the manuscript to declare.

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