

Simple questionnaire and urine reagent strips compared to microscopy for the diagnosis of *Schistosoma haematobium* in a community in northern Ghana

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Abstract

OBJECTIVES To evaluate the utility of a simple questionnaire and urine reagent strip testing for the rapid diagnosis of *Schistosoma haematobium* in rural northern Ghana.

METHODS Cross-sectional parasitological and questionnaire survey in a community in northern Ghana. Participants provided two urine specimens that were examined under a microscope using a centrifugation method. The first urine sample was additionally subjected to reagent strip testing. A short questionnaire was administered to all participants.

RESULTS Microscopy of urine samples obtained from 208 individuals aged 1–77 years revealed an *S. haematobium* prevalence of 6.8%. The presence of any blood or protein on a urine reagent strip was 100% and 42% sensitive, and 93% and 80% specific for *S. haematobium* diagnosis. Questionnaires were completed by 198 individuals. Self-reported haematuria showed a sensitivity of 53% and a specificity of 85%. A dichotomous two-question panel was helpful in *S. haematobium* diagnosis, with working and playing near the river significantly associated with *S. haematobium* infection ($P < 0.001$).

CONCLUSION The use of urine reagent strips, coupled with questions pertaining to water contact patterns, might be considered for point-of-contact diagnosis of *S. haematobium* where microscopy is unavailable.

keywords schistosomiasis, *Schistosoma haematobium*, diagnosis, questionnaire, urine reagent strip, microscopy, Ghana

Introduction

Urogenital schistosomiasis due to chronic infection with *Schistosoma haematobium* is a public health problem in sub-Saharan Africa (Fenwick *et al.* 2009; Schur *et al.* 2011a,b) and is strongly associated with squamous cell carcinoma of the bladder (El-Bolkainy *et al.* 1981). The construction of large dams and irrigation systems has a history of altering the risk of schistosomiasis (Steinmann *et al.* 2006). In Ghana, for example, the construction of the Akosombo Dam in the 1960s created suitable breeding grounds for *Bulinus* spp., snails that act as intermediate hosts for *S. haematobium*. This resulted in a major increase in the incidence of infection in the then formed Lake Volta (Paperna 1970; Scott *et al.* 1982). Dam construction in

the northern part of Ghana further contributed to *S. haematobium* transmission (Hunter 2003).

In addition to the establishment and maintenance of community-based helminth control efforts, better clinical prediction tools are necessary for the rapid identification of individuals at high risk for schistosomiasis in endemic settings. Several indirect tools have been used to aid in the field diagnosis of *S. haematobium*, including school-based questionnaires (Lengeler *et al.* 2002a,b) and urine reagent strips (Brooker *et al.* 2009; Kosinski *et al.* 2011). Short questionnaires used in isolation often fail to diagnose infected individuals, particularly those with light infection intensities (Ansell *et al.* 1997; Guyatt *et al.* 1999). Urine reagent strips positive for haematuria have yielded varied results for *S. haematobium* diagnosis,

I. I. Bogoch *et al.* ***S. haematobium* in northern Ghana**

with sensitivities ranging between 70% and 97% and specificities ranging from 59–80% (Mott *et al.* 1983; Robinson *et al.* 2009; Kosinski *et al.* 2011), prompting concerns as to the utility of this as the sole method for screening populations.

We conducted a cross-sectional survey and assessed the prevalence of *S. haematobium* in a community in northern Ghana. We determined the accuracy of a modified short questionnaire, in combination with urine reagent strips for the diagnosis of *S. haematobium*, using light microscopy based on two urine samples as our 'gold' standard.

Methods

This study was carried out in February 2008 with investigators working alongside local dracunculiasis public health teams. Permission was granted by the Tolon District Health Director. Tolon/Kumbungu District is a primarily rural region in northern Ghana and consists of 257 communities with an estimated population of 161 160 according to the census from 2000. Kuli, a small village in the district, lies 1.5 km from the White Volta River and has an estimated population of 360 (United States Geological Survey 2012). Empiric therapy with albendazole and ivermectin, as part of the global programme to eliminate lymphatic filariasis (Molyneux & Zagaria 2002), began twice yearly in the district starting in November 2004, and Kuli was last treated 4 months prior to this study. Kuli had empiric therapy for schistosomiasis 2 years prior with praziquantel, although at the time of this study, no ongoing schistosomiasis control efforts were in place.

Announcements were made via a portable public address system that voluntary screening and treatment for *S. haematobium* would occur concurrently with routine dracunculiasis control/elimination efforts. Written informed consent was obtained from all adult participants and from parents/guardians of minors. Overall, 280 individuals aged 1–77 years were screened for *S. haematobium* by light microscopy. In brief, two urine specimens were collected from each individual between 10:00 and 14:00 h on consecutive days and processed at Tamale Teaching Hospital. Ten millilitres of urine was centrifuged and examined under a microscope by an experienced biomedical scientist and laboratory technician for the presence of *S. haematobium* eggs. We defined cases of schistosomiasis as individuals having at least one *S. haematobium* egg present on microscopic examination of urine on either day. The presence of blood and protein in urine were determined semi-quantitatively using urine reagent strips (Combur 10 Test Strip; Roche) on the first day of urine collection.

In addition, 198 individuals completed a simple questionnaire with the aid of local public health officials. The questionnaire assessed dichotomous 'yes/no' variables pertaining to water exposure for occupational and/or recreational activities and self-reported blood in urine. Children who could not answer the questions were aided by older family members accompanying them.

We calculated the sensitivity and specificity of urine reagent strip results and questionnaire responses for the diagnosis of *S. haematobium* using the centrifugation results (two urine samples examined under a microscope by a trained laboratory technician) as diagnostic 'gold' standard. McNemar's test was used to compare correlated proportions for diagnostic tests. We used Fisher's exact test to compare binary categorical variables and chi-squared test for trend in binomial proportions to assess for trends in ordinal variables. All participants who tested positive for *S. haematobium* were treated with praziquantel (40 mg/kg, single oral dose) free of charge.

Results

The 280 individuals screened had a mean age of 18.6 years (range: 1–77 years), 126 (45.0%) were females. 19 (6.8%) participants were found to have *S. haematobium* eggs in their urine by microscopy. Of those infected, the mean age was 15 years (range: 1–38 years), 7 (36.8%) were females.

The sensitivity and specificity of blood detected by urine reagent strips were 100% and 93%, respectively (Table 1). Self-reported blood visualised in the urine was 41% sensitive and 86% specific for having a urine reagent strip

Table 1 Sensitivity and specificity of haematuria by urine reagent strip and self-report, and proteinuria by urine reagent strip for *Schistosoma haematobium* diagnosis

| Variable | Urine microscopy for <i>S. haematobium</i> (two specimens) | | Sensitivity | Specificity |
|--------------------------------------|------------------------------------------------------------------|----------|-------------|-------------|
| | Positive | Negative | | |
| Haematuria (by urine reagent strip) | | | | |
| Positive | 19 | 18 | 100% | 93% |
| Negative | 0 | 243 | | |
| Total | 19 | 261 | | |
| Haematuria (by self-report) | | | | |
| Positive | 9 | 27 | 53% | 85% |
| Negative | 8 | 154 | | |
| Total | 17 | 181 | | |
| Proteinuria (by urine reagent strip) | | | | |
| Positive | 8 | 53 | 42% | 80% |
| Negative | 11 | 208 | | |
| Total | 19 | 261 | | |

I. I. Bogoch *et al.* ***S. haematobium* in northern Ghana**

positive for blood and was 53% and 85% specific compared with microscopy. The probability of self-reporting haematuria increased as the reagent strip blood score increased ($P < 0.001$). Presence of protein in the urine was associated with *S. haematobium* infection detected by microscopy ($P = 0.04$), although sensitivity was only 42% and specificity 80%. Working and playing near the river was significantly associated with *S. haematobium* infection ($P < 0.001$). The sensitivity and specificity of working/playing near the river for *S. haematobium* infection was 100% and 23%, respectively.

Discussion

Epidemiological studies pertaining to *S. haematobium* in Ghana tend to be concentrated around high-risk areas in the Lake Volta region, with much less data stemming from northern regions (Scott *et al.* 1982). Studies carried out in the 1970s (Lyons 1974) and more recent investigations (Amankwa *et al.* 1994; Anto *et al.* 2011; Kosinski *et al.* 2011) revealed that *S. haematobium* is endemic in the northern part of the country. Recently, a Bayesian geostatistical model demonstrated a <10–20% prevalence of *S. haematobium* in this northern district, with closer distances to water predicting greater risk of infection (Soares Magalhães *et al.* 2011). Consistent with this study, we found a prevalence of 6.8% in a cross-sectional survey in a small community in rural northern Ghana. Of note, we included infants, preschool-aged children, adolescence and adults, while previous schistosomiasis surveys primarily focused on school-aged children (Schur *et al.* 2011a,b). Two urine samples subjected to a centrifugation technique and examined under a microscope served as our diagnostic ‘gold’ standard, which is a reasonably sensitive approach (Savioli *et al.* 1990). However, a true gold standard for schistosomiasis diagnosis has proved to be elusive, and currently, most studies utilise at least three concentrated urine specimens (or three stool specimens) as a ‘gold’ standard for the diagnosis of *S. haematobium* (or *S. mansoni*).

Several studies have assessed indirect methods for the diagnosis of *S. haematobium*, particularly the use of urine reagent strips and simple questionnaires (Lengeler *et al.* 2002b; Brooker *et al.* 2009). Early studies from Ghana showed a strong correlation between microscopic haematuria and greater *S. haematobium* egg burden (Mott *et al.* 1983), with one study reporting sensitivity of 86% when >16 eggs/5 ml of urine were present and 97% when >64 eggs/5 ml of urine were present (Mott *et al.* 1985). A recent study from southern Sudan demonstrated that urine reagent strips were 97.8% sensitive, but only 58.8% specific in the diagnosis *S. haematobium*, high-

lighting the need for subsequent evaluation of haematuria-positive samples by microscopy (Robinson *et al.* 2009). By contrast, a recent study from lightly infected children in Ghana (<50 eggs/10 ml), who were screened three times, demonstrated only a 70% sensitivity and 80% specificity for urine reagent strips positive for haematuria and *S. haematobium* infection (Kosinski *et al.* 2011).

A weakness of our study is that we did not quantify egg burden. By only assessing the presence or absence of eggs in urine, it is not possible to correlate intensity of infection with the degree of haematuria, the latter determined by specific colour reactions on the urine reagent strips. Nevertheless, haematuria in our population was 100% sensitive and 93% specific, possibly attributable to high egg burdens in infected individuals. Although we screened individuals on two consecutive days with microscopy, it is conceivable that further examinations would have revealed additional infections, mainly of light intensity (Kosinski *et al.* 2011). Another weakness is that we only screened for *S. haematobium*. Intestinal schistosomiasis and soil-transmitted helminthiasis are also endemic in the region, with polyparasitism being common in focal regions (Soares Magalhães *et al.* 2011). The most widely used diagnostic approach for these diseases is the Kato-Katz technique based on multiple stool examinations. Future studies should therefore collect both urine and stool samples for microscopic examination.

Our short questionnaire was extrapolated from available questionnaires that have been thoroughly validated and widely used in community-based schistosomiasis control programmes across sub-Saharan Africa (Lengeler *et al.* 2002a,b). The simple dichotomous ‘yes/no’ answer for water contact, as previously used in a Chinese population (Zhou *et al.* 1998), was significantly associated with *S. haematobium* infection. Indeed, a simple dichotomous three-question panel was 86.2% sensitive and 97.6% specific for the diagnosis of *S. japonicum* in Hunan Province, People’s Republic of China.

Surveys of health-seeking behaviour from rural Ghana reveal that individuals are more likely to seek care with gastrointestinal symptoms rather than urinary symptoms such as haematuria or dysuria (Danso-Appiah *et al.* 2004). In that study, of the 30% who sought care with perceived blood in urine, half opted to self-medicate with traditional therapies. We found that the perception of blood in urine had poor correlation with urine reagent strip–documented haematuria (41% sensitivity; 86% specificity); a study from Malawi reported higher sensitivity (68%) but lower specificity (74%) (Kapito-Tembo *et al.* 2009). Given the rather modest reliability of self-reported haematuria for individual diagnosis and the ease and low cost of urine

I. I. Bogoch *et al.* **S. haematobium** in northern Ghana

reagent stick analysis, which had 100% sensitivity and 93% specificity in our study, we propose urine reagent strips, alongside with history of recent contact with fresh water, as a suitable point-of-care diagnosis of urogenital schistosomiasis. It will be interesting to study health-seeking behaviour and to monitor changes in *S. haematobium* prevalence over time now that preventive chemotherapy efforts are scaling up in Ghana and elsewhere in sub-Saharan Africa.

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I. I. Bogoch *et al.* **S. haematobium in northern Ghana**

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