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The performance of haematuria reagent strips for the rapid mapping of urinary schistosomiasis: field experience from Southern Sudan

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Summary The implementation of programmes to control neglected tropical diseases (NTDs) requires up-to-date information on the prevalence and distribution of each NTD. This study evaluated the performance of reagent strip testing for haematuria to diagnose *Schistosoma haematobium* infection among school-aged children in the context of a rapid mapping survey in Southern Sudan. The reagent strips were highly sensitive (97.8%) but only moderately specific (58.8%). The proportion of false positive diagnoses was significantly higher among girls than boys, especially among girls aged 5–10 years. These findings suggest that reagent strips alone are not sufficient for rapid mapping surveys. A two-step approach is thus recommended whereby haematuria-positive urine samples are subsequently examined using urine filtration.

keywords urinary schistosomiasis, *Schistosoma haematobium,* diagnosis, neglected tropical diseases, mapping, Southern Sudan

Introduction

There is increasing interest in the implementation of programmes to control neglected tropical diseases (NTDs) (Lammie *et al.* 2006). To ensure that these programmes target the areas of greatest need, there is an operational requirement for up-to-date information regarding the prevalence and distribution of each NTD. Screening using rapid, indirect tests has been proposed as a procedure to simplify mapping surveys (Brooker & Utzinger 2007). For urinary schistosomiasis, caused by *Schistosoma haematobium*, testing urine with reagent strips for microhaematuria is one such simple, indirect diagnostic method, particularly for use among school-aged children (Mott *et al.* 1983); school-based blood in urine questionnaires are another rapid, low-cost screening approach (Lengeler *et al.* 2002). At present, parasitological diagnosis remains the preferred screening approach for the other main schistosome species in sub-Saharan Africa, *S. mansoni,* which causes intestinal schistosomiasis (Brooker *et al.* 2009).

Several research studies report high sensitivity and specificity of reagent strips compared to urine filtration (Savioli *et al.* 1989), the considered diagnostic gold standard. Operational research studies in Africa show that screening using reagent strips is an effective method to identify school children requiring treatment and to subsequently monitor control (Savioli *et al.* 1989; French *et al.* 2007; Ugbomoiko *et al.* 2009). However, because of regional variation in the performance of reagent strips (Mott *et al.* 1985), evaluation at country level is necessary to establish reliability for their use during large-scale mapping. Here, we report on the performance of reagent strips during community surveys conducted as part of the mapping phase of a national integrated NTD control programme in Southern Sudan (Rumunu *et al.* 2009).

Materials and methods

The study was conducted from February to May 2009 in Northern Bahr-el-Ghazal State, Southern Sudan, as part of

a large-scale integrated NTD mapping survey for schistosomiasis, soil-transmitted helminth infection, lymphatic filariasis and loiasis (Sturrock *et al.* in press). School enrolment is under 30% in the area and therefore school-based questionnaire surveys were deemed unfeasible for mapping of schistosomiasis. Details of the study area, recruitment method, and parasitological surveys are provided elsewhere (Sturrock *et al.* in press). In brief, a quasi-random two-stage cluster sampling method was employed, whereby communities were selected on the basis of potential risk of filariasis and schistosomiasis, and households were randomly selected within each community. Each household head was requested to provide written consent, and all children aged 5–16 years were asked to give verbal consent before providing urine samples; adults were only sampled for testing of lymphatic filariasis. Individuals who did not provide consent were excluded from the study. Urine samples were generally collected from each child between 10 am and 2 pm and tested using Hemastix® reagent strips (Bayer Diagnostics, Basingstoke, UK). Samples positive for haematuria were subsequently filtered through a hydrophilic, 12 μm polycarbonate membrane, and the number of *S. haematobium* eggs was counted per 10 ml of urine. A heavy infection was classified as >50 eggs per 10 ml urine, and a light infection as between 1 and 50 eggs per 10 ml. For each haematuria-positive sample, an age-sex matched negative sample was also filtered. Data were double entered in Microsoft Excel and analysed in STATA 9.0 (Stata Corporation, College Station, TX, USA). Comparisons of infection prevalence by sex and age group were tested with the χ^2 test. The diagnostic performance of reagent strips was assessed by calculating sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). 95% exact binomial confidence intervals (CIs) were calculated, and non-overlapping CIs were indicative of a statistical difference.

This study was part of an integrated mapping protocol, which received ethical approval from the Directorate of Research, Planning and Health System Development, Ministry of Health (MoH), Government of Southern Sudan, and from the Ethics Committee of the London School of Hygiene and Tropical Medicine, UK. Clearance to conduct the surveys was obtained from Northern Bahr-el-Ghazal State MoH, followed by County Health Departments.

Results

A total of 4901 children from 74 communities provided urine samples, of whom 370 (7.5%) had detectable haematuria. Of these, 357 samples were subsequently examined by urine filtration, and matched to 320 reagent strip negative samples that were also filtered. The prevalence of *S. haematobium* infection, determined by a positive filtration result, was 3.0% (95% CI, 2.5–3.6%). Prevalence did not significantly differ by sex, but was significantly higher in children aged 11–16 years compared those who were 5–10 years old (4.7% *vs.* 2.4%, $P < 0.001$). Table 1 presents the diagnostic performance of reagent strips overall and by age-group and sex, and shows that reagent strips had high overall sensitivity and NPV, but only moderate specificity and poor PPV. Diagnostic indices were consistently better among boys compared to girls (Table 1). Of the children who had haematuria but no detectable *S. haematobium* eggs, 71% (158/222) were female and 51% (113/222) were girls aged 5–10 years old. Sensitivity was not related to intensity of infection: 100% (95% CI, 95–100%) among those

Table 1 Diagnostic performance of haematuria reagent strips according to age, sex, and *Schistosoma haematobium* prevalence in Northern Bahr-el-Ghazal State, Southern Sudan 2009

	Number examined	Sensitivity	Specificity	PPV	NPV
Overall*	677	98 (94–99.5)	59 (55–63)	38 (33–43)	99 (97–99.8)
Boys: 5–10 years	186	100 (93–100)	68 (60–76)	52 (42–63)	100 (96–100)
Boys: 11–16 years	98	100 (87–100)	74 (62–83)	58 (52–72)	100 (93–100)
Boys: all ages	284	100 (95–100)	70 (63–76)	54 (45–93)	100 (98–100)
Girls: 5–10 years	270	97 (85–99.9)	52 (45–58)	24 (17–31)	99 (96–99.9)
Girls: 11–16 years	122	93 (76–99)	52 (42–63)	37 (25–49)	96 (87–99.5)
Girls: all ages	392	95 (87–99)	52 (46–57)	28 (22–34)	98 (95–99.6)
Low prevalence payams†	444	100 (94–100)	54 (49–60)	26 (21–32)	100 (98–100)
Moderate prevalence payams‡	155	96 (89–99)	75 (64–84)	78 (69–86)	95 (87–99)

*One record was missing data for age and sex.
†>0% and <10% prevalence. 15 of the 21 payams, with payams with 0% prevalence excluded.
‡≥10% prevalence. One of the 21 payams.
PPV, positive predictive value; NPV, negative predictive value. 95% exact binomial CI in parenthesis.

harbouring heavy infections and 96% (95% CI, 88–99%) among those with light infections. By contrast, specificity and PPV were lower in low prevalence communities (Table 1).

Discussion

Previous research studies in different African settings report sensitivities of reagent strips for micro-haematuria ranging from 67–93%, and specificities of 67–99% (Brooker *et al.* 2009), including a sensitivity of 87% in White Nile Province in Sudan (Eltoum *et al.* 1992). The present study showed that in the context of an integrated NTD survey in Southern Sudan, reagent strips had comparably high sensitivity. Specificity was, however, considerably lower than reported by previous studies, and was especially poor among young girls and in low prevalence communities. The high prevalence of false positive diagnoses among girls compared to boys is consistent with studies in Ghana (Hall & Fentiman 1999) and Tanzania (Hatz *et al.* 1990). Some of the observed false positives among older girls may be explained by menstruation. Among younger girls, urinary-tract infections, which are more common in girls than boys and can be the result of female circumcision, may also play a role. Female circumcision is very common custom in northern Sudan, occurring in girls as young as 4 year olds (Satti *et al.* 2006), and is also practiced by some tribes in Southern Sudan.

Reagent strip testing has been proposed as a simple, indirect method for identifying children with *S. haematobium*, and hence a useful way to rapidly map the prevalence of infection to identify areas warranting mass treatment with praziquantel. Our experience in Southern Sudan shows that if reagent strips are used as the sole diagnostic tool, the observed low specificity would result in overestimation of infection prevalence, especially among low transmission villages, and potentially lead to mass treatment in communities or target groups that do not require treatment. For example, using the WHO cut-off of 10% to denote the need for mass treatment using praziquantel of school-aged children, 19 of the surveyed villages would have received mass treatment if the decision was based only on reagent strips, whereas only four villages would warrant mass treatment based on urine microscopy. Positive results obtained by reagent strip in the context of a rapid mapping survey should thus be confirmed by urine filtration.

Ultimately, it would be useful to have a single rapid diagnostic tool that could reliably detect more than one of the parasites causing NTDs. For schistosomiasis, the ongoing refinement of reagent strips to test for circulating cathiodic antigen is likely to result in such tool for simultaneous detection of both *S. haematobium* and *S. mansoni* (Bergquist *et al.* 2009).

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