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Mapping of *Schistosoma mansoni* in the Nile Delta, Egypt: Assessment of the prevalence by the circulating cathodic antigen urine assay

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ABSTRACT

In line with WHO recommendations on elimination of schistosomiasis, accurate identification of all areas of residual transmission is a key step to design and implement measures aimed at interrupting transmission in low-endemic settings. To this purpose, we assessed the prevalence of active *S. mansoni* infection in five pilot governorates in the Nile Delta of Egypt by examining schoolchildren (6–15 years) using the Urine-Circulating Cathodic Antigen (Urine-CCA) cassette test; we also carried out the standard Kato-Katz (KK) thick smear, the monitoring and evaluation tool employed by Egypt's national schistosomiasis control programme. Prevalence rates determined by the Urine-CCA test for all governorates were higher than those determined by KK ($p < 0.01$). Of 35 districts surveyed in the five governorates, *S. mansoni* infection was detected in 19 districts (54.3%) using KK, and in 31 districts (88.6%) by Urine-CCA ($\chi 2 = 9.94$; $P = 0.0016$). *S. mansoni* infections were detected by Urine-CCA, but not by KK in 12 districts (34.3%), and infection was not detected by either of the two diagnostic methods in four districts in Qalyubia governorate. Males and higher age-groups have significantly higher Urine-CCA prevalence rates. Based on the findings of the current S. mansoni mapping exercise, authorities of the Ministry of Health and Population (MoHP) adopted a new elimination strategy by readjusting thresholds for mass treatment with praziquantel and targeting all transmission areas. MoHP is now planning to remap in all other endemic governorates using Urine-CCA with the aim of identifying all areas of transmission where the elimination strategy should be applied.

1. Introduction

Two forms of schistosomiasis (intestinal caused by *S. mansoni* infection and urogenital by *S. haematobium* infection), have been endemic in Egypt since ancient times. *S. haematobium* infection prevails along the Nile Valley south of Cairo, whereas *S. mansoni* infection is restricted to the Nile Delta. The National Schistosomiasis Control Programme (NSCP), established in 1977, has been successful in significantly decreasing the prevalence of the two forms (El Khoby et al., 2000).

Prevalence of *S. mansoni*, as assessed by a single Kato-Katz thick smear, had consistently decreased among the general population in the Delta from 14.8% in 1993–2.7% in 2002, and further declined to 1.5% in 2006, due to application of intensive control measures (WHO, 2007; WHO, 2011). Also, the intensity of infection, measured by egg count, has decreased considerably. However, there were still "hot spot" transmission foci with prevalence rates of about 10% in 2006. The number of the "hot spots" was 136 in 2010 and decreased to 88 in 2013, of which 83 were in Lower Egypt (Nile delta governorates) and 5 in Upper Egypt (Barakat, 2013). Currently, *S. mansoni* endemic areas can be grouped in three categories: areas with prevalence of ≥3%, areas with prevalence of <3% and those

Abbreviations: CCA, circulating cathodic antigen; CIs, confidence intervals; KK, Kato-Katz; MDA, mass drug administration; MoHP, Ministry of Health and Population; NSCP, National Schistosomiasis Control Programme; WHO, World Health Organization.

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with no autochthonous cases. Thus, most of the endemic areas are currently of low transmission and hence the Ministry of Health and Population (MoHP) aims for elimination of the infection (reducing incidence of infection to zero), in line with World Health Assembly Resolution 65.21 (2012; "Elimination of schistosomiasis"), and the recent World Health Organization (WHO) strategy (WHO, 2009, 2013).

The current *S. mansoni* epidemiological data are based on detection of schistosome eggs using a single Kato-Katz (KK) thick smear, the standard monitoring and evaluation tool employed by the MoHP's NSCP. However, the sensitivity of a single examination, especially in areas of low transmission, can be very low due to a combination of factors. These include variation in the distribution of eggs within a single stool specimen, day-to-day variations in egg excretion and random distribution effects (Hall, 1981; De Vlas et al., 1992; Engels et al., 1996; Engels et al., 1997; Kongs et al., 2001; Utzinger et al., 2001). The sensitivity of KK can be improved by examination of multiple samples, but this is impractical for field work. Recently, a cassette format test for active *S. mansoni* infection, based on detection of adult worms' circulating cathodic antigens (CCA) in urine samples, has been developed, evaluated, and is currently commercially available (Shane et al., 2011; Coulibaly et al., 2011; Tchuem Tchuenteí et al., 2012; Colley et al., 2013). Previous studies in African countries indicated that the Urine-CCA test is more sensitive than triplicate KK examinations in areas of low endemicity (i.e. low prevalence and intensity of infection) (Coulibaly et al., 2011). The present study aimed at more accurately mapping the distribution of intestinal schistosomiasis in five Nile Delta governorates as a first step towards extensive remapping in all *S. mansoni* endemic areas, in the framework of Egypt's efforts to achieve transmission elimination. In particular it assessed the prevalence of *S. mansoni* infection using the Urine-CCA test in schoolchildren, compared it with data obtained by the standard KK thick smear, and contributed to revision and updating of the MoHP's mass treatment policy.

2. Material and methods

2.1. Ethics statement

The present work was conducted as a standard and regular part of the MoHP's NTD Programme of public health fieldwork to evaluate the status of intestinal schistosomiasis in schoolchildren in anticipation of moving from morbidity control to elimination (WHO, 2013). The Ethics Review Committee of the Faculty of Medicine, Ain Shams University reviewed and approved the study protocol. The work included only non-invasive collections of stool and urine specimens and their examination by assays of two different sensitivities in order to obtain population data needed for programmatic decisions concerning elimination efforts. Thus, individual consent was not obtained, but rather consent was obtained at the school and community administrative levels for this public health programme.

2.2. Study population

The present work was carried out in five Nile Delta governorates (i.e. Behira, Dakahlia, Kafr El Sheikh, Qalyubia and Sharqia governorate), during March–April 2016. A convenience sampling methodology was employed to maximise the probability of identifying endemic settings. In each governorate a number of schools in rural areas of a study district were sampled, with 100 children selected per school. [3] Names of participating children were not recorded; they were anonymously coded according to their number of the classroom list. Based on previous data from Kato-Katz (KK) stool examinations, three endemicity settings were selected: (1) areas reporting *S. mansoni* prevalence of ≥3%; (2) areas with prevalence of <3% and more than zero percent, in the last school assessment (last scholastic year 2014–2015); and (3) areas reporting zero prevalence during the last three years. In each category, schoolchildren, 6–15 years of age, were examined.

The last annual schistosomiasis treatment, prior to this work, was implemented during the 2014–2015 scholastic year. The MoHP strategy calls for implementing targeted treatment of schoolchildren using praziquantel (PZQ) in each school where prevalence in a sample of its population is ≥2%. Moreover, the entire population aged ≥3 years of a village or satellite village (Ezba or sub-village, average population 1000) is treated (i.e. mass drug administration, MDA) when community prevalence, assessed in ≥100 of its inhabitants, is ≥3%.

2.3. Stool examination

Field assistants collected stool samples from schoolchildren enrolled in the study. Well trained laboratory technicians prepared and examined stool samples using a single KK thick-smear. The results were reported as negative/positive. Approximately 10% of the KK negative slides were reexamined by a senior laboratory technician. Eggs of soil transmitted helminths (STH; *Ascaris lumbricoides*, hookworm, and *Trichuris trichiura*) were also reported.

2.4. Urine collection and urine-CCA diagnosis

The WHO Representative Office, in Cairo, supplied MoHP with 15,000 Urine-CCA cassette tests (Rapid Medical Diagnostics, Pretoria, South Africa; batch number 50174). Urine samples for the CCA test and stool samples for KK examination were collected from children in target schools. Urine samples were transferred to the district laboratory and processed within 2–3 h from collection. The Urine-CCA test was performed according to the manufacturer's instruction. Briefly, one drop of urine was added to the sample well of the cassette and allowed to absorb. Then, one drop of test buffer, provided with the kit, was added to the well and the assay was allowed to develop. The test was read 20 min after the buffer was added. Any line in the test area was considered positive. The test was considered invalid if the line developed after 25 min after the buffer was added or no control line was developed. The test was read and agreed upon by two observers (laboratory assistant or lab technician), and in case of disagreement results were discussed with a senior lab technician. Positive colour reactions were compared to the colour of the control line and arbitrarily scored as trace (faint-very faint band), weak (+), medium (++) and strong (+++).

The original study protocol called for testing only KK negative subjects by the Urine-CCA test. However, because the number of KK positives was expected to be small and to allow laboratory technicians to see intense positive bands, urine samples from all children examined by KK were also tested by the Urine-CCA.

2.5. Statistical analysis

Data were checked for its completeness and consistency. Data entry was done on Microsoft Excel database spreadsheet. Qualitative data was summarised by frequencies and percentages. Chi-square test was used in the analysis. Confidence intervals and odds ratio were calculated with STATA 10 Programme. The rest of the analysis was done with SPSS programme version 13.0. Non-overlapping 95% confidence intervals (CI) or a "P value" of less than 0.05 was considered statistically significant.