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The Ethiopian SORT IT Course

Does mass drug administration affect *Schistosoma mansoni* infection trends in West Dembia district, Northwest Ethiopia?

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Abstract
Introduction: Schistosomiasis is one of the Neglected Tropical Diseases in Ethiopia. Since 2015, yearly school-based mass drug administration (MDA) using praziquantel has become the major control strategy. This study aimed to assess trends of *Schistosoma mansoni* infection in a high-endemic area in Northwest Ethiopia.
Methodology: Data were extracted from routine laboratory logbooks at two health centers in West Dembia district, Amhara region, for the period 2013-2018. Wet-mount direct microscopy was used to diagnose intestinal parasites. Chi-square test was used to compare proportions of *S. mansoni*-positive results before and after the start of MDA with praziquantel, across sex, age groups, and seasons.
Results: Data of 8002 stool tests was extracted. The proportion of *S. mansoni* progressively decreased from 9.6% in 2013 to 4.1% in 2018 in the overall patient population and from 20.3% in 2013 to 8.8% in 2018 in school-aged children. However, a declining trend of *S. mansoni* was observed before the launch of MDA and remained constant after the start of the MDA. The positivity rate was significantly higher in males and in the 5-14 years age group. *S .mansoni* infection in school aged children showed significant seasonal variation.
Conclusions: The declined trend of *S. mansoni* positivity rate is encouraging and may be related to the existence of intervention packages. Although the timing of MDA was related with low positivity rate of *S. mansoni* infection, it has not resulted in the expected beneficial effect. Therefore, the district health office should work on both MDA and other interventions.

Key words: Schistosomiasis; deworming; neglected tropical diseases; Ethiopia; operational research.

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Introduction
Schistosomiasis, also known as snail fever or bilharziasis, is a chronic neglected tropical disease (NTD) caused by parasitic flatworms of the genus *Schistosoma*. It affects people in tropical and sub-tropical countries, particularly poor communities that lack access to safe drinking water and adequate sanitation [1-5]. The two major forms of human schistosomiasis are hepatointestinal and urogenital. *Schistosoma* parasites are transmitted through contact with cercaria contaminated water. Around 240 million people worldwide are infected and a further 700 million people in 78 countries are at risk of infection [6,7]. Children in rural areas are particularly often affected [8].

Ethiopia is one of the developing countries in Sub-Saharan Africa. Seventeen out of 21 diseases on the WHO list of NTDs are found here, and the Ministry of Health (MoH) has identified eight priority NTDs for control and elimination, including schistosomiasis [9,10].

Previous studies have reported a high prevalence of schistosomiasis in school children in Northwest Ethiopia: 38% in Zarima Town in 2009 and 90% in Sanja Town in 2013 [11,12].

School- or community-based mass drug administration (MDA) using praziquantel is the major control strategy for schistosomiasis. As in most other endemic countries, the MDA strategy in Ethiopia mainly focuses on school-aged children via yearly school-based treatment. These campaigns started in 2015 and are currently targeting 6.4 million children in endemic areas countrywide. The Ethiopian MoH has classified districts according to burden of disease and plans to achieve the elimination of schistosomiasis-related morbidity by 2020 and tobreak the transmission by 2025. Short-term targets of the elimination program are to cover at least 75% of school-aged children with MDA; to extend MDA to all adolescents and adults in high-endemic districts; and to decrease infection rates by 65-90% compared to baseline estimates [9].

To assess the effect of MDA campaigns on infection prevalence, cross-sectional community-based surveys are conducted. In Ethiopia, some of these surveys have shown high infection prevalence among school-aged children despite repeated yearly MDA campaigns [13,14]. This phenomenon has also been observed in other countries [15] and has raised questions about the adequacy of school-based MDA to control schistosomiasis [13,15]. However, such surveys provide cross-sectional snapshots in geographically limited areas and in specific population groups. They do not allow general overviews or assessments of long-term trends.

Long-term trends of *S. mansoni* infection in high-endemic areas of Ethiopia in the context of yearly MDA to school-aged children have not been assessed to date. Such evidence, however, is crucial to understand the effects of MDA on infection and morbidity trends and to inform policy makers about the effectiveness of MDA as a tool to reach elimination targets. Therefore, the present study aims at assessing the trend of *S. mansoni* over the last six years (2013-2018) in two routine laboratories in a schistosomiasis endemic area. This can be usedas aproxy for the trend of the disease in the area which may contribute to evidence-based decision on schistosomiasis control activities.

Methodology

Study design and setting

A retrospective study was conducted using routine laboratory data from primary health centers in West Dembia, a district in Amhara region, Northwest Ethiopia.This district is located about 46 km south of Gondar, on the northern shore of Lake Tana, the largest lake of Ethiopia and source of the Blue Nile. It is found at the 10º 38’ 36N latitude, 39º 18’ 37E longitude, and at an altitude of 2556 meters above sea level [16]. Based on the 2007 census, West Dembia had a population of 271,053. It is classified as a high-endemic district for schistosomiasis (prevalence ≥ 50%) [17]. According to the district health office, health education and snail control activities have been promoted for the past ten years (personal communication, April 09, 2019). In 2016, the district also started to organize school-based MDA campaigns using praziquantel. West Dembia district has five health centers, of which the oldest two are located in Chuahit and Gorgora. In these centers, laboratory services have been part of the routine activities since 2009. The most commonly performed diagnostic tests are stool microscopy (direct wet-mount technique), urine analysis, and blood film examination for malaria.

Study population, period and sampling

The target population consisted of all stool microscopy results registered in the laboratory logbooks from January 2013 to December 2018. Since the number of stool samples tested was very large, we used a systematic sampling technique: all the information registered in the first week of every month over the six years was included. Patients whose laboratory result was eligible and with full information for the study were included in the study.

Data collection

The hand-written laboratory logbooks were the main source of information for this study. We extracted test date, patient sex and age, and stool test result (positive or negative for schistosomiasis). In these health centers, direct wet mount stool microscopy is used for intestinal parasitosis diagnosis. Data regarding MDA campaigns with praziquantel in the district were obtained from West Dembia District Health office.

Analysis

Data were double-entered directly from the laboratory register into EpiData version 3.1. Chi-square tests with the level of significance set at 95% were used to compare proportions of *S. mansoni*-positive results before and after MDA with praziquantel, and across sex and age groups. The data were analysed using SPSS 20 software package and the graphs were made with Microsoft Excel.

Ethical considerations

Permission for the study was obtained from the Research and Ethical Review Committee of the University of Gondar and from the Union Ethics Advisory Group of the International Union against Tuberculosis and Lung Disease, Paris, France.

Results

Trend of S. mansoni infection over six years

The results of 8002 stool microscopy tests were systematically extracted from Gorgora and Chuahit health centers. Of these, 408 (5.1%) had a diagnosis of *S. mansoni* infection. The proportion of *S. mansoni* infection decreased from 9.6% in 2013 to 4.1% in 2018 (Figure 1). The main decrease occurred before the start of MDA in 2016 (p<0.001). The patterns of *S. mansoni* positivity for the total population and for the subgroup of school-aged children were similar, but in school-aged children, the decrease was more pronounced: from 20.3% in 2013 to 9.3% in 2015 and from 9.6 in 2016 to 8.8% in 2018. For comparison, the trends of other helminth (*Ascaris lumbricoides*, *Hookworm*, *H. nana* and Taenia species) and protozoan infections (*E. histolytica* and *G. lambilia*) are also indicated on Figure 1: protozoan infections showed a significant increase, while other helminths remained almost constant.

Stool test results stratified by age, sex, and MDA period

The mean age of the patients providing stool samples was 26.3 years (standard deviation 17.2 years), and 50.5% were males. The proportion of *S. mansoni*-positive results was significantly higher in the 5-14 years' age group (10.4%) than in the other age groups (1.4% in children under five and 4.1% in patients of 15 years or older; p<0.001). The proportion of infection was significantly higher in males (6.5%) than in females (3.7%), both before and after the start of MDA in 2016 (p<0.001). The proportion of infection was significantly higher in 2013-2015 (7.1%; before the start of MDA) than in 2016-2018 (3.7%) in all age and sex groups (Figure 2).

Seasonal variation of S. mansoni positivity

The proportion of *S. mansoni* positive results varied over the seasons, particularly in school-aged children and in the years after MDA (Figure 3).

Figure 2. Age- and sex-related patterns of *S. mansoni* positivity in two health centers of West Dembia district, Northwest Ethiopia, 2013-2018.

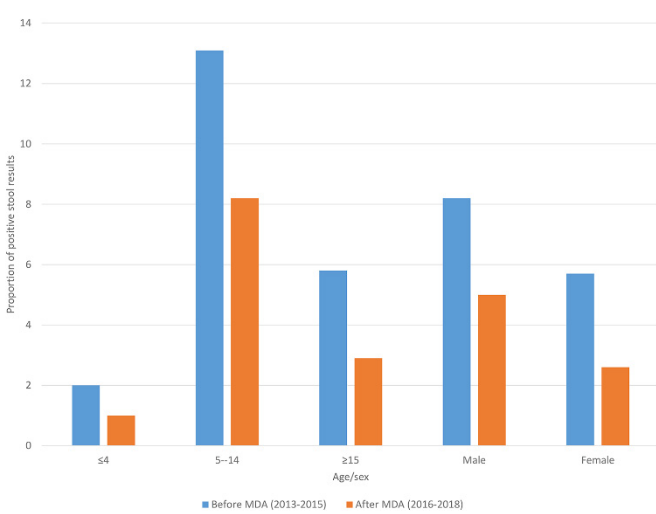
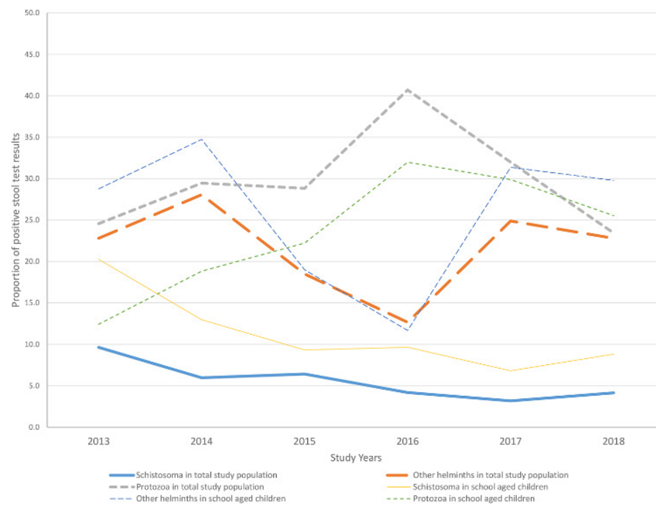


Figure 1. Trends of S. mansoni and other intestinal parasites in the total study population (n = 8002 samples) and in the subgroup of school-aged children (n=1535 samples) in two health centers of West Dembia district, Northwest Ethiopia, 2013-2018.



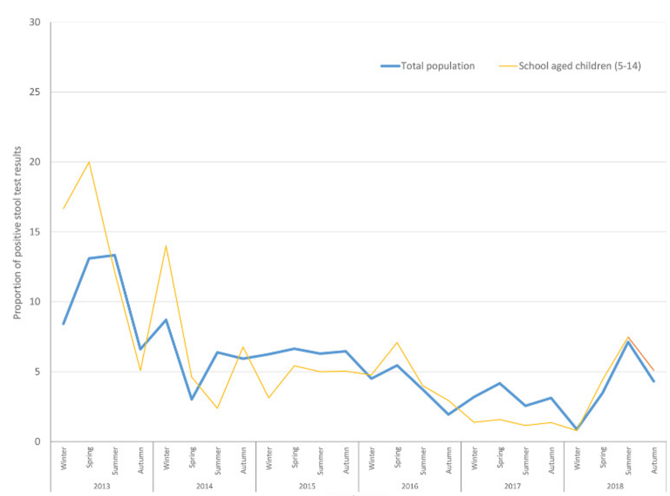
Stool test results stratified by health center

Out of the 8002 stool test results, 74.5% were from Chuahit health center. The overall proportion of infection due to *S. mansoni* over the six years was 5.5% in Chuahit and 3.9% in Gorgora. The proportion of *S. Mansoni* positive results dropped significantly in Chuahit health centre while it remained relatively constant in Gorgora. The trends for the other parasites are also shown in Figure 4.

Mass drug administration campaigns

Since at the end of 2015, MDA campaigns using praziquantel have been conducted in the district once

Figure 3. Seasonal fluctuation of *S. mansoni* positivity in different population categories attending two health centers of West Dembia district, Northwest Ethiopia, 2013-2018.



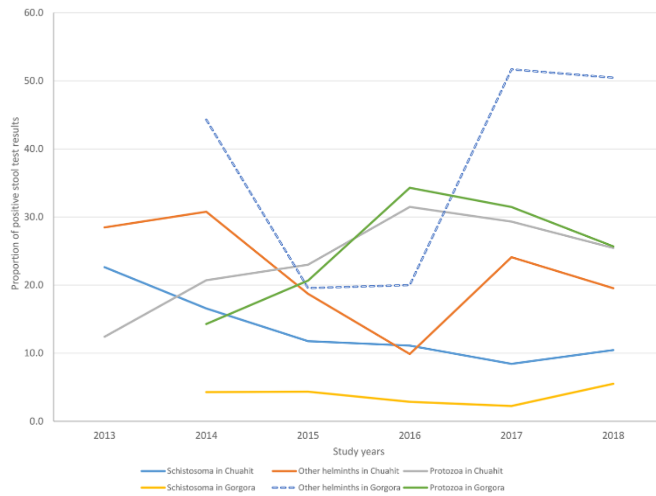
every year, in November or December. During these MDA campaigns, health extension workers give the drug to all the children who attend primary school. The information on the number of children treated in 2015 was not available.The average MDA coverage among schoolchildren in the district for the period 2016-2018 was 71% (Table 1).

Discussion

Over the six years' study period, there was a 57% reduction in *S. mansoni*-positive stool test results: the proportion decreased from 9.6% in 2013 to 4.1% in 2018. The patterns in the total study population and in school-aged children were similar. Although this is an encouraging finding, it is difficult to interpret because the main decrease occurred before the start of MDA. MDA has been introduced as the major control strategy against the disease since 2015 [9], and according to the district health office, the coverage for the target population in Dembia district was around 70% in 2016-208, which is close to the target of 75%. Nevertheless, the infection proportions remained relatively stable from 2016 onwards. One possible explanation for this unexpected phenomenon could be the work of health extension workers who were trained and assigned to different districts to improve the health condition of the people in rural areas and has been promoted by the Ethiopian MoH since the 2010s. These professionals have been working hard especially in the first years after their employment, and in that period, the coverage of latrine construction and improved sanitation may have been higher than ever. A second explanation may be that MDA is given only once a year and not to the whole population (report from the district health office). Thus, reinfection may be frequently occurring, and this may have been a driver of the relatively constant proportion of *S. mansoni* infection. Thirdly, there may have been problems with the implementation and documentation of the MDA campaigns and the true coverage could be lower than what is reflected in the reports.

The overall frequency of *S. mansoni* in this study was 5.1%, which is low compared to previous cross-sectional studies conducted in different parts of Ethiopia such as Wolita Zone, Southeast Ethiopia (81.3%) [18], Sanja town in Northwest Ethiopia (89.9%) [12], Southwest Ethiopia (44.8%) [19], South Tigray in North Ethiopia (73.9%) [20], and Fincha valley Wollega in South Ethiopia (67.9%) [21]. A possible reason for the lower proportion of infection in the present study could be the diagnostic tests used. In our study, a single direct wet-mount microscopy test was used in both health centers, whereas the other cross-sectional studies used Kato-katz which is more sensitive technique. Other explanations for the discrepancy could be differences in the skill of the laboratory personnel, the type of study population, the type of control measures used in the area, and the local climatic conditions.

Figure 4. Patterns of *S. mansoni* and other parasite positivity by health center in West Dembia district.



The proportion of *S. mansoni* was higher in men than in women, regardless of the MDA period. This is in agreement with reports from other parts of Ethiopia such as Jimma [22] and Wondo Genet [23]. Most people in West Dembia are farmers. Men are engaged in agronomic activities like irrigation, ploughing and planting during which they are exposed to the infective cercarial stage of the parasite. Children less than five years of age were the least affected group in this study. This observation could be because they spend most of their time at home which makes them less exposed to the infection. The 5–14 years age group was the most affected in both sexes. This may be due to their

Table 1. Number of children treated with praziquantel in 2016-2018, West Dembia district, Northwest Ethiopia.

Year	Month of MDA	Number of children treated	Number of children registered in primary schools	MDA coverage (%)
2016	November	27254	38634	71
2017	November	28979	40756	71
2018	December	31199	43587	72

engagement in agricultural activities and the habit of taking baths and washing clothes in local rivers. Individuals who are 15 years and older may have equal risk of exposure to *S. mansoni* infection as those in the 5-14 years' age group. However, their immune system is more protective than the younger age group [24]. Moreover, there is a practice of taking Praziquantel and other treatments from private pharmacies by the communities prior to seeking care in the local health facilities. Hence, these reasons could explain why the infection rate among this group is lower than in the 5-14 years age category.

The proportion of *S. mansoni* infection varied across seasons, especially in school-aged children. The difference was more pronounced after the introduction of MDA. For example, in 2016 and 2017, MDA was given in November (autumn) and in 2018 in December (winter). During these study periods, infection proportions were lower than in any other season. This may suggest that MDA resulted in a significant reduction of the infection but that rapid reinfection may have masked the beneficial effect of MDA over longer periods of time.

Although Gorgora is located near the shores of Lake Tana, the proportion of *S. mansoni* infection was lower in Gorgora than in Chuahit. However, in Chuahit, the decrease in infection was more pronounced. As the turnover of laboratory technicians was limited in both health centers, it is unlikely that changes in staff explained the differing trends. More likely explanations are differences in the activities by health extension workers and in MDA coverage.

The major limitation of this study is that routine data of direct wet-mount microscopy was used for analysis. This may have led to an underestimation of the true proportion of *S. mansoni* infection, which complicates the comparison of our findings with those of other studies in the country. Moreover, the report about MDA coverage may not be robust since we observed incomplete documentation of health intervention activities in the district. However, the large sample size and the possibility to analyze trends are strengths of the study.

Conclusion

Despite the limitations, this study allowed to observe the trend of *S. mansoni* positivity rate over the six years period. Although the positivity rate was relatively lower on months/seasons where MDA was given, a slight increment of the infection was observed on seasons or months without MDA. This may suggest that, while MDA resulted in a reduction of the infection, there may exist a rapid reinfection rate and this may mask the beneficial effect of MDA over longer periods of time. Therefore, the district health office should work on both MDA and other interventions that can minimize reinfection rates of the parasite.

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Authors' contributions

AJZ was involved in study conception and design, protocol development, data collection, analysis, and drafting of the manuscript. KV and FV contributed to protocol development. EMK and KV were involved in data analysis and drafting of the manuscript. All authors contributed to the interpretation of the findings and they critically reviewed and approved the manuscript.

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