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Brief Communication

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An integrated mass drug administration against hymenolepiasis and schistosomiasis in Sudan

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Abstract

Hymenolepis nana, commonly known as the dwarf tapeworm, affects 50 to 75 million people worldwide. To date, no studies have explored the disease burden of *H. nana* infection in Sudan. This study aimed to determine the national prevalence of *H. nana* across 189 districts and 18 states in Sudan and the number of individuals infected with *H. nana* who did not receive treatment during the mass drug administration (MDA) campaign targeting schistosomiasis. In addition, the study sought to evaluate the extent of co-infection of *H. nana* with schistosomiasis and soil-transmitted helminthiasis. This involved a secondary analysis of a nationwide survey conducted in 2017 in Sudan. Binomial family generalized linear models with a logarithmic link function were used to estimate the prevalence ratio of potential risk factors, including sex and water and sanitation conditions in schools and households. For the nationwide survey, a 2-stage sampling method was used, in which 105,167 students were selected from 1,772 schools. A total of 96,679 stool samples were collected, of which 4,706 (4.9%) tested positive for *H. nana*. Of these, fewer than 1% were co-infected with schistosomiasis (either *Schistosoma haematobium* or *Schistosoma mansoni*), and a mere 0.1% had co-infections with soil-transmitted helminths. At an 8% threshold for village-based MDA, approximately 1.1 million infected adults are ineligible to receive praziquantel from the village-based MDA. Children residing in households with improved latrines had a lower odds of *H. nana* infection than those without improved latrines did (adjusted odds ratio=0.87, 95% confidence interval=0.80–0.94, *P*=0.001). In countries where *H. nana* is endemic, such as Sudan, providers making MDA decisions should consider the prevalence of either *H. nana* or schistosomiasis, rather than focusing solely on the latter.

Keywords: *Hymenolepis nana*, mass drug administration, sanitation, Sudan

Hymenolepis nana, which is commonly referred to as the dwarf tapeworm, is the primary parasite responsible for hymenolepiasis, causing 50 to 75 million cases of the disease worldwide [1]. Although hymenolepiasis is typically asymptomatic, it can sometimes lead to mild clinical symptoms including diarrhea, abdominal pain, anorexia, and nonspecific gastrointestinal manifestations [2]. In some cases, infection with *H. nana* may lead to severe diseases, including life-threatening conditions, particularly in individuals with HIV who are immunosuppressed [3]. Direct human-to-human transmission is a common route of *H. nana* infection [4,5]. However, because rodents, such as mice and rats, along with arthropod intermediate hosts, serve as reservoirs of the infection, *H. nana* infection is classified as a zoonosis. The significance of each reservoir varies with the environment [6]. In conditions of poor hygiene and sanitation, especially in densely populated urban areas, transmission risks are particularly high [7,8]. Co-infection with other enteric parasites, including soil-transmitted helminths, *Giardia*, *Entameba coli*, *Blastocystis*, and *Chilomastix*,

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is common, with fecal-oral contamination occurring frequently [9-12]. Notably, the clinical severity of this polyparasitic infection is primarily intensified by *H. nana* [9].

There are increasing concerns about the invasive nature of *H. nana*, which may have been overlooked in many regions and is more pathogenic than previously recognized; furthermore, this disease primarily affects children [13]. Despite its significance, to the best of my knowledge, no previous studies have investigated the disease burden of *H. nana* infection in Sudan. In this region, praziquantel is primarily distributed through mass drug administration (MDA) campaigns that target schistosomiasis. Although praziquantel can treat *H. nana*, individuals infected with or at risk of *H. nana* have not been considered in these efforts in Sudan.

This study determined the prevalence of *H. nana* across 189 districts and 18 states in Sudan. In addition, I sought to analyze the extent of co-infection with schistosomiasis and soil-transmitted helminthiasis. Ultimately, the aim of this study is to provide programmatic recommendations for addressing both schistosomiasis and *H. nana* in Sudan. This research involved a secondary analysis of a nationwide survey conducted in Sudan in 2017. Previous reports have documented the prevalence of schistosomiasis and soil-transmitted helminthiasis [14,15].

Sudan, the third largest country in Africa, is divided into 18 states and 189 districts. In 2020, the population of the country was approximately 40.2 million [16]. A 2-stage sampling method was used for the nationwide survey, with 105,167 students selected from 1,772 schools. From this group, 96,679 stool samples were collected. Ethical review and approval were obtained both from the Institutional Review Board of Federal Ministry of Health, Sudan (FMOH/DGP/RD/TC/2016; January 15, 2017) and the Korea Association of Health Promotion (130750–20,164-HR-020; May 16, 2016).

The data collectors visited a school early in the morning, distributed stool and urine containers to selected students, and collected samples on the same day, which were then processed within 24 h. Laboratory technicians used the Kato–Katz technique to examine the eggs in the stool samples. They prepared and examined 2 slides for each student's stool sample. Two senior supervisors from the Federal Ministry of Health oversaw the quality of the specimen examinations and interviews. Each day, 1 supervisor reexamined 10% of the slides. In addition, independent supervisors from Al Neelain University and the Blue Nile National Institute for Communicable Disease, University of Gezira, were assigned to reexamine 5% of the samples collected during their visits. Fewer than 10 slides had a discrepancy between the findings of the supervisors and the state-level laboratory technicians. To account for this discrepancy, the examination results from the supervisors were considered as the accurate values.

To estimate the prevalence at the state level, I applied sampling weights by state and district, taking into account each district's sex ratio and population size. For district-level prevalence, I referred only to the sex ratio, as the population size was unknown at levels smaller than the district. Because the survey included only school-aged children (SACs), age was not weighted. I estimated the prevalence and number of infected individuals using the prevalence data for SACs, acknowledging the limitations described. To create a map of *H. nana* infections, geographical information system software (QGIS v.3.2; QGIS Development Team, Bern and Chur, Switzerland) was used. I gathered information on the MDA target population for schistosomiasis and identified districts that were excluded from the MDA intervention. Based on this information, I estimated the number of individuals infected with *H. nana* who did not receive praziquantel treatment during the MDA campaign against schistosomiasis. To estimate the prevalence ratio of probable risk factors, including sex and water and sanitation conditions at schools and households, binomial family generalized linear models with a logarithmic link function were used. I used the log-likelihood ratio to assess the inclusion of each variable in the final model. This study reported 95% confidence intervals (CIs), with statistical significance set at $P<0.05$. Statistical analyses were performed using Stata version 16.0 (College Station, TX, USA).

Supplementary Table S1 presents the number of schools, students, and their ages. Of the participants, 45% were girls. The average age of the students was 11.1 years (SD=2.41) for boys and 10.7 years (SD=2.21) for girls.

Table 1 details the prevalence rates. A survey conducted across 1,722 schools in Sudan collected 96,679 stool samples from 105,167 students, of whom 4,706 (4.9%) tested positive for *H. nana*. The state-level weighted prevalence varied, with the lowest being 0.7% (95% CI=0.5%–1.0%) in East Darfur and the highest being 7.2% (95% CI=6.6%–7.9%) in Khartoum. Following closely were the South Darfur and Blue Nile states, with prevalence rates of 6.3% (95% CI=5.9%–6.7%) and 6.1% (95% CI=5.4%–6.9%), respectively.

Fig. 1. shows the geographical distribution of *H. nana* at the district level. As compared with schistosomiasis, *H. nana* was more evenly distributed.

Table 1 also presents the co-infection status of *H. nana* with schistosomiasis and soil-transmitted helminthiasis. Among the 4,706 children infected with *H. nana*, less than 1% were co-infected with schistosomiasis (either *Schistosoma haematobium* or *Schistosoma mansoni*). Furthermore, a mere 0.1% of these children had a co-infection with soil-trans-

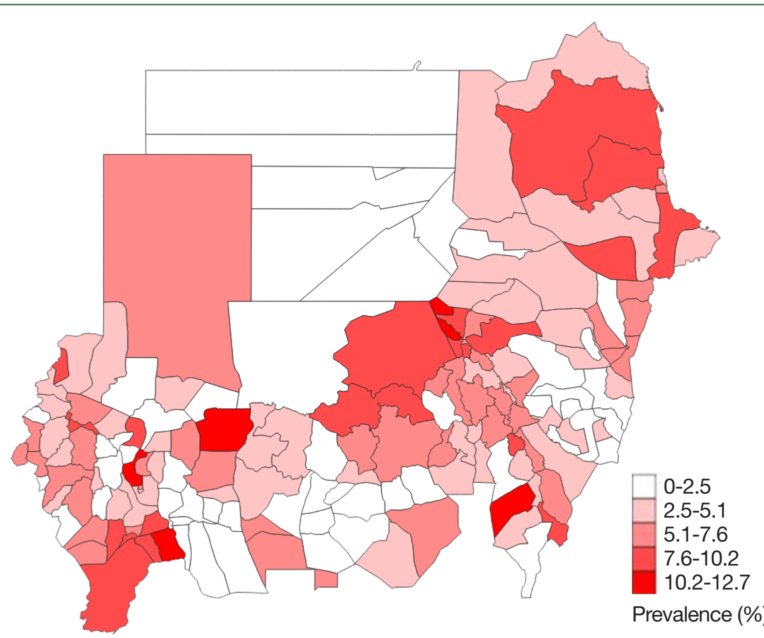

Fig. 1. *Hymenolepis nana* prevalence at district level in Sudan.

Table 1. Prevalence of *Hymenolepis nana* and number of cases of co-infection

	H. nana		No. of cases co-infection	
	n/N[a]	Prevalence[b] (95% CI)	*H. nana* + *Schistosomiasis*	*H. nana* + Soil-transmitted helminth
Blue Nile	240/3,709	6.1 (5.4–6.9)	12	2
Al Gazeira	309/5,710	4.9 (4.4–5.4)	9	0
Central Darfur	185/3,175	4.3 (3.7–5.0)	9	0
East Darfur	34/4,252	0.7 (0.5–1.0)	6	0
El Gadaref	169/5,821	2.6 (2.3–3.0)	10	0
Al Khartum	436/5,514	7.2 (6.6–7.9)	12	0
North Kordofan	220/3,578	5.9 (5.2–6.7)	4	0
Northern	34/3,578	0.9 (0.6–1.2)	1	1
West Darfur	178/3,976	4.1 (3.5–4.7)	1	0
West Kordofan	352/10,190	3.3 (3.0–3.7)	18	0
Kassala	165/3,441	4.6 (4.0–5.3)	5	0
North Darfur	311/6,562	4.6 (4.1–5.1)	14	0
Red Sea	198/2,425	5.9 (5.2–6.8)	1	0
River Nile	125/2,988	3.4 (2.8–4.0)	1	1
Sinnar	175/2,763	5.7 (4.9–6.6)	1	0
South Darfur	922/14,048	6.3 (5.9–6.7)	174	0
South Kordofan	324/8,402	3.5 (3.2–3.9)	13	0
White Nile	383/6,579	5.1 (4.6–5.6)	26	1
Total	4,706/96,679	4.2 (4.1–4.4)	317	5

[a]*n/N,* positive for *H. nana*/number of samples tested.
[b]Weighted prevalence (taken into consideration sex ratio and district population).

mitted helminthiasis.

Table 2 displays the number of individuals infected with *H. nana* who did not benefit from praziquantel because their districts were excluded from MDA interventions as a result of the low prevalence of schistosomiasis. With an 8% threshold for village-based MDA, approximately 1.1 million infected adults are unable to receive praziquantel. Similarly, under the current school-based MDA program at the 3% threshold for school-based MDA, 360,838 infected students are unable to receive praziquantel.

Table 3 shows the association between *H. nana* infection and probable risk factors. Children residing in households equipped with an improved latrine had a lower likelihood of being infected with *H. nana* as compared with those in households without such facilities (adjusted odds ratio=0.87, 95% CI=0.80–0.94, *P*=0.001). However, when compared with households without a latrine, the presence of any type of latrine in a household did not significantly alter the odds of *H. nana* infection (adjusted odds ratio=1.03, 95% CI=0.95–1.10, *P*=0.49). In addition, no correlation was found between access to improved water sources, open defecation practices, and *H. nana* infection.

This study indicated that approximately 4.2% of the SACs in Sudan were infected with *H. nana*. Notably, the prevalence of *H. nana* was significantly higher than that of the 3 soil-transmitted helminthiases, which stood at only 0.1%. Unlike schistosomiasis, this disease is more evenly distributed across all 18 states of Sudan [14,15]. The observation of the highest prevalence in Khartoum may be associated with the state's dense population.

Infection with *H. nana* can lead to fever, headache, abdominal pain, diarrhea, and ane-

Table 2. Estimated number of people with *Hymenolepis nana* who would be excluded from MDA if the thresholds are based solely on schistosomiasis prevalence

State	Students[a]	Adults[b]
Khartoum	104,613	308,283
Al Gezira	40,580	138,910
North Kordofan	23,414	78,582
White Nile	12,103	73,839
North Darfur	31,020	72,381
Red Sea	29,929	69,834
Kassala	23,202	57,348
Sinnar	17,449	53,963
South Darfur	14,205	53,322
South Kordofan	4,444	31,695
Blue Nile	13,264	30,949
West Kordofan	10,371	29,426
El Gadaref	9,442	27,247
Central Darfour	5,241	25,182
River Nile	10,042	24,896
West Darfur	9,193	21,449
Northern	1,789	4,175
East Darfur	540	1,837
Total	360,838	1,103,317

MDA, mass drug administration.
[a]Number of students with *H. nana* who would be excluded from MDA when school-based MDA threshold for schistosomiasis prevalence is 3%.
[b]Number of adults with *H. nana* who would be excluded from MDA when village -based MDA threshold for schistosomiasis prevalence is 8%.

Table 3. Association between risk factors and *Hymenolepis nana*

Variables			Crude OR	95% CI	*P*-value	Adjusted OR	95% CI	*P*-value
Gender	Male	4.34 (2,043/47,041)	0.94	0.89–0.99	0.04	0.91	0.86–0.97	0.003
	Female	4.61 (2,657/57,661)						
Having any type of household latrine	Yes	4.52 (3,732/82,479)	1.04	0.97–1.12	0.28	1.03	0.95–1.10	0.49
	No	4.36 (968/22,223)						
Having an improved household latrine	Yes	4.12 (680/16,490)	0.94	0.83–0.98	0.02	0.87	0.80–0.94	0.001
	No	4.54 (4,080/89,961)						
Open defecation	Yes	4.37 (881/20,152)	0.97	0.90–1.04	0.45	0.98	0.91–1.06	0.63
	No	4.49 (3,879/86,599)						
Having improved water	Yes	4.53 (4,310/95,129)	1.12	1.01–1.24	0.04	1.11	0.99–1.23	0.06
	No	4.07 (390/9,573)						

OR, odds ratio; CI, confidence interval.

mia. In the absence of treatment, it may result in malnutrition, including stunting and micronutrient deficiencies, due to impaired intestinal permeability, enteritis, or intestinal leakage of micronutrients [7].

Niclosamide has been proven effective in treating *H. nana* infections in humans [17]. Some studies have reported that both albendazole and praziquantel have successfully eradicated *H. diminuta* and adult *H. nana* infections [18].

The most significant finding of this study is that several districts that had a high prevalence of *H. nana* were excluded from the mass administration of praziquantel because of the low prevalence of schistosomiasis in those areas. It is estimated that about 2 million Sudanese individuals are infected with *H. nana*, and approximately 1.1 million did not receive praziquantel because they resided in areas not targeted by the MDA intervention. A more effective strategy would likely be addressing both schistosomiasis and *H. nana* concurrently.

In countries such as Sudan, where *H. nana* is endemic, I recommend that decisions regarding MDA be based on the prevalence of either *H. nana* or schistosomiasis, rather than exclusively on schistosomiasis. Although further evidence is required to confirm the economic feasibility of this approach, I believe it offers significant cost-effectiveness and a favorable benefit–cost ratio [1]. Although effective drugs such as praziquantel and albendazole are available to treat *H. nana* infections, they are insufficient for controlling the parasite in endemic foci where transmission rates are high [19]. Reinfection occurs quickly under these conditions, necessitating preventive measures such as education, improved hygiene, and enhanced sanitation. Some studies have suggested that the prevalence of hymenolepiasis could serve as an indicator of the level of hygiene practice and fecal contamination in a village [20]. This study provides evidence that supports this argument.

With regard to sanitation, a significant association was found between only schistosomiasis and the presence of an improved latrine (at school or household). Merely having any type of latrine at school or in a household did not reduce the odds of hymenolepiasis infection. After adjusting for water and sanitation in the analysis, boys had a higher odds of developing hymenolepiasis than girls did, indicating that they may have other unknown risk factors. A possible explanation for this disparity could be their greater exposure to contaminated fields or soil.

The ingestion of fecal contaminants is a recognized transmission pathway for *H. nana*. This study shows that simple pit latrines, whether in schools or households, do not provide protection against *H. nana* in SACs. Furthermore, access to improved water, as defined by the World Health Organization/United Nations Children's Fund, was not associated with a reduced risk of infection in children.

Although the World Health Organization has emphasized the importance of integrated interventions for neglected tropical diseases (NTDs) by publishing the NTD–water, sanitation, and hygiene (WASH) integrated strategy, many projects aimed at controlling NTDs continue to focus solely on preventive chemotherapy. Communities using the WASH strategy have consistently stressed the significance of eliminating open defecation and ensuring access to household latrines. However, the results of this study demonstrate that simply ending open defecation and possessing a household latrine are not enough; it is crucial to have an improved latrine.

Fortunately, numerous WASH experts have begun to explore the impact of sanitation interventions on disease reduction. To the best of my knowledge, few studies have investigated the relationship between WASH interventions and *H. nana* infections.

Food hygiene, which encompasses aspects such as food storage and rodent infestation at home, represents a potential risk factor for *H. nana* infection. These factors were not assessed in this study and thus merit further investigation.

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Supplementary Information

Supplementary material is available with this article at https://doi.org/10.3347/PHD.24056.

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