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REVIEW

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Strategies and achievements in controlling and eliminating schistosomiasis from Egypt

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Abstract

Schistosomiasis is an old parasitic disease in Egypt primarily caused by *Schistosoma mansoni*, transmitted through infected water canals, and disproportionately affects rural areas. Despite substantial reductions in the disease prevalence over the years, it still affects more than 5% of the population in some governorates, highlighting the need for sustained control efforts. Among the recent control measures: (a) mass drug administration with large-scale, biannual administration of praziquantel, which remains the cornerstone of the control program targeting the interruption of vector transmission cycles. (b) Improving disease diagnostics, including point-of-care tests, which facilitate early detection and case management, particularly in remote areas. (c) Snail control using targeted molluscicide aims to reduce parasite transmission by controlling intermediate snail hosts. And (d) behavioral change communication focusing on raising awareness regarding hygiene practices and safe water access.

Even if control attempts have shown positive results, several challenges still exist, including (a) drug resistance, especially to praziquantel, the most commonly used drug, which calls for ongoing observation and monitoring. (b) Sustainability of funding to avoid program disruptions and setbacks. And (c) social and environmental factors like poverty, poor sanitation, and access to clean water. The transition from disease control to elimination requires meticulous planning and vigilance. Robust surveillance systems, enhanced case management, and continued community engagement are vital for such elimination. Strengthening research on drug resistance, snail control methods, and innovative diagnostics would further support elimination efforts. This report aims to address the most recent data regarding the prevalence and control measures for schistosomiasis in Egypt and provide the information required to lead the transition from disease control to elimination.

Keywords Control, Egypt, Elimination, *Schistosomiasis*, *Schistosoma haematobium*, *Schistosoma mansoni*

Introduction

Schistosomiasis is a persistent parasitic infection caused by a trematode worm (blood flukes) of the genus *Schistosoma* and is transmitted to the definitive human host through an intermediate snail host [1]. *Schistosomiasis* is always considered one of the significant endemic infections that result in human acute and chronic diseases in the tropics and subtropics, coming in order after malaria among parasitic infections that have economic and public health importance [2, 3]. *Schistosomiasis* is common in tropical and subtropical settings, particularly in disadvantaged people with limited access to safe drinking water and sanitation. According to the World Health Organization (WHO), it was estimated that at least 236.6 million persons needed *schistosomiasis* preventive treatment in 2019, with more than 105.4 million of them receiving treatment. At least 90% of those who need *schistosomiasis* treatment live in Africa [4]. In the less developed African continent, *schistosomiasis* alone is responsible for about 300,000 annual deaths [5]. Strong

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evidence was obtained from some countries that morbidity due to *schistosomiasis* can be eliminated whenever financial resources and logistics exist. However, eliminating an endemic public health threat like *schistosomiasis* is not easy [6, 7]. *Schistosomiasis* has been diagnosed in Egypt since pharaonic times (3200 B.C.) by recovering *Schistosome* eggs and antigens in ancient mummies [8]. Two species that were found to cause significant disease in humans, namely *S. haematobium* and *S. mansoni*, have been known to represent a significant problem in Egypt due to the high prevalence and disease morbidity, especially in rural areas [7]. Egypt began fighting the disease shortly after discovering the parasite's life cycle in 1915 by establishing control campaigns depending on snail control [7]. *S. haematobium* is responsible for urogenital *schistosomiasis*, with hematuria as its primary manifestation, while *S. mansoni*, the prevalent species in Egypt, is causing intestinal schistosomiasis with liver-related sequelae [9]. Infection causes chronic inflammation and granuloma formation within the intestines, leading to abdominal pain, diarrhea, and blood in stool (hemorrhages). Long-term complications can include malnutrition, stunted growth in children, and liver damage in severe cases. Unlike S. haematobium, S. mansoni does not directly affect the urinary tract, but chronic infection can contribute to secondary bacterial infections and associated urinary symptoms [10–12].

Being a disease with close relations to cultivation, the changes in farming-related activities could impact the disease epidemiology. Barakat et al. reported that in a study involving nine Egyptian Governorates, the mode of parasite transmission in the Nile Delta was changed, with a noticeable reduction owing to the change in irrigation type and care of irrigation canals [2].

Overall, eliminating schistosomiasis can be achieved using a combination of different measures, including improved diagnosis, vector control, proper treatment, vaccination, and raising disease awareness (of patients and decision makers). Integrating the target of disease elimination into the national health system will help prioritize disease management [13]. It is worth mentioning that the development of an effective vaccine is required to improve current control measures for schistosomiasis, leading to its eventual elimination together with the deployment of current interventions. Although many vaccine candidates have been identified, very few have gone to clinical trials. A revolutionary and effective anti-schistosome vaccine pipeline is urgently needed to develop and test novel vaccines [14].

Schistosomiasis journey in Egypt from discovery to near eradication (Fig. 1)

Following the discovery of the parasite's life cycle in 1915, Egypt began its fight against it by launching several pilot initiatives aimed at snail control or disease treatment. Approximately 2.5 million cases of *schistosomiasis* were detected and treated in Egypt between 1989 and 1996. The Egyptian Ministry of Health and Population (MOHP) has launched a campaign aiming to declare the final elimination of *schistosomiasis* in 2020, following the success in reducing the prevalence of *schistosomiasis* to about 0.2% by the end of 2016 [15]. Since 1922, schistosomiasis eradication has been on the agenda of the Egyptian Ministry of Health and Population (MOHP) [16]. Despite significant progress, achieving elimination remains a challenge. While the intensity of infection reported in some studies involving children shows a decrease, with a majority experiencing light or moderate infection in 2022 (e.g., 98.2%, $n=111$ out of 113 total children in one study), overall prevalence still varies across the country, ranging from below 1% to over 50% in different regions [17]. Sustained efforts and vigilance are crucial to achieve the goal of nationwide elimination. Egypt was one of the first countries to take comprehensive steps in the

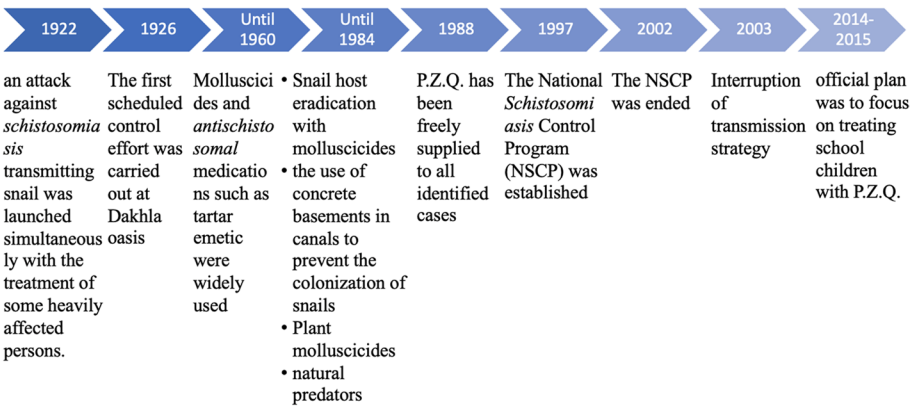

Fig. 1 Timeline of different elimination strategies throughout *Schistosomiasis* journey in Egypt

schistosomiasis control program, which was implemented through different strategies [16].

The control of transmission strategy

This technique was chosen per WHO recommendations to reduce *schistosomiasis* transmission by eliminating snail intermediate hosts and treating infected cases with antischistosomal therapy. Adopting risky behaviors and environmental factors that enhance snail survival and infection were responsible for the infection's persistence. Schistosomiasis elimination in hotspots requires an integrated control approach that combines preventive chemotherapy with other complementary measures [17].

Egypt was one of the countries where molluscicides were used to control *schistosomiasis* successfully [18]. The start was in 1922 when an attack against *schistosomiasis*-transmitting snails was launched simultaneously with the treatment of some heavily affected persons. In 1926, The first scheduled control effort was carried out at Dakhla Oasis, with molluscicide (copper sulfate) applied to all irrigation channels and tartar emetic administered to nearly a third of the population [19, 20]. Molluscicides were widely used in transmission regions, reclamation sites, and places transitioning from seasonal to perpetual irrigation until 1961. Copper sulfate, sodium pentachlorophenate, and niclosamide were employed as molluscicides. Meanwhile, *antischistosomal* medications such as tartar emetic, given through the intravenous route with significant side effects, and hycanthone and astiban, also given intramuscularly, were employed [20].

Egypt succeeded in interrupting disease transmission by using chemical mollusciciding campaigns. As a result, both the incidence and prevalence of *S. haematobium* and *S. mansoni* infections were significantly reduced [18, 21]. However, it should be noted that Snail host eradication with molluscicides is a costly operation and should be performed regularly to avoid snail reinfestation of water channels [22]. Moreover, the use of molluscicides can cause environmental harm. Despite this, this technique was carried out successfully till the beginning of 1984. However, due to the expansive movement of people, lack of health awareness, and the fact that school-aged children were reinfected during the summer months in the same regions where molluscicides were used, the prevalence of infection began to rise again in the middle of the twentieth century [23, 24]. Other measures were simultaneously used to control snail hosts, including using concrete basements in canals to prevent the colonization of snails [25]. Plant molluscicides, such as Ambrosia maritime, have been utilized in Egypt for many years (Damsissa) [26]. Other natural predators, such as tilapia fish, ducks, and water insects, can also operate as biological control agents (Figs. 2 and 3) [27].

Control of morbidity strategy

This strategy focuses on combating the disease by treating infected personnel and interrupting the disease transmission. Egypt's MOHP has a long history of tackling schistosomiasis. In the 1960s, 1970s, and early 1980s, large-scale efforts to combat schistosomiasis involved treating individuals over 5 years old with tartar emetic injections. While effective in reducing prevalence, this method raised concerns about side effects and toxicity. Recognizing these limitations, the Egyptian Ministry of Health and Population (MOHP) launched a Schistosomiasis Research Project in 1988 [16]. This marked a shift towards Mass Drug Administration (MDA) using praziquantel (PZQ), which offered a safer and more efficient approach. Notably, the widespread use of PZQ for MDA from 1988 onwards coincides with a significant decline in the prevalence of hepatitis C virus (HCV) infection in Egypt, suggesting a potential link between schistosomiasis control and reduced HCV transmission [29, 30]. Although the research is complicated and the precise nature of the potential link is still being examined, there may be a connection between tartar emetic medications, HCV, and schistosomiasis. Two points should be summed up, though: First, schistosomiasis and HCV co-infection: individuals with schistosomiasis are at increased risk of acquiring HCV due to factors like (a) increased susceptibility: chronic inflammation caused by schistosomiasis might damage the liver, making it more receptive to HCV infection, (b) exposure risks: shared exposure to contaminated water sources can occur for both infections and (c) immune modulation: schistosomiasis can alter the immune system, potentially affecting the body's ability to fight off HCV [16, 31]. Second, Tartar emetic drugs and HCV: (a) tartar emetic (sodium antimony tartrate) was an older treatment for schistosomiasis used before praziquantel. (b) Its use has been linked to an increased risk of hepatitis B and HIV due to potential contamination issues during administration. (c) Limited evidence exists directly linking tartar emetic to HCV compared to other bloodborne infections. More research is needed to assess any potential connection. Finally, while co-infection with schistosomiasis and HCV seems to increase the risk of complications, the role of tartar emetic specifically in this context is unclear [12, 32, 33].

Egypt's fight against schistosomiasis has evolved over time. One key tactic has been the transition from treating individuals regularly based on need to a more targeted approach using praziquantel (PZQ). This shift proved successful, as evidenced by the dramatic reduction in *S. haematobium* prevalence in Middle and Upper Egypt from 29.3% in 1977 to less than 3% by the late 1990s [34]. This success paved the way for the establishment of the

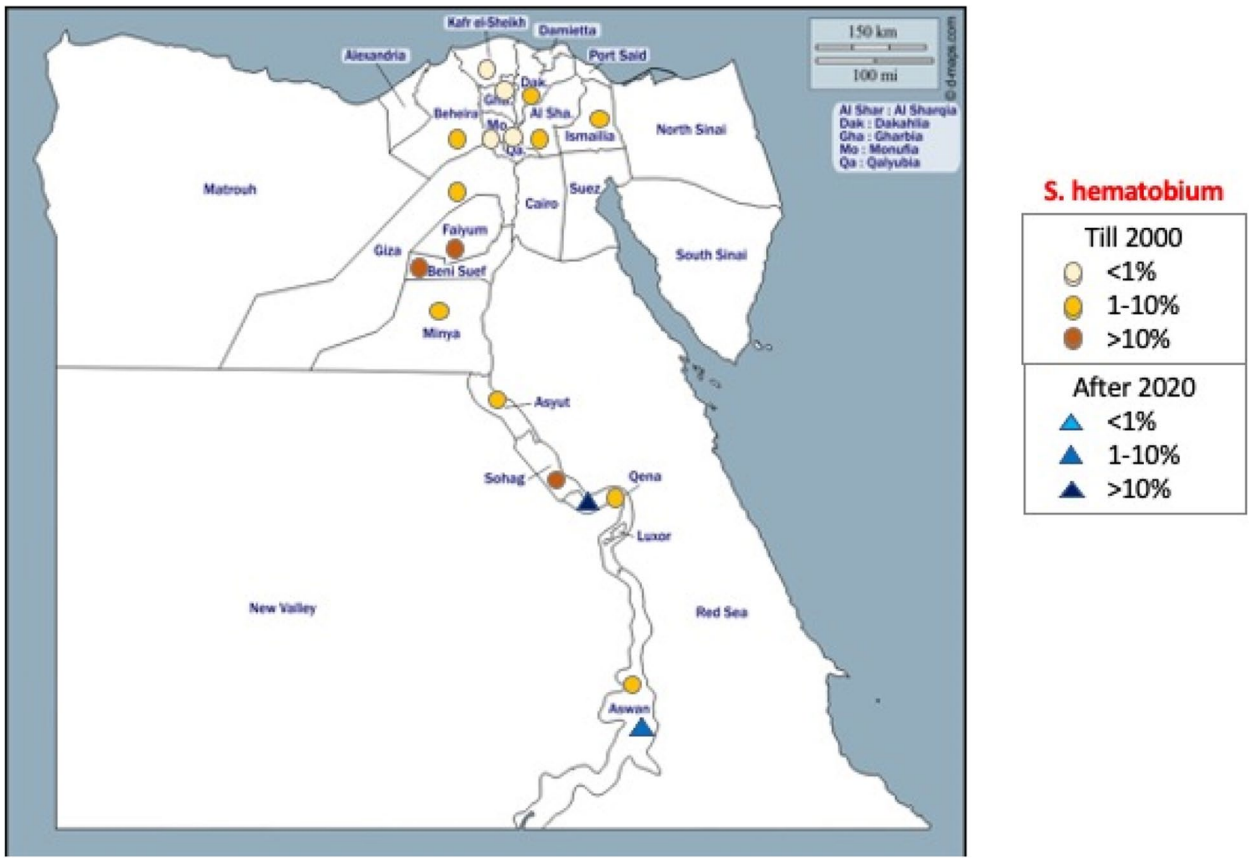

Fig. 2 Distribution of *S. haematobium* in Egypt [28]

National Schistosomiasis Control Program (NSCP) in 1997. The NSCP focused on mass PZQ treatment targeting specific groups with the highest transmission risk: school-aged children (6–8 years old). This age group serves as a reservoir for infection, so early intervention is crucial. Also, for communities with high prevalence (20% or more): targeting endemic areas allows for broader impact and interruption of transmission chains. In addition to Individuals diagnosed with schistosomiasis, Treating confirmed cases helps contain the spread and prevent further complications. This targeted approach ensured efficient resource allocation and maximized the impact of the program. While challenges remain, the NSCP's efforts have undoubtedly contributed to significant progress in tackling schistosomiasis in Egypt [19].

PZQ PZQ The NSCP was ended in 2002, with positive results. Following six rounds of regular yearly treatment, the prevalence of *schistosomiasis* dropped from 20 to 10% in 1999, then to 5% in 2000, reaching 3.5% in 2002 and 3% in 2003 [35]. For example, the disease prevalence in Beheira (one of Egypt's largest and most populous governorates) was lowered from 26 to 3.8% [36]. Even though it was evident that using PZQ as an M.D.A. for *Schistosomiasis* control in Egypt has been effective in terms of morbidity and prevalence, it has not been able to break the parasite's transmission cycle, even when repeated [37]. Furthermore, P.Z.Q., a key component of M.D.A., is ineffective against juvenile *schistosomes* and does not prevent reinfection [2]. Ross et al. [38] recently advised a yearly split dosage of 60 mg/kg PZQ plus six mg/kg artemether rather than a single oral dose of 40 mg/kg. The goal was to employ artemether to use PZQ against the adult and early stages of the parasite. Unfortunately, *Schistosomal* resistance to PZQ emerged early in Egypt, with recorded treatment failure after the first or second dosage of treatment [39].

Interruption of transmission strategy

This technique was initially implemented in 2003, focusing solely on afflicted areas and relying on annual monitoring surveys tailored to the prevalence rate to stop the spread. Villages with a prevalence of 3% or more were administered mass treatment with P.Z.Q., while villages with less than 3% were given selective chemotherapy. Targeted molluscicides, water delivery, and environmental sanitation were implemented [40]. In 2006, *S. mansoni*

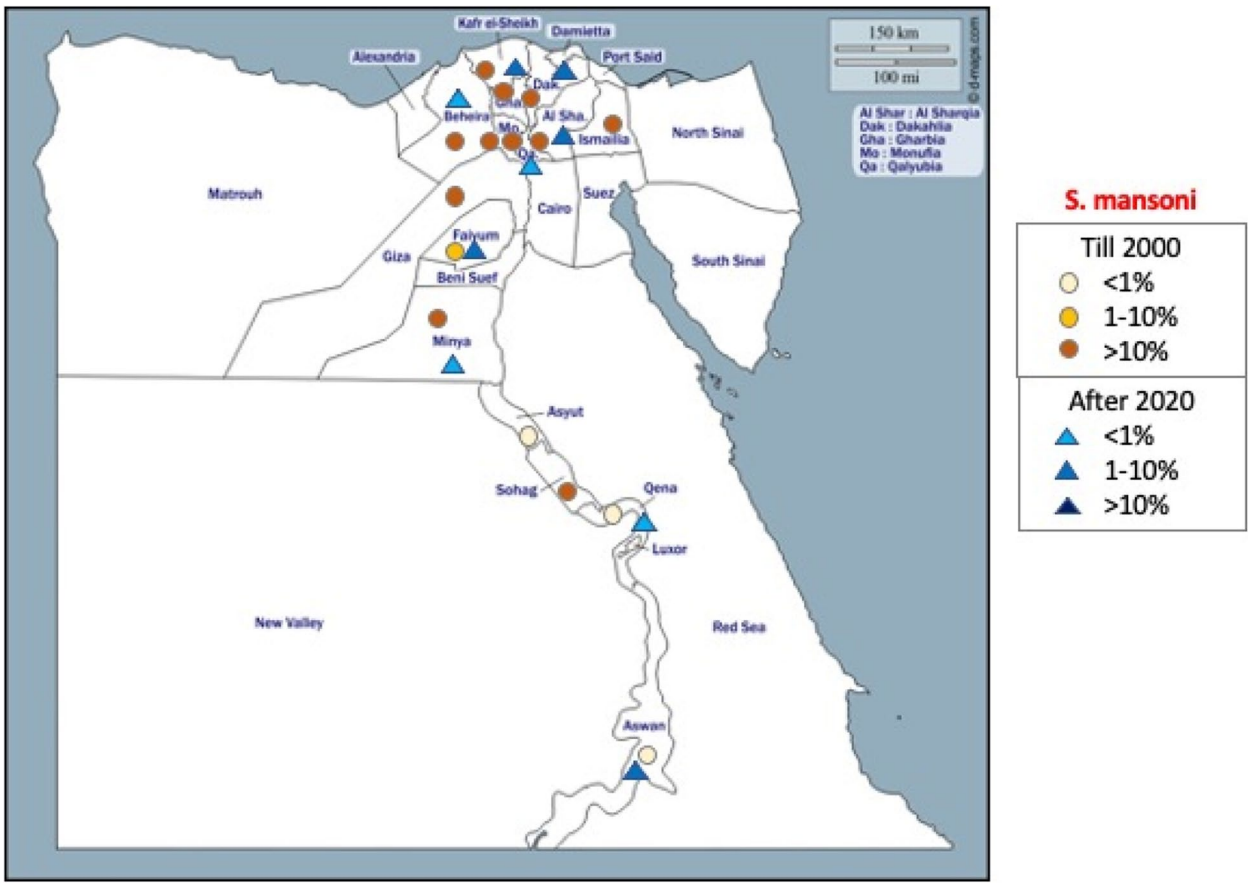

Fig. 3 Distribution of *S. mansoni* in Egypt [28]

and *S. haematobium* were found in 1.5% and 1.2% of the population [34, 36]. Despite the presence of "hot spots" transmission foci with a 10% incidence rate in 2006, the number of hot spots increased to 136 in 2010, then reduced to 88 in 2013. Most of these regions were located in Lower Egypt, with only five in Upper Egypt (Barakat, 2013). According to the Egyptian MOHP, only 20 villages across the country had a prevalence of infection of more than 3.5%, and no villages showed more than 10% [34].

During 2014–2015, the official plan was to focus on treating school children with PZQ PZQ when the prevalence of infection in a sample of the population is 2% and M.D.A. to the entire population aged 3 years of a hamlet or satellite village where the prevalence in a hundred of its people is 3% [34]. The longevity of these hotspot locations could be due to high levels of immature infection resulting from the enhanced transmission, necessitating a changed chemotherapeutic strategy, given that PZQ is ineffective in early infection [37, 41]. Another reason for the persistent hot spots after PZQ treatment could be the worms' diminished susceptibility to the medicine due to the drug's long-term use in the country [29]. PZQ susceptibility was reduced in some countries, including Egypt [39]. One of the important issues was the presence of many high-risk communities in Egypt, like the case of Kafr El-Sheikh Governorate, located in the northern section of the Nile Delta. In 2014, the prevalence rate was as high as 26.6%. Excess fisheries, a lack of latrines on fishers' boats in Lake Manzala, and vast rice farming were to blame [37]. Rice cultivation necessitates constant water contact during the hot summer months when snail shedding is high [40]. Also, Elmorshedy et al. [42] concluded that in high- and low-prevalence areas in the Nile Delta, Egypt, PZQ treatment resulted in a significant reduction in infection prevalence and intensity; however, the high-prevalence village returned after the second round. Despite this, transmission continues to be a significant issue in both settlements. In both high- and low-prevalence communities, data revealed a modest degree of knowledge and lack of population awareness regarding disease transmission and the role of human excreta in contaminating water. Compared to the low-prevalence village, the high-prevalence village had higher water contact activities [28].

Schistosomiasis in Egypt: progress, challenges, and the road ahead

Egypt has made significant strides in combating schistosomiasis, a debilitating parasitic disease. However, recent studies reveal pockets of persistence and emerging challenges demanding continued vigilance. Progress achieved: the MOHP deserves commendation for its dedicated efforts, and (b) studies like Ahmed et al.'s (2021) highlight that infection rates have dropped: 4.7% and 1.25% prevalence of *S. haematobium* and *S. mansoni*, respectively, in rural areas [28]. Despite progress, challenges remain such as (a) In some areas, schistosomiasis still exists. According to Elmorshedy et al. 2020, colonic schistosomiasis affected 12.4% of symptomatic rural residents in the Nile Delta [40, 42], (b) potential drug resistance to PZQ, the primary treatment, necessitates exploring alternative medication combinations or substitutes [41], and (c) high co-endemicity of viral hepatitis (B and C) poses additional challenges, requiring strategies to address their potential exacerbation after schistosomiasis eradication [43, 44]. For moving forward, sustained commitment and funding are crucial to maintain achievements and tackle remaining challenges. In addition to innovative approaches, including tackling social and environmental factors impacting transmission, are essential. However, continued research on drug resistance and alternative therapies is paramount., and addressing co-infections like viral hepatitis requires integrated healthcare strategies.

Conclusion

Egyptian governmental efforts and plans for screening the risky population are required to eliminate the persistent *schistosomiasis* transmission in the Nile Delta's rural areas. Consequently, a robust National program should be launched to draw an accurate map of the residual areas that reflect the actual extent of the spread of *schistosomiasis*. Accordingly, the necessary measures to permanently eliminate *schistosomiasis* are to be taken, in addition to follow-up and treat disease complications. Moreover, the Health Authorities should consider the snail intermediate host side by side with the actively infected patients as a source of infection. Community health awareness and media campaigns targeting students and young patients are needed to avoid the transmission of this water-borne disease. An integrated control strategy that combines preventive chemotherapy with additional complementing interventions is necessary to eliminate schistosomiasis in hotspots. Finally, Egypt can achieve its goal of schistosomiasis elimination by continuous health awareness, mass treatment of patients, and vaccine development can cut the *Schistosoma* life cycle and write a fitting end for this dramatic story in Egypt.

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M.E.K., M.E.: study design; R.E.: data collection and writing up of the first draft of the paper. All authors revised and approved the final version of the manuscript.

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Consent for publication
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