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Towards elimination of schistosomiasis after 5000 years of endemicity in Egypt

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ABSTRACT

Schistosomiasis is a snail-transmitted infectious disease caused by a long lasting infection with a blood fluke of the genus *Schistosoma*. *S. haematobium* and *S. mansoni* are the species endemic in Egypt. The country has been plagued and seriously suffered from schistosomiasis over the past 5000 years. Great strides had been done in controlling the disease since 1922. The history, epidemiology and the different control approaches were reviewed. Currently, Egypt is preparing towards schistosomiasis elimination by 2020. The new strategy depends on four main axes; large scale treatment in all areas of residual transmission by targeting entire populations with PZQ, intensified snail control, heath education and behavioral changes and expansion of the complementary public health interventions. While on the road towards elimination, we addressed here the important challenges, lessons and the key issues from the different control strategies to help the achievement of our goal. Notably, frangibility of the drug based control, emergence of resistance against PZQ, persistence of some hot spots areas, the need of further control efforts to the high risk individuals and community involvement in the control programs, reconsideration of diagnostic tests used in surveillance, and continous monitoring of the field to detect changes in the snail intermediate host. Importantly, the adaptation between the parasite and its intermediate snail host throughout water bodies in Egypt merits attention as *Schistosoma* infection can be introduced to the new reclaimed areas. This review may help supplying information for the policy makers to tailor control measures suitable to the local context that could help in the transfer from control to elimination.

1. Introduction

Schistosomiasis is one of 17 neglected tropical diseases (NTDs) listed by the World Health Organization (WHO). The disease is endemic at variable rates in 78 countries and is estimated to affect over 290 million individuals worldwide, the majority of them live on the Africa continent (Global burden of disease study, 2015; WHO, 2015). Concerning the burden of the disease, schistosomiasis ranks third after soil-transmitted helminthiasis and leishmaniasis and causes a global burden of 3.3 million disability-adjusted life years (DALYs) (Hotez et al., 2014). Being a disease of poverty, the incidence of the infection is mainly in poor communities with lack of clean water and sanitation (Bergquist and Whittaker, 2012). It is widely acknowledged that children at school age who are engaged in recreational swimming and individuals where occupational exposure to fresh water bodies occurs daily as those working in fisheries and rice farming are at high risk. Furthermore, bathing and laundry that is carried out mainly by women are among the activities leading to infection (Taman et al., 2014; Grimes et al., 2015).

Schistosomiasis is a snail-transmitted infectious disease caused by a long lasting infection with a blood fluke of the genus *Schistosoma*. The disease is manifested in two major forms; urogenital disease is caused by *S. haematobium* while the intestinal form is caused mainly *S. mansoni* and *S. japonicum*. *S. intercalatum*, *S. mekongi* and *S. guineensis* can also cause intestinal schistosomiasis but their distribution is geographically limited (Davis, 2009). *S. haematobium* and *S. mansoni* are the species endemic in Egypt.

Egypt has been plagued by schistosomiasis since the time of pharaohs and the disease has been a major health problem thousands of years ago. Since 1922 schistosomiasis control has been one of the important priorities for the Egyptian Ministry of Health. Strong upgrading of the activities were implemented in 1976 through regular control projects leading to a remarkable decline in both mortality and prevalence (WHO, 2007; World Bank, 2008).

Based on the successful achievement of the control programs, Egyptian Ministry of Health and Population (MoHP) is preparing for elimination of schistosomiasis by 2020 following the call of the World Health Assembly (WHA) Resolution 65.21 at 2012 (WHO, 2012; MoHP, 2017). The global schistosomiasis alliance (GSA) has been developed to

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meet this goal and acts as partnership with endemic countries to concentrate on health requirements, inequity and rural poverty (Savioli et al., 2017). Unfortunately, Egypt was not presented in the first conference of the Research Working Group of the Global Schistosomiasis Alliance (GSA) held in June 2016 in People's Republic of China. In this international meeting, there was a discussion about the current progress in schistosomiasis control, identification of the research gaps and the importance of applying other measures in addition to PZQ to make elimination a reality. The value to switch from the modified Kato technique for the intestinal type of the disease and the urine filtration for urogenital infection to more sensitive diagnostic approaches had been emphasized in areas of low level of infection. For hotspot areas, there is an urgent need to increase data collection and mapping together with other control measures and this must go side by side with encouragement of surveillances in areas with low level of infection. Due to the high heterogeneity of endemic areas for schistosomiasis and partly due to the different schistosome species involved, there was an agreement to better tailor controlling measures to the local situations to each endemic areas (Bergquist et al., 2017).

This article reviews the history and the epidemiology of schistosomiasis in Egypt and describes the different control strategies that had been implemented in the country. Moreover, reviewing the local achievement and the lessons addressed from these strategies and from other researches were undertaken. This may help supplying information for the policy makers to tailor control measures suitable to the local context that could help in the transfer from control to elimination.

2. Ancient roots of schistosomiasis in Egypt

Imported infected humans and baboons from Land of Punt to Thebas at Pharaonic times and their dispersal in Upper and Lower Egypt were blamed to be the cause of introduction of schistosomiasis in the country (Abou-El-Naga, 2013). Following the distribution of their intermediate host (IMH), *S. hematobium* became established in Upper and Lower Egypt while *S. mansoni* was established in Nile Delta (Lower Egypt) (Adamson, 1976).

The mysterious disease "â-a-â" that was referred to in many papyri of the ancient Egyptians was considered by many Egyptologist to be hematuria and dysuria (Ebbell, 1937). However, overt expression of schistosomiasis induced hematuria in the papyri was not clear. Ancient Egyptians believed that "â-a-â" was an evil 'influence' that was brought about by either a god (usually Zeth) or a dead person (Ziskind, 2009). On the other hand, remedies for hematuria including sedatives, antispasmodic, antimony based remedies and honey have been reported in different papyri suggesting the serious suffering from the disease (Taha and Waked, 2010).

There is no clear evidence of the presence of *S. mansoni* at the same ancient Egyptian time with *S. hematobium*. However, Abou-El-Naga (2013) suggested that both *Schistosoma* species were present during the same time in ancient Egypt where *S. hematobium* prevailed in Upper and Lower Egypt while *S. mansoni* was restricted to Lower Egypt only. This suggestion had been based on different facts. Mummies were better preserved in Upper Egypt due to the dry air in contrast to humid Lower Egypt where most of the mummies have perished. It is well known that perfect mummification was performed mainly in the high classes, while in low social classes which were highly exposed to the infection, an inadequate mummification was done. Later on, in the later dynasties, people in all classes were well mummified. *S. mansoni* infection may be overlooked due to its less dramatic symptomatology than *S. hematobium*. Some papyri focused on proctology and described bowel treatment most likely referring to treating *S. mansoni* (Jonckheere, 1944).

Ibn Battouta described the marshes of Lower Egypt in an old Arabic book of geography after he visited Egypt eight centuries ago. He reported that the male inhabitants of these districts used to pass blood with urine (Ibrahim, 1948).

Theodor Maximilian Bilharz was a German anatomist and helminthologist. In 1851, he was 25 year old, he came to Egypt and accepted a job in Cairo as an assistant to the director of the Egyptian Department of Hygiene. During the course of autopsies on patients with hematuria, he noted pathological changes in the mucous membranes of the ureters, bladder and intestines. In 1852 he discovered that the causative parasite was unknown worm-parasite and named it *Distomum haematobium*. In 1853, Bilharz published the description of pairs of adult schistosomes and two kinds of lateral – spined eggs without realizing the difference between both species (Tan and Ahana, 2007, Pai-Dhungat, 2015). The name Bilharzia has been widely used in many countries as well as in Egypt. In 1902, Sir Patrick Manson diagnosed intestinal schistosomiasis in the West Indies where notably lateral spine eggs alone were present and this species was named *S. mansoni* (Samboon, 1907).

In 1910, Ruffer discovered calcified *S. hematobium* eggs in the kidneys of two Egyptian mummies dating from the 20th dynasty (Ruffer, 1910; Cox, 2002). Radiological examination revealed calcified *Schistosoma* eggs and calcified bladders in several mummies (Contis and David, 1996; David, 1997). Later on, the antigen detected by immunodiagnostic tests identified cases of schistosomiasis back to 5000 years ago (Deelder et al., 1990). In 1915, the life cycle of *Schistosoma* was elucidated by Lieper who showed the existence of two separate intermediate hosts, *Bulinus* and *Biomphalaria* for *S. hematobium* and *S. mansoni* respectively (Leiper, 1915).

3. Epidemiology of schistosomiasis in Egypt

The first nation-wide survey that described the pattern of schistosomiasis throughout Egypt was conducted by Scott in 1937. He found that both *Schistosoma* species were highly prevalent in the Northern and Eastern parts of the Nile Delta (Lower Egypt) where 60% of people were infected with *S. mansoni* and 85% were infected by one or both species. Interestingly, the infection rate of *S. mansoni* in Southern part of the Delta was 6% probably due to scanty number of snail intermediate host (IMH). *S. mansoni* infection and its snail host were completely absent from the Nile Valley (Upper Egypt). The prevalence of *S. hematobium* in the Nile Valley was 60% where perennial irrigation was used while the infection rate reached less than 5% in areas with basin irrigation. Scott clearly documented the correlation of *S. hematobium* prevalence with the irrigation system in the country. (Scott, 1937; Barakat, 2013).

It is possible that the construction of Aswan High Dam in 1964 had changed the distribution of *Schistosoma* infection. The shift from basin to perennial irrigation had increased the prevalence of *S. hematobium* infection. Furthermore, the decrease Nile water velocity especially in the Delta, created a favorite habitat for breeding of *Biomphalaria alexandrina* (*B. alexandrina*) and *Bulinus truncatus*, the snail intermediate hosts of both intestinal and urinary schistosomiasis. Undisturbed populations of these snail hosts are present in the irrigation canals and drains throughout the year (Malek, 1975).

The IMH of *S. mansoni* that was restricted to Nile Delta is now being found in the Nile in Upper Egypt and reach the Aswan city and Lake Nasser. Consequently, *S. mansoni* was detected in some foci in Upper Egypt (Mallett and Aboul-Ela, 1979; Kloos and David, 2002; Abou-El-Naga, 2013). Furthermore, *S. mansoni* had replaced *S. hematobium* in the Nile Delta as its snail IMH prefers the slow flowing water as well as it has more capacity to adopt to the increase in the pollution and the low level of oxygen resulting from massive irrigation practice than the snail IMH *Bulinus truncatus* of *S. hematobium* (Kloos and David, 2002; Barakat, 2013).

In 2000, the Schistosomiasis research Project implemented by the Egyptian MoHP in collaboration with United States Agency for International Development (USAID) revealed that in Upper Egypt the prevalence of *S. hematobium* ranged from 4.8% to 13.7% while *S. mansoni* was rare, having the highest prevalence of 4.3% in Fayoum Governorate. Oppositely, in Lower Egypt the infection with *S. hematobium* was scarce and reached 1.8% only in Ismailia city and the