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Human Schistosomiasis Disease: Diagnosis, Management and Treatment according to WHO Guidelines

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ABSTRACT: Human schistosomiasis is a parasitic disease brought on by blood worms that infect the liver, colon, bladder, and urethra among other organs. With the use of Praziquantel, vaccinations, and gene therapy, this illness might be cured. One of the neglected tropical illnesses that has a major impact on people's health in Ethiopia is schistosomiasis. The sole medication used to treat human schistosomiasis in the nation is praziquantel. These parasites have two types of hosts throughout their life cycles: snails and mammals. Schistosomiasis symptoms can be acute or persistent. Fever and headache are two examples of acute schistosomiasis's clinical symptoms. Dysuria and hyperplasia are two signs of persistent infections. The five species that can infect people. *S. haematobium, S. japonicum*, and *S. mansoni* are the three strains that are most common. The Kato-Katz and PCR are two methods for schistosomiasis detection. The only medication that effectively treats this condition at the moment is praziquantel.

Keywords: *Schistosomiasis, Praziquantel*, *Schistosoma mansoni, S. japonicum*, PCR, Sporocysts.

INTRODUCTION

More than 230 million individuals in tropical and subtropical regions are afflicted with schistosomiasis, one of the neglected tropical diseases (NTDs). Concentrated in African nations are more than 90% of the cases. In endemic nations, schistosomiasis causes roughly 4.5 million DALYs (Disability-Adjusted Life Years). Six Schistosoma species are responsible for human schistosomiasis. Three species, *Schistosoma mansoni, Schistosoma haematobium,* and *Schistosoma japonicum*, account for 99% of human schistosomiasis. The first two are the most common and extensively dispersed, whilst *S. japonicum* is only found in China, Indonesia, and some regions of the Philippines. Schistosomiasis in humans is one of the most common parasite illnesses. The illness, which is present in 75–76 nations, is listed as the second parasitic disease after malaria. (Alemu *et al.,* 2018). Numerous developing nations in Africa, Asia, South America, and a number of Caribbean islands all have schistosomes. Nonendemic regions are equally susceptible to schistosomiasis. It can spread through immigration and water-based development initiatives.

Schistosomiasis can be managed using either treatment or prevention. Important measures to prevent schistosomiasis include eliminating snail hosts and enhancing sanitation. Schistosomiasis vaccines are not yet available. Vaccines will be crucial in the future in the fight against this illness. Potential vaccinations have been made available, such as *S. japonicum* insulin receptor and *Schistosoma mansoni* Chaptesin B1 (SmCB1) (rSjLD1). Currently, schistosomiasis is treated with the medication praziquantel. Furthermore, vaccines and snail control are two other ways to prevent this illness. Genetic engineering and additional medications might also be advantageous (Nelwan *et al.,* 2019).

The preferred medication for treating infections caused by any schistosoma species is praziquantel and is generally safe, well-absorbed, and efficient. For the treatment of human schistosomiasis, an oral dose of 40 mg/kg body weight is advised. Alternatively, this dose may be spread out over the course of a day (2 × 20 mg/kg doses given every 4 hours). The recommended dose of praziquantel for treating human schistosomiasis in children is 60 mg/kg. Drug typically paralyses the worm and harms the tegument within an hour of consumption. Praziquantel, however, has little to no impact on eggs and young worms. Praziquantel is frequently used to treat infected people, and its widespread use among schoolchildren raises questions regarding the drug's effectiveness in endemic areas. As a result, numerous nations reported that praziquantel had unsatisfactory treatment outcomes (Silva *et al.,* 2005; Teesdale *et al.,* 1976).

In Ethiopia, praziquantel is often used for both patient treatment and mass drug administration (MDA) among school-age children. There are few studies on praziquantel's effectiveness in the nation. After

administering the recommended dose of praziquantel, the cure rate (CR) was calculated as the conventional method for evaluating pharmacological efficacy. Egg reduction rate (ERR) has recently been suggested by WHO as a different method to evaluate the effectiveness of anthelminthic medications (Teesdale and Amin 1976; WHO, 2022).

WHO GUIDELINES

In order to guide action against NTDs from 2021 to 2030, WHO published a new road map in 2020. The road map aims to cease schistosome transmission among people in a number of countries by 2030 and end schistosomiasis as a public health concern. The accomplishment of these goals will make it simpler to move toward the Sustainable Development Goal, which is to "guarantee healthy lives and promote well-being for people at all ages". A key component of the WHO's plan to control and eradicate human schistosomiasis is prevention treatment for at-risk populations, greater access to drinking water and sanitation, hygiene education, environmental management, and snail control.

With the help of this advice, governments can make progress toward schistosomiasis transmission ceasing and controlling the disease's morbidity as a public health concern. The recommendations in this publication will assist countries in implementing national schistosomiasis control and elimination programmes and in efforts to verify the cessation of transmission (WHO, 2022).

The specific objectives are to provide guidance on:

- Cutoffs for prevalence, target age groups, and frequency of prophylactic chemotherapy for schistosomiasis.
- Setting up WASH and snail control programmes to help with schistosomiasis management and eradication.
- Performing diagnostic tests on people in low-transmission areas, as well as moving to those areas and determining whether schistosomiasis transmission has stopped.
- Tools for determining whether Schistosoma species have infected their snail hosts.
- Schistosomiasis diagnostic methods for identifying the disease in animal reservoirs of infection.

SCHISTOSOME LIFE CYCLE

The two hosts for the schistosome life cycle are mammals and snails. Reproduction can be asexual or sexual, depending on the type of host. For instance, freshwater snails have asexual reproduction. This occurs in the snail when the miracidia change into a sporocyst. When sporocysts replicate, they develop into cercariae. Mammalian hosts are where parasites grow, mature, mate, and lay their eggs. People, mice, and canines are examples of mammalian hosts (Nelwan *et al.,* 2019; Mouahid *et al.,* 2018; Van Dam *et al.,* 2004).

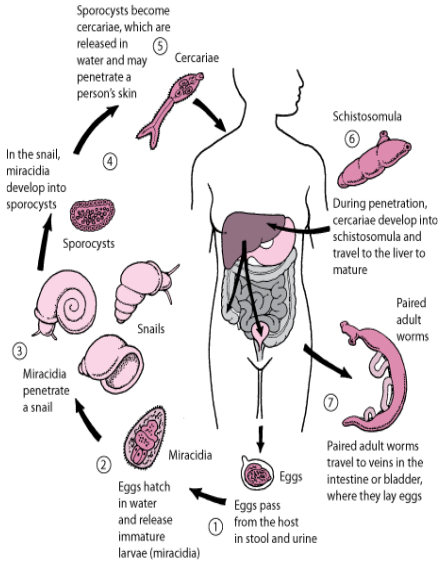

Fig. 1. Life cycle of schistosome.

SNAIL HOSTS

Mammalian hosts discharge worm eggs into the environment via their faeces or urine. In fresh water, these eggs develop into miracidia, which hatch and infect snails (Nelwan *et al.,* 2019; Geyer *et al.,* 2018). The Bulinus snails are impacted by *S. haematobium.* Oncomelania snails become infected when exposed to *S. japonicum.* Snails of the *Neutricula* genus are affected by the *S. mekongi* virus. Biomphalaria snails become ill with *S. mansoni*. The mother sporocyst gives birth to daughter sporocysts after the miracidium sheds the ciliated plates while it is inside (Nelwan *et al.,* 2019; Gurarie *et al.,* 2018).

Daughter sporocysts produce either cercaria *(cercariogenoussporocysts)* or further daughter sporocysts *(sporocystogenoussporocysts)*. Re-differentiation into new daughter sporocysts is another possibility for daughter sporocysts. Snails may expel hundreds of cercariae per day; *S haematobium* can expel 200, *S japonicum* can expel 15–160, and *S. mansoni* can expel 250–600 (Nelwan *et al.,* 2019; Mouahid *et al.,* 2018).

MAMMALIAN HOSTS

Cercariae shed their forked tails after entering human skin to become schistosomula. The schistosomula travel between body tissues via blood flow. From schistosomula, adult worms and schistosomes are formed. Males of these adult worms have ZZ chromosomal pairs, whereas females have ZW chromosome pairs (Nelwan *et al.,* 2019; Gurarie *et al.,* 2018). Adult worms can be found in many places in humans, depending on the species. *S. haematobium* can also be found in the rectal venules, in addition to the bladder and ureters. The small intestine is where *S. japonicum* is more usually found. The *S. mansoni* worm can reside in the small or large intestine and can travel between those two regions. By ingesting water contaminated with cercariae, human schistosomiasis can develop (Nelwan *et al.,* 2019; Tamirat *et al.,* 2021).

There are both acute (Katayama syndrome) and chronic clinical symptoms of schistosomiasis. About 14 to 84 days are needed for Katayama syndrome to develop. Fever, headache, myalgia, rash, and respiratory problems are only a few of the signs and symptoms of Katayama syndrome. Clinical signs of the long-term illness can result in dysuria and hematuria in *S. haematobium.* Additionally, it might harm the vaginal tract and make people more vulnerable to contracting other illnesses. Persistent infections may contribute to bladder cancer. Some of the clinical indications of the chronic condition include blood in the stool, constipation, and diarrhoea (Nelwan *et al.,* 2019; Tamirat *et al.,* 2021).

SCHISTOSOMIASIS TRANSMISSION

The construction of dams and irrigation systems could result in schistosomiasis outbreaks. Schistosomiasis can spread as a result of population movements, such as those from rural to urban regions. Schistosomiasis infection epidemics can also result from seasonal employee movements, and the disease can spread through refugees (Nelwan *et al.,* 2019; Mohamed *et al.,* 2018). Schistosomiasis can be stopped in its tracks with a clean water supply, good hygiene, vector control, and health education. There are five different methods for treating water: heating, filtration, chlorination, and ultraviolet light. Sadly, there are no trustworthy design recommendations for water treatment to prevent schistosomiasis. This shows that additional study is needed to identify an efficient water treatment method. Schistosomiasis can be managed with the aid of sanitation and water filtration. Schistosomiasis should be managed at the provincial, district, and municipal levels by governments in endemic areas. People from endemic nations should also be tested and treated for schistosomiasis in particular in nonendemic countries (Nelwan *et al.,* 2019; Braun *et al.,* 2018).

DIAGNOSIS

For the diagnosis and detection of schistosomes, various methods are employed. Although several immunological and molecular diagnostic methods have been created, some of them have been employed in Africa, where the usual method is the microscopy-based detection of eggs in urine or faeces (Gobert *et al.,* 2005; Lunde *et al.,* 1980; CDC, 2019). The most common method for schistosomiasis diagnosis is the microscopic detection of eggs in faeces and urine (*S. haematobium*) (*S. mansoni*). While *S. haematobium* infections are diagnosed by urine microscopy, followed by urine filtration*, S. mansoni* eggs are found in faeces using the Kato-Katz (KK) method (Dazo *et al.,* 1974; Utzinger *et al.,* 2007). These techniques, however, have limited application in low-socioeconomic endemic field settings since they are expensive, time-consuming, necessitate a considerable laboratory infrastructure, and demand specialized training. *S. haematobium* in a cross-sectional study conducted along Lake Malawi's southwest shoreline in Sub-Saharan Africa, eggs were found in the semen of fisherman, suggesting a significant lodgment of eggs in men's reproductive organs (CDC, 2019; Kayuni *et al.,* 2019). Eggs discovered in semen have an unclear origin, however they may have started in the bladder and travelled down the urethra with urine drops before being expelled with the semen. By using a light microscope, S. haematobium eggs are easily identifiable, and semen has been found to contain cell-free circulating schistosome DNA several weeks after receiving a single dose of PZQ (CDC, 2019; Kato-Hayashi *et. al.,* 2013). Enzyme-linked immunosorbent assays (ELISA) or lateral flow assays based on monoclonal antibodies can be used to identify active infections in addition to worm-derived circulation anodic antigens (CAAs) and circulating cathodic antigens (CCAs) in blood and urine (WHO, 2013). These screening techniques can identify an infection before the worms start to lay eggs. However, they do not distinguish between past, present, or future infections, which is particularly problematic in endemic areas where patients may continue to test positive for years after receiving treatment (CDC, 2019; WHO, 2011).

TREATMENT

Preventive chemotherapy (PC) employing MDA with PZQ is the mainstay of schistosomiasis treatment and control in endemic regions of Africa. PZQ has been shown to be a safe and effective oral treatment that is active against adult worms of all *Schistosoma* species, despite the fact that the precise nature of its method of action is yet unknown. It cannot be used for chemoprophylaxis and is ineffective against migrating schistosomula because of its short half-life. When people with Katayama syndrome show up, usually within two months of being exposed to cercariae, corticosteroids are helpful as an adjuvant in addition to PZQ to reduce immune responses and prevent acute disease. Two further drugs that have showed promise in the treatment of schistosomiasis are oxamniquine for *S. mansoni* and metrifonate for *S. haematobium*, but they are either no longer widely available or have been abandoned due to significant toxicity. The WHO recommends a combination PC with both PZQ and albendazole, especially for SAC and other high-risk groups, due to the prevalence of co-infections with Schistosoma species and soil-transmitted helminths (STH) in many endemic regions of Africa (Teesdale and Amin 1976; Lunde *et al.,* 1980).

PZQ is given to SAC between the ages of 5 and 15, who have the highest infection rates and are simpler to reach through school-based initiatives. PC frequently starts with an assessment of the disease's prevalence, which determines how frequently the area receives treatment. For instance, regions with a 50% or higher illness prevalence often only require one annual treatment, whereas regions with a 10% prevalence require treatment every three years. As of 2019, 57.1% (61.8 million) of SAC who require treatment have already gotten PZQ (Lunde *et al.,* 1980). Apart from praziquantel, there are different types of anti-schistosomal drugs that are shown in Table 1.

Table 1: Different types of anti-schistosomal drugs.

Anti-schistosomal drugs	Application
Metrifonate	Metrifonate is solely effective against *S. haematobium*, and it has been taken off the market due to economic and medical regulations.
Oltripaz	Oltripaz is a different anti-schistosomal medication that has been used in the past but has since been taken off the market and discontinued in order to treat schistosome infections since it causes photosensitivity and takes longer to cure the infections—roughly 2 months.
Oxamniquine	It is more effective against males than female when given orally. It works best when *S. mansoni* infection is present because it stops the development of chronic *S. mansoni* infection and posture. Only Brazil uses oxamniquine on a big basis.

CONCLUSIONS

This review revealed that Praziquantel is the only medication that can currently be used to treat schistosomiasis. There are three main species of worm i.e., *S. haematobium, S. japonicum,* and *S. mansoni*. that can infect humans. In the schistosomiasis life cycle, hosts include both snails and animals. Snails can reproduce asexually, while mammals can only reproduce sexually. Two further drugs that have showed promise in the treatment of schistosomiasis are oxamniquine for *S. mansoni* and metrifonate for S. haematobium, but they are either no longer widely available or have been abandoned due to significant toxicity.

FUTURE SCOPE

We can re-evaluate suggestions for the timing and frequency of drug-based treatments for disease control as we gain a better understanding of the timing and kinetics of illness formation as well as the true incidence of schistosoma in endemic locations. An efficient vaccination will be needed, together with the implementation of additional interventions, to improve on present controls for schistosomiasis and eventually lead to its extinction.

Conflict of Interest: None.

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