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Review Article

Review on Schistosomiasis: Epidemiology and Clinical Manifestation up to Date

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Abstract

Schistosomiasis is a parasite disease that affects both humans and animals and is brought on by the blood flukes of the genus Schistosoma. It is one of the world's most enduring neglected tropical diseases. Sub-Saharians make up more than 90% of them, and a significant portion of Ethiopians are afflicted and at risk. It spread across the entire nation and was correlated with the rapid development of water resources and population growth. The two species of freshwater snails, *Biomphalaria pfeifferi* and *Biomphalaria sudanica,* are responsible for the parasite's transmission in Ethiopia. Compared to the three primary schistosomes that infect people, *Schistosoma mansoni, Schistosoma haematobium, Schistosoma japonicum, Schistosoma intercalatum, and Schistosoma mekongi* have less of an epidemiological impact. Geographically, *S. haematobium and S. mansoni* are more common in Africa than other species. Epidemiological coverage is also influenced by seasonal distributions throughout the post-rainy season, as well as the cold and dry seasons. The organs and systems implicated in its pathogenic dissemination include the intestines, urogenital systems, the pulmonary system, the liver, spleen, and the brain. Ecological change and sociocultural influences are risk factors for water contamination. Regarding clinical symptoms, the penetration of cercariae into the dermis, cercarial dermatitis, acute schistosomiasis, and the chronic stage of infection are significant. Mammals and snails serve as the two hosts for the schistosome life cycle. It can be diagnosed through clinical exams and laboratory techniques. Praziquantel can be used to treat this condition, and it can be prevented by taking precautions during ecological shifts that may result in epidemics. Other measures to take include providing clean water, maintaining good hygiene, controlling mosquitoes, and spreading health awareness.

Keywords: Schistosomiasis, Epidemiology, Snails, Hosts, Parasites

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Introduction

In developing countries with inadequate medical infrastructure and unhygienic environmental conditions, neglected diseases are primarily documented in the underprivileged members of society. Schistosomiasis (bilharziasis and snail fever) is one of them and is a neglected helminthic zoonosis with a worldwide distribution (1,2). It is a parasitic disease that affects both humans and animals. It is brought on by the blood flukes of the genus Schistosoma. According to public health experts, schistosomiasis is the most significant water-related disease (3). Human schistosomiasis, one of the most pervasive parasite diseases in the world, is widespread, with 76 different countries having it (4,5).

This neglected tropical disease, a prevalent parasitic disease, affects more than 236 million people globally. Sub-Saharan Africa is home to more than 90% of these individuals (6). In Ethiopia, 5.01 million people had schistosomiasis, and 37.5 million more were at risk of contracting the parasitic disease. Schistosomes have multiplied across the entire nation as a result of the development of water resources and substantial population movements (7). In this altitude range, where 1000-2000 m is the best height category for Schistosoma mansoni transmission, are the majority of the country's endemic locations. According to estimates, 90% of the country may be affected by it (8).

Two types of freshwater snails, Biomphalaria pfeifferi and Biomphalaria sudanica, are responsible for the parasite's spread in Ethiopia (9). The three main schistosomes that infect individuals are S. mansoni, Schistosoma haematobium (S. haematobium), and Schistosoma japonicum, with Schistosoma intercalatum and Schistosoma mekongi having less of an epidemiological impact. Schistosomiasis' importance for public health has increased significantly in recent years as a result of an increase in migration and international travel (10).

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way, with the disease's symptoms and outward manifestations getting increasingly worse. Nearly 90% of individuals have a full neurological picture within two months (34). Granulomatous lesions, egg deposition accompanied by edema and broad mass effects, and vasculitis and thrombosis-type lesions that may be caused by eosinophil poisoning are the signs of cerebral schistosomiasis (33).

Associated Risk Factors

Ecological Transformation

The development of irrigation systems and other ecological changes brought about by humans, including dam construction, are currently the main risk factors for the resurgence of parasitic diseases. Many agro-industrial projects around the world are well-recognized to be closely related to parasitic disease epidemics (35).

Water Source and Toilet Usage

Schistosomiasis may spread to non-endemic regions as a result of environmental changes brought on by the development of water resources and migrations according to research. Numerous surface irrigation systems in Africa foster snail reproduction, promoting the spread of schistosomiasis. For example, *S. mansoni* was brought to Mauritania and Senegal with the building of the large Diama dam on the Senegal River (36) and the Koka dam in Ethiopia (37). The construction of the Nile and Aswan dams, respectively, has reportedly worsened the transmission of urogenital schistosomiasis in Sudan and Egypt.

The vast majority of studies offer evidence to back up the claim that initiatives to develop water resources will invariably have a detrimental effect on both human health and the environment. Furthermore, studies have shown that the development of irrigation programs greatly changed the environment, facilitating the spread of vector-borne diseases, including schistosomiasis (3).

Toilets, the major source of water, the distance to the open source of water, bathing and washing at open water sources, and fetching water were all significantly associated with the transmission of Schistosoma. Our results are consistent with observations from other studies (38,39). Human activity has a substantial impact on schistosomiasis transmission, which is fueled by human excreta containing Schistosoma eggs contaminating surface waters and their environs (40).

Socio-cultural Factors

Schistosomiasis is a disease brought on by poverty (41,42). Poverty frequently coexists with subsistence farming, low levels of education, filthy housing, restricted access to clean water, and inadequate sanitation in African nations south of the Sahara, all of which raise the risk of getting schistosomiasis (42).

The parasite that causes schistosomiasis prefers unfavourable socioeconomic conditions, and both the disease's occurrence and spread are associated with these conditions (43). Both humans and mollusks can become affected in freshwater bodies that have been contaminated by schistosome-infected people's faeces. The geographical distribution of the illness is influenced by the presence of the Biomphalaria mollusk, inadequate or nonexistent sanitation, human cultural practices, and the length of the parasite's life cycle (44,45).

Clinical Manifestations

Cercarial Dermatitis or Swimmer's Itch

An itchy maculo-papular rash that only affects areas submerged in water occurs a few hours following contact with freshwater contaminated with cercariae (46). The itching usually worsens after a few hours or days of exposure, and a rash with papules and vesicles develops frequently. Itching is occasionally the sole symptom patients have due to the disorder's brief duration; the illness goes away on its own in 1-3 weeks (47). The early stages of an infection make detection extremely difficult despite recent advancements in diagnostic procedures such as polymerase chain reaction (PCR) or antigen testing (33).

Dermatitis can be caused by a variety of illnesses, but its history strongly points to acute schistosomiasis. Initial results from serology may be negative, and there are no eggs in either the urine or the faeces. In samples obtained from the patients during brief travels, serology was the technique that most frequently resulted in a diagnosis, indicating a low parasite load (21).

Acute Schistosomiasis

Acute schistosomiasis, which primarily affects non-immune people (travelers), is a typically self-limiting sickness caused by a cercariae-induced hypersensitivity reaction. Thus, it is necessary to determine the history of exposure to freshwater (lakes or rivers) to aid in the diagnosis of acute schistosomiasis. To this end, it is vital to ask about activities such as bathing, crossing lakes or rivers, or even taking a shower (48). The most common symptoms include a high body temperature, asthenia, myalgia, urticaria, and an unproductive cough. The majority of patients experience a spontaneous recovery after 2-10 weeks despite the fact that some individuals experience more severe and extended illness, including weight loss, diarrhoea, generalized stomach discomfort, hepatomegaly, dyspnea, and extensive skin rash.

In around 50% of patients, eosinophilia is present (33). Since eosinophilia often appears late, 21 days after fever and up to 47 days (in the range of 25-119) after exposure (49), the diagnosis of acute schistosomiasis must be established by repeating laboratory testing in two to three weeks.

From a clinical standpoint, schistosomiasis has three stages. The acute stage begins 3-8 weeks after acute schistosomiasis, and the chronic stage occurs months or years later as a result of the development of granulomas in the tissues around the schistosome eggs (11). Cercarial dermatitis is the initial symptom, which appears 24 hours after the cercariae enter the dermis. Schistosomiasis prevalence rates are higher in poor rural populations, particularly those where fishing and farming are practiced. When conducting household chores such as washing clothes and getting water from hazardous sources, women and children are at risk of getting sick. Poor hygiene habits and recreational activities, including swimming and fishing, increase the risk of illness in children (12).

In Ethiopia, the distribution and transmission of Schistosoma species (*S. mansoni and S. haematobium*) are influenced by water temperature, the presence or lack of intermediate hosts such as snails, population movement, and the construction of water dams for irrigation and hydropower generation (13). The current recommended course of treatment for all clinical symptoms of the disease is praziquantel. This treatment is affordable and safe and reduces the risk of developing severe clinical symptoms and fatal instances of schistosomiasis (14,15).

The objectives of this paper are as follows:

- To highlight the public health importance of this disease up to date
- To provide awareness of schistosomiasis increasing with drastic changes in world climate
- To review epidemiological coverage of schistosomiasis and the complication of its clinical manifestations

Schistosomiasis: Epidemiology and Clinical Manifestations

Geographical Distribution

The Eastern Mediterranean region, which includes 16 nations, has the second-highest prevalence of the illness, with 42 countries in Africa having endemic cases as illustrated in Figure 1. Ten countries in the Americas, six in the Western Pacific, three in Southeast Asia, and Turkey, the sole affected nation in Europe, all have schistosomiasis as an endemic disease (Figure 1).

Several species are distributed, geographically. *S. haematobium* is more common in the Middle East and Africa, and *S. mansoni* is more widespread in the Caribbean, South America, and Africa. In addition, *S. japonicum* is more common in China, Indonesia, and the Philippines. The Global Atlas of Helminthes Infection of *S. haematobium* in Ethiopia recently provided a useful overview of the issue, limiting it to lowland regions such as the northeastern part of the country following the middle and lower Awash valley, the eastern part of the country around the lower Wabe Shebele valleys, and Kurmuk on the Ethio-Sudan border (16).

Seasonal Distribution

Many studies have also shown a connection between snail distribution, abundance, and rainfall. Rainfall has many effects on the state of the snail habitat. While they

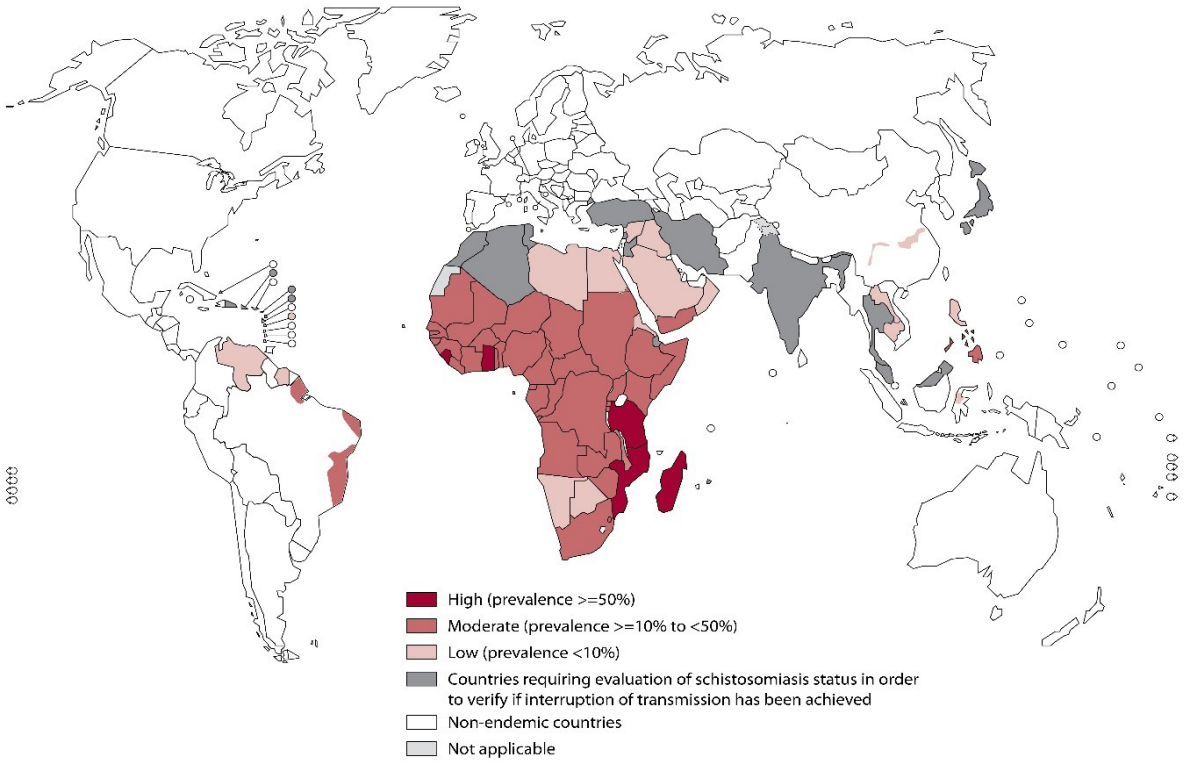

Figure 1. Worldwide geographical distribution of schistosomiasis (Permission copyright from WHO)

require water to exist, snail populations can decline when there is too much of it (17). Because snails are transported by heavy rainfall, rain helps the development of both temporary and permanent snail homes. Rainfall may also significantly lower population densities, as the quantity of snails may be hampered by flowing water speeds greater than 0.3 m/s (18). To better understand the intricate link between water velocity and vector snail density, we did not measure the water velocity, a crucial metric. Both *B. globosus* and *Bio. Pfeifferi* found adequate habitats in the pools (along the streams) and dams throughout the post-rainy, cold, and dry seasons (19,20).

Pathological Distribution

Intestinal Schistosomiasis

The quantity of parasite eggs in the colon and rectum, in particular, where they cause an inflammatory reaction and the growth of granulomas, ulcers, and fibrosis, as well as the frequency of exposure, influences the severity of the condition (21). Diarrhoea, asthenia, weight loss, anorexia, and chronic or occasional stomach pain are among the most common non-specific symptoms (22). In severe cases, anaemia can follow chronic colitis due to bleeding from colon and rectum ulcerations, which might mimic chronic colitis brought on by several aetiologies, including inflammatory bowel disease (23).

Furthermore, patients are more likely to develop colorectal polyps, particularly rectal polyps (24). However, all these polyps were discovered during colonoscopy and showed as large polyps rather than cecal thickening (25). Granulomatous inflammation is the most common intestinal lesion in chronic intestinal schistosomiasis and can degenerate into polyps and even induce dysplasia to manifest.

Urogenital Schistosomiasis

The location of *S. haematobium* worms at the terminal venules appears to make it easier for deposited eggs to get through to the bladder, pelvic organs, and in highly rare cases, the stomach organs. The ureter is the main organ that is most profoundly damaged by the deposited eggs. The developed lesions in the bladder and ureters result in sandy patches, ulcerations, and polypoid lesions, all of which can lead to cancer (26), haematuria, urinary obstructions, calcified bladder walls, and haematuria. Typical early warning indicators include dysuria, proteinuria, and hematuria (26,27). The onset of urological abnormalities brought on by *S. haematobium* infection is associated with the severity of the illness.

The most frequent urogram abnormalities were hydronephrosis, calcium urinary bladders, calcified ureters, and non-functioning kidneys. A hydronephrosis and multiple or bilateral abnormalities, including a calcified bladder, a malformed ureter, and non-functioning kidneys, were discovered as well (28). The degree of infection and the presence of urinary tract abnormalities are clearly correlated with considerably higher incidences of hydronephrosis, calcified urinary bladders, and deformed ureters in students who had more severe infections (excreted > 250 eggs/10 mL of urine). Recent studies have shown that symptoms such as pain during urination, urgency, loin pain, and fatigue by midday, as well as self-reported frothy urine, self-perceived haematuria, self-reported schistosomiasis in the previous year, detected haematuria, and the presence of *S. haematobium* eggs in urine, were major risk factors for urinary tract abnormalities detected by ultrasound (26,28).

Hepatosplenic Schistosomiasis

The symptoms of hepatosplenic schistosomiasis can range from being nonexistent to being life-threatening. Upper gastrointestinal bleeding caused by hepatosplenic schistosomiasis frequently leads to severe anaemia. In contrast to cirrhosis, hepatosplenic schistosomiasis often preserves hepatic function. Organomegaly, a test for illness severity, has revealed a correlation between the number of generated faecal eggs and the severity of the condition in numerous investigations (29,30).

Neuro Schistosomiasis

Neuro schistosomiasis, which affects fewer people, can influence any component of the central nervous system (CNS), but it is most common in the brain and spinal cord according to previous research (31). The prognosis depends on receiving treatment quickly (32). However, an African autopsy analysis demonstrated that 50% of the patients with urinary schistosomiasis had brain abnormalities. The migration of adult larvae to the CNS and the deposit of eggs are required to initiate the chronic granulomatous inflammatory response. The Batson vertebral epidural venous plexus, embolisation from portosystemic shunts, and even left heart cavities are possible routes for the eggs to enter the CNS. To establish themselves, adult worms may also go to regions close to the CNS. Characteristics in a species' clinical appearance may be explained by some morphological characteristics. As a result, the smaller eggs of *S. japonicum* are more likely to reach the CNS, whereas the larger eggs of other species, including those of *S. mansoni* and *S. haematobium*, are more frequently discovered in the lower spinal cord (33).

Pulmonary Schistosomiasis

The neurological side effects of this parasitosis can appear at any stage of the illness, although they tend to be more prevalent in the chronic stage. The reaction is more inflammatory when the symptoms are more severe. Usually beginning a few weeks after infection, neurological symptoms increase in an acute or subacute

Chronic Schistosomiasis

The accumulation of eggs released into the tissues causes granulomatous inflammation, which is the main contributing factor to chronic schistosomiasis because of the parasite's propensity to promote inflammation and fibrosis (50). The eggs migrate through the portal venous system and, before reaching the other tissues, embolize in the liver, spleen, or, if they make it to the systemic circulation, the lungs, brain, or spinal cord. Eggs that are stuck in tissues and secreting proteins and carbohydrates trigger the host's Th-2 immune response, causing an eosinophilic granulomatous reaction (11).

Life Cycle

Mammals and snails serve as the two hosts for the schistosome life cycle (Figure 2). Reproduction can be asexual or sexual depending on type of the host. For instance, freshwater snails have asexual reproduction. The transformation of the miracidia into a sporocyst triggers this in the snail. Sporocysts become cercariae as a result of their replication. In their mammalian hosts, where they mate and lay their eggs, parasites mature into maturity (51). Mammalian hosts include things such as humans, mice, and dogs.

Snails

Worm eggs are dispersed into the environment by mammalian hosts through their faeces or urine (51, 52). These eggs, known as miracidia, develop in fresh water and infect snails (51,53). Snails in the genus *Bulinus* contract *S. haematobium*. *Oncomelania* snails are affected by the *S. japonicum* infection. *Neutricula* snails are contaminated by *S. mekongi. S. mansoni* affects snails belonging to the *Biomphalaria* genus (54). After penetration, the miracidium removes the ciliated plates, matures into a mother sporocyst, and then generates more daughter sporocysts (sporocystogenous sporocysts). Additionally, daughter sporocysts can undergo redifferentiation to form additional daughter sporocysts (51). Snails can expel 100 cercariae every day; as shown in Figure 2, they can expel 200, 15-160, and 250-600 cercariae for *S. haematobium*, *S. japonicum*, and *S. mansoni* (55,56), respectively.

Mammalian Host

For *S. mansoni* and *S. haematobium*, people are their sole hosts. In about two weeks, cercariae penetrate the human's undamaged epidermis, change into schistosomula, enter the bloodstream, mature, pair up, and begin generating eggs (41). Over the course of their lifetime, adult schistosome worm pairs produce eggs, some of which are expelled through the urine (*S. mansoni*) or faeces (*S. haematobium*), the details of which are depicted in Figure 2.

Diagnosis of Schistosomiasis

Palpating the abdomen during a physical examination is a good way to check for hepatomegaly and/or splenomegaly. During the disease's acute stage, there may also be generalized lymphadenopathy and crackles on pulmonary auscultation (57). It is crucial to be aware of the occurrence of a condition known as cercarial dermatitis, which may be observed as an emerging issue and is a risk factor for non-endemic people who have *S. mansoni*. According to their clinical presentations, their symptoms are different (58).

Only laboratory tests, which are typically quick and simple to perform, can confirm the diagnosis of schistosomiasis since the clinical picture is highly broad and vague (59). Despite its drawbacks, microscopic examination of urine or stool continues to be the gold standard for schistosomiasis diagnosis. Lutz and Kato-Katz are the two primary methods for examining stools, with the latter having the most relevance for estimating the parasite burden by looking for eggs in the faeces after 45 days of infection.

The stool test, however, has low sensitivity, particularly in regions where *S. mansoni* infection is prevalent but worm load is low (59,60). Rectal biopsy or bladder testing may be helpful if the search for disease-causing eggs in the urine or faeces is negative and the suspected condition persists (60). Rectal biopsy, for instance, is crucial in the control of healing and has a greater positive response rate than parasitology of faeces (59). Enzyme-linked immunosorbent assay is another applicable tool that is similar to PCR.

Treatment, Prevention, and Control

Treatment: Efforts to eradicate schistosomiasis often focus on preventing infection with chemotherapy. Using praziquantel to treat schistosomiasis is economical. For all species and age groups, the World Health Organization (WHO) advises a single dose of 40 mg/kg (61). Praziquantel does not eradicate young worms that are already present in the body at the time of therapy, posing a limitation to this advice (62). For this reason, a second round of treatment is required after two to four weeks (63).

The quantity of intermediate snail hosts declines with snail management. Molluscicide is frequently used to achieve it. However, using this method will result in environmental damage. *Oncomelania hupensis* nails should be killed using linalool *Cinnamomum camphora* (L) extracts to prevent this according to previous data (64). The infection caused by *S. japonicum* may also be treated with linalool. Linalool-treated snails exhibited cell degeneration and gill damage. Linalool-treated snails' hepato-pancreas also shrunk and detached from the connective parenchyma. In comparison to snails without linalool, these snails exhibited substantially

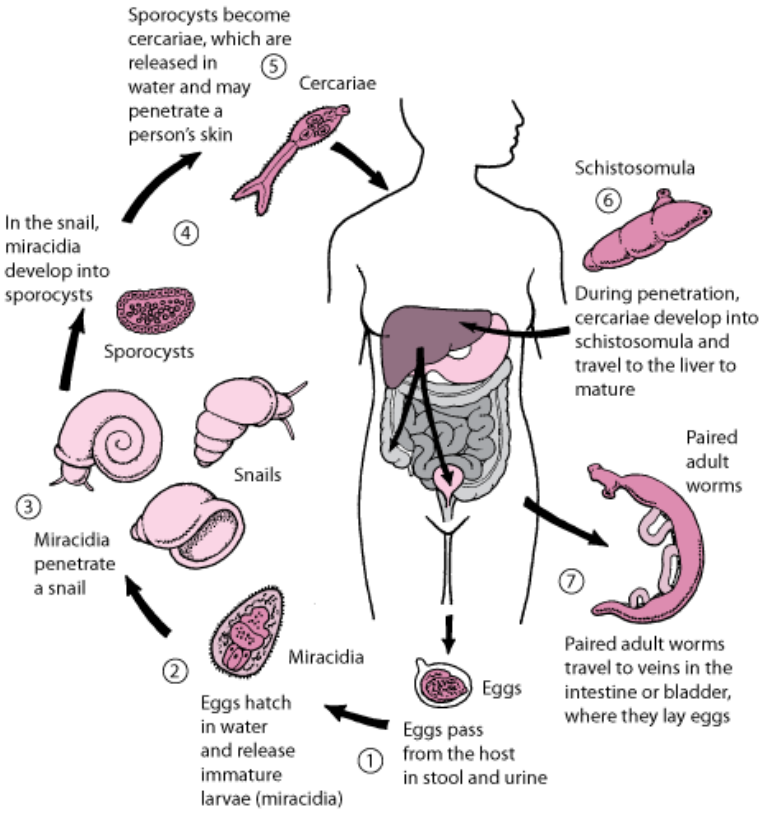

Figure 2. Schistosomiasis life cycle (Permission copyright from WHO)

smaller tubular lumen and fewer oval black granules. The findings suggested that gill injury and hepato-pancreas disease might be the primary killers (64), demonstrating that linalool extracts are effective in treating snail schistosomiasis and pose no environmental hazards.

Control: Extreme caution should be exercised while building dams, doing irrigation projects, relocating refugees, or moving people because these activities can spread the disease (63). Schistosomiasis can be stopped in its tracks by providing clean water, maintaining good hygiene, controlling vectors, and promoting good health (65,66). Furthermore, researchers (55) suggested that water filtration could lessen schistosomiasis. Storage, heating, chlorination, filtration, and UV radiation are the five available methods for treating water. There are no trustworthy design standards for water treatment to prevent schistosomiasis, which is unfortunate (55), implying that further investigation is needed to identify an efficient water treatment method.

Prevention: In endemic locations, effective public policies, interdisciplinary health and education programs, and community involvement in the entire disease control process are all important components of *S. mansoni* prevention. These tactics, which are detailed in the WHO document, include effective mass treatment, simple sanitation initiatives to lessen water contamination or contact with it, alterations to the living arrangements of the population at risk, and the creation of a potent vaccine (57,59).

Conclusion and Recommendations

In general, Schistosomiasis is a parasite causing neglected tropical disease which is detected following the water base. It causes high mortality and morbidity worldwide. After entering the human body, it can cause from mild itching to highly carcinogenic infections. Its epidemiology is host, environment, and causative agent dependent.

Thus, based on the above conclusions:

- Changes in the environment, marshy areas, irrigation projects, movements of populations, and migrations of employees play a role in the spread of schistosomiasis.
- By providing access to clean water, maintaining good hygiene, controlling vectors, and promoting good health, we can stop the spread of schistosomiasis.
- Finally, we would like to recommend that many studies should be performed on this disease to make it easily preventable, and the WHO should focus on its eradication.

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Authors' Contribution

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Competing Interests

There is no conflict of interests.

Ethical Approval

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