

## Review Article

# Update on *Schistosomiasis mansoni*: Epidemiology, Pathogenesis, Diagnosis, Treatment and Prevention

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**Abstract**

This study aims to present an update on *schistosomiasis mansoni*. *Schistosomiasis* is a parasitic disease caused by trematode flatworms of the genus *Schistosoma*. *S. mansoni* is the only species of importance in the American continent. This disease is considered a serious public health problem in some countries. It is found in 72 countries and is endemic in at least 52 of them. Its pathogenesis depends on the parasite-host interaction and can affect different organs and systems, such as lungs, liver and urinary tract. The diagnosis includes detailed history, physical examination and laboratory tests, with the gold standard being the microscopic analysis of stool or urine. Currently, praziquantel has been widely used in the treatment of *schistosomiasis*. Moreover, the implementation of socio-educational intervention measures is essential to minimize the impact of this endemic disease.

**INTRODUCTION**

*Schistosomiasis*, also known as bilharzia or snail fever, is a parasitic disease caused by trematode flatworms of the genus *Schistosoma* [1-3]. The first records of this disease were made in the basins of the rivers Nile in Africa and the Yangtze, in Asia. From these points of origin, it disseminated to other continents, following the migratory flows [2]. Currently, *schistosomiasis* is found in 72 countries in all continents and it is an endemic disease in at least 52 of them [1].

Several species of *Schistosoma* can cause diseases in humans, the main ones being *S. mansoni*, found in Latin America, Africa and the Middle East, *S. japonicum*, found in East Asia, *S. haematobium*, found in Africa and that causes hematuria and granulomatous disease of the bladder, resulting in chronic obstructive uropathy, *S. intercalatum*, typical in countries of Central Africa and *S. mekongi*, common in the valley of the Mekong river in Laos and Cambodia. Therefore, *S. mansoni* is the only species of importance in the American continent [1,3,4].

The World Health Organization (WHO) includes *schistosomiasis* as a neglected tropical disease. The disease is believed to affect approximately 200 million individuals in many countries and kills more than 100,000 people a year, with

most cases occurring in Africa, the Eastern Mediterranean and the Americas. Furthermore, the disease is considered a risk for 650 million people living in endemic areas [1,4,5]. In Brazil, it is estimated that six million individuals are infected, mainly in the states of Minas Gerais, Bahia, Sergipe, Alagoas, Pernambuco and Paraíba, in addition to 1.5 million people living in areas at risk of contracting the disease [2,4].

In this sense, *schistosomiasis* is considered a major public health problem in some countries [6]. The main factors that favor disease transmission in endemic areas are poor socioeconomic conditions, which result in the use of contaminated natural water for agriculture, domestic use and leisure, difficulties in access to health services, migratory movements and inadequate water and sewage treatment. This close association with poverty and low economic development justifies the concept of some authors to consider *schistosomiasis* as an important socioeconomic indicator [6,7].

Thus, this study aims to present, through a brief literature review, an update on the clinical picture, diagnosis, control and management of *schistosomiasis mansoni*.

**PATHOGENESIS**

The transmission of *schistosomiasis* to humans occurs when

they come into contact with contaminated water [8,9]. The cercariae, the larval form of the parasite, swims freely in fresh water and penetrates the human skin with the aid of proteolytic enzymes [4,8].

Inside the human body, after invading intact skin cercariae transform into schistosomula, which enter the vasculature of the host, the larvae migrate to peripheral vessels, lung and liver, mature and mate in liver vessels and form adult worms, living in the venous system, where the females lay their eggs [8,9]. These eggs produce proteases, which induce inflammatory reactions necessary for their passive transfer through the walls of the intestine and the bladder, being eliminated in stool and urine [4]. The eggs that are trapped in the tissues cause an immune reaction, with the formation of granuloma and fibrosis around them, with consequent damage to the organs [9].

The infection of fresh waters mollusks by eggs eliminated in human feces complete the life cycle of the parasite [4]. These freshwater mollusks are the *Biomphalaria*, especially the species *Biomphalaria tenagophila*, *Biomphalaria glabrata* and *Biomphalaria straminea*, known as planorbids and popularly as snails [10].

## NATURAL HISTORY OF THE DISEASE

After cercarial penetration, local urticarial reaction can occur at the site, which only occurs after the first exposure, typically in a few hours and may persist for up to one week [11,12].

The acute form of the disease (Katayama syndrome) is characterized by a hypersensitivity reaction, which typically occurs from one to four weeks after infection and can be triggered by the laying of eggs in the tissues or by schistosome migration or maturation. The symptoms of this phase are fever, headache, fatigue, abdominal pain and nonproductive cough, among others [11,12].

Chronic *schistosomiasis* develops when the eggs trapped in the host's tissues secrete enzymes, triggering inflammatory and granulomatous reactions. In this case, urinary, intestinal or hepatosplenic *schistosomiasis* can occur, as well as neuro *schistosomiasis* [11-13].

In the intestinal or hepatosplenic form, which is caused by the laying of eggs on the walls and mesentery of the rectum and large intestine, as well as in the liver, there can be abdominal pain, anorexia and diarrhea. Finally, in neuro *schistosomiasis*, which occurs due to abnormal migration of adult schistosomes and the laying of eggs in the brain or spinal cord, there may be focal or generalized seizures, nystagmus, headache, backache and muscle weakness [12,13].

Adult schistosomes can live for years in the human host, with survival of approximately three to ten years having been reported [11].

## CLINICAL DIAGNOSIS

In non-endemic areas, the diagnosis of *schistosomiasis* might not be recalled [14]. Therefore, a detailed history, including geographical history (patient origin and recent travels) and contact with rivers, lakes and streams is a key element of the investigation [14,15].

On physical examination, one should perform abdominal palpation, searching for hepatomegaly and/or splenomegaly. There may also be crackles on pulmonary auscultation during the acute phase of the disease, as well as generalized lymphadenopathy [15].

It's important to note the existence of an entity known as cercarial dermatitis that may be considered an emerging problem and in *schistosomiasis mansoni* is a risk factor for non-endemic people. Its symptoms include pricking sensation and pruritus associated with rash that may begin within one hour, to as long as five days following exposure. The rash is most common on the legs and feet and may be macular, urticarial or manifest as diffuse erythema with progression to papules and vesicles [16].

Cercarial dermatitis is also known as "swimmer's itch" and is caused by the cercariae of certain species of schistosomes whose normal hosts are birds and mammals other than humans. These cercariae attempt to, and, sometimes enter human skin, but do not mature into adults in the human body. One species of schistosome often implicated in cases of cercarial dermatitis is *Austrobilharzia variglandis*, whose normal hosts are ducks. The snail, *Nassariusobsoletus*, is the intermediate host for this species and can be found at marine beaches in temperate climates. Cercarial dermatitis should not be confused with sea bather's eruption, which is caused by the larval stage of cnidarians (e.g., jellyfish). The areas of skin affected by sea bather's eruption are generally under the garments worn by bathers and swimmers where the organisms are trapped after the person leaves the water. Cercarial dermatitis occurs on the exposed skin outside close-fitting garments [17].

Because the clinical picture of *schistosomiasis* is a broad and nonspecific one, diagnosis can only be confirmed by laboratory tests, which are usually fast and easily performed [14].

## LABORATORY DIAGNOSIS

In spite of its limitations, the microscopic analysis of stool or urine remains the gold standard for *schistosomiasis* diagnosis [18,19]. The two main techniques for stool examination are the Lutz and Kato-Katz, the latter with great applicability in determining the parasite load by detecting the presence of eggs in the faeces, which occurs after the 45th day of infection. However, the stool test has low sensitivity, especially in areas dominated by *S. mansoni* infection with low worm burden [14,15].

Where the search eggs in the faeces or urine is negative and the suspected disease persists, rectal biopsy or bladder may be useful [15]. Rectal biopsy, for example, has a higher positive than the parasitology of faeces, being important in the healing control [14,19].

In some situations, they make immunological tests necessary, especially in the chronic phase of *schistosomiasis*. The main techniques are the intradermal reaction, the complement fixation reaction, the indirect immunofluorescence and the Enzyme linked immunosorbent assay (ELISA) and ELISA capture. The positivity of the immunological tests does not necessarily indicate active infection with *S. mansoni*, for circulating antibodies remain after cure of the disease. Thus, these tests are not useful for proving the efficacy of drug treatment [14,19]. Some studies suggest that

the ELISA-IgM is in a potentially useful method for diagnosis of *schistosomiasis* in individuals with low parasite load [20].

The detection of *Schistosoma* circulating antigens in serum, urine and saliva host is becoming a promising tool for the diagnosis of active infection. The two described antigens are associated with intestinal parasite: the circulating anodic antigen (CAA) and the circulating cathodic antigen (CCA). Serum levels of these antigens are related to the parasitic load and intensity of infection and decrease rapidly after drug treatment, and may be useful in assessing the therapeutic response and to determine the cure [19].

The development of ELISA based on the use of monoclonal antibodies specific for CAA some portions became possible to detect these antigens in a sensitive and highly specific. The CAA-ELISA determines CAA levels in serum for all kinds of human *Schistosoma* with virtually 100% specificity, but it loses sensitivity to diagnose mild infections [19].

Due to the disadvantages presented by the ELISA method, a lateral flow assay was developed for the CCA detection in urine. The format of this laboratory test was developed at a rapid test Point-of-Care (POC-CCA) highly available in the world, but not recommended by WHO. Overall this test has been shown to be sufficiently sensitive and specific, being recommended by some studies as more sensitive in detecting infection than stool examination of Kato-Katz, especially in areas of low endemicity [19].

In addition to this, other non-specific tests may help in the diagnosis, such as complete blood count, which shows eosinophilia in over 80% of patients; coagulation profile, which can show high prothrombin time in chronic and advanced cases; urea, electrolytes and liver function tests [14,15].

## COMPLICATIONS

There are several possible disease complications, which vary according to its form. Urinary *schistosomiasis*, for instance, may be associated with proteinuria or nephrotic syndrome, fibrosis or calcification of the bladder or ureters distally, renal colic, hydronephrosis and kidney failure [8,11].

Ulceration, microscopic bleeding and colonic or rectal stenosis can occur in the intestinal disease. Splenic disease is associated with the development of esophageal varices, portal hypertension, splenomegaly, glomerulonephritis and pulmonary hypertension [11,12]. Growth retardation, anemia, as well as memory and cognitive impairment can occur in children [13].

## TREATMENT

The treatment of *schistosomiasis mansoni* aims at reducing egg production by decreasing the parasite load, reducing morbidity and mortality, even without complete parasite elimination [21]. The importance of treatment consists in reversing the chronic or early acute disease, preventing complications associated with chronic infection, preventing neuro *schistosomiasis* and also minimizing the production and laying of eggs as a form of primary prevention [14,18,21]. The anthelmintic oxmniquine was used for 30 years to treat Brazilian patients with *schistosomiasis*, but were registered several cases of parasitic infections resistant

to treatment. This drug has reduced effectiveness, being active only in infections caused exclusively by *S. mansoni*, single species in Brazil. Thus, currently, *schistosomiasis* control is performed mainly by preventive chemotherapy with praziquantel, which exhibits pharmacological activity much higher than oxamniquine [14,22].

Praziquantel is derived from the isoquinoline-pyrazine nucleus and has a broad anthelmintic spectrum, by changing the structure of the adult worm tegument, increasing membrane permeability to cations, especially calcium, which accumulates in the cytosol, leading to muscle contractions and consequently spastic paralysis. The damage to the helminth membrane also induces an immune host response to parasite antigens [22-24]. Its schistosomicide action occurs within 15 minutes after administration and adverse effects occur in approximately one-third of patients. These effects are usually mild, lasting 24 to 48 hours and include nausea, dizziness, headache, vomiting, abdominal pain, diarrhea, rash, palpitation, drowsiness, hyporeflexia, hypoacusis, visual disturbance and tremors [14,21,24].

Cure rates for *schistosomiasis mansoni* with the use of praziquantel ranges from 60% to 90%, being highly effective against infection by several species of trematodes and cestodes [14,25,26]. Paziquantel is excreted in breast milk, it is considered category B for pregnant women and a higher incidence of prematurity and low birth weight has been observed in infants born to mothers infected with *S. haematobium*. Moreover, it is contraindicated in severe liver, kidney and heart failure, as well as in the decompensated hepatointestinal form of *schistosomiasis mansoni* [14,21].

Oxamniquine is derived from tetrahydroquinoline; it has a lower cost compared to praziquantel and is active in the intestinal and hepatosplenic forms of infections caused exclusively by *S. mansoni* [14,21,27]. It is known that after the drug administration, oviposition cease by adult worms and the eggs are taken through the portal circulation to the liver, where they are involved in the inflammatory process and phagocytosed. The cure rate is similar to that of praziquantel and the most common effects are dizziness, drowsiness, headache, neuropsychiatric manifestations, fever, systemic arterial hypertension, leukopenia and transient lymphopenia [14,18,22]. It is contraindicated in pregnant women, infants, children under two years of age, patients with decompensated kidney, liver and heart failure and individuals with epilepsy [14,21,27].

Patients in the acute phase, with cercarial dermatitis, should be treated with symptomatic drugs for pruritus, with local antihistamines and topical corticosteroids, associated with specific anthelmintic drugs [6,28]. Acute *schistosomiasis* syndrome should be controlled by reducing inflammation with corticosteroids and praziquantel administration should be started only after the acute symptoms are resolved [29,30].

In patients with chronic disease, praziquantel should be started and its use is more effective from the fourth to sixth weeks after exposure, when the infection is well established and the worms are fully matured [21,31,32]. Specific conducts and surgical interventions can be adopted according to their

intestinal, hepatointestinal and hepatosplenic forms [14,33]. Monitoring of clinical manifestations, eosinophil count and microscopic analysis of stool are essential for treatment follow-up. In areas with high parasite load, imaging studies are essential to determine disease progression [13,34].

## PREVENTION

*Schistosomiasis mansoni* prevention is related to multidisciplinary health and education strategies, as well as adequate public policies in endemic areas, with the participation of the population in the entire disease control process. These strategies are present in a document prepared by the World Health Organization, published in 1993, and include effective mass treatment, basic sanitation programs to reduce water contamination or contact with the latter, changes in the living conditions of the population at risk and development of an effective vaccine [14,35-37].

Therefore, the implementation of socio-educational intervention measures is essential to minimize the impact of this endemic disease, which is difficult to control by health care services. After all, the dissemination of intermediate hosts, the precarious condition of health education and basic sanitation, as well as the disease chronicity have facilitated the dissemination and progression of the disease in its more severe forms.

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