CHAPTER 2

SCHISTOSOMIASIS MANSONI IN THE STATE OF MARANHÃO, BRAZIL: AN INTEGRATIVE MINI-REVIEW

Submission date: 03/09/2024 *Acceptance date: 01/10/2024*

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ABSTRACT: Schistosomiasis is a chronic parasitic disease characterized by its significant prevalence, the severity of its clinical forms, and its progression, making it a major public health issue in the country.

The etiological agent is *Schistosoma mansoni*, with snails of the genus *Biomphalaria* serving as intermediate hosts. The endemic disease affects nearly 240 million people worldwide; however, 700 million people live in endemic areas. Currently, schistosomiasis is reported in Brazil across 19 federative units, distributed throughout all regions of the country, making it the largest endemic area in the Americas. In the state of Maranhão, schistosomiasis has been known since 1920. According to a 2011 epidemiological situation report, the disease was considered endemic in 20 municipalities and focal in 29 of the 217 existing municipalities. The species *S. mansoni* is the only one described in Brazil. The lack of sufficient financial investment and trained human resources severely limits the effectiveness of programs in addressing the population's demands for a long-term solution. Consequently, what we see are shallow achievements, never leading to a definitive result. As a disease linked to underdevelopment, to achieve the elimination of schistosomiasis and other infectious and parasitic diseases, governments will need to promote significant improvements in the socioeconomic conditions of the population, along with a safe water supply and sanitation improvements in urban centers and rural areas.
KEYWORDS: Schistosomiasis, Public Health Endemic Disease

GENERAL ASPECTS OF THE PARASITIC DISEASE

Schistosomiasis is a chronic parasitic disease whose magnitude of prevalence, severity of clinical forms, and evolution characterize it as a significant public health problem in the country. Commonly referred to as Bilharzia, Snail fever, and Katayama fever, this parasitosis is part of an important group known as Neglected Tropical Diseases (BRAZIL, 2017; WHO, 2018).

Initially, schistosomiasis is a predominantly rural disease, but it has become urbanized with the extensive migration from rural areas to cities. This process often occurs in an unorganized manner, leading to the formation of peripheral urban conglomerates with no planning. In these areas, the state of basic sanitation, coupled with low levels of education and economic status of the population, creates favorable environmental conditions for the establishment of infectious-parasitic diseases, including schistosomiasis. Thus, it is considered a disease associated with poverty and underdevelopment. People become infected when they come into contact with water infested with the parasite's larval forms. These occurrences are generally linked to labor or leisure activities in rural areas, such as washing clothes, bathing, and fishing, as well as contact with water contaminated by domestic sewage in peripheral urban areas (COLLEY et al., 2014).

Transmission of schistosomiasis occurs through the complex life cycle of the worm, which requires two hosts (an intermediate and a definitive host) as well as specific environmental conditions for infection to occur.

As a strategy for controlling its transmission, various prophylactic measures and treatment methods are required, such as mollusk control, treatment of infected individuals with medication, provision of potable water, adequate sanitation, and health education for exposed populations (WHO, 2018).

EPIDEMIOLOGY OF SCHISTOSOMIASIS

Schistosomiasis is a tropical disease. Endemicity affects nearly 240 million people worldwide, yet 700 million live in endemic areas. Its transmission has been recorded in 78 countries, primarily in Africa and the Eastern Mediterranean, affecting regions such as the Nile Delta and countries like Egypt and Sudan. Estimates show that at least 219.9 million people required preventive treatment for schistosomiasis in 2016, of which 89 million were reported as having been treated. In 2017, 98.7 million people received preventive treatment in 52 countries, where moderate to high transmission is reported (WHO, 2018-A; WHO, 2018-B).

The first recorded case of schistosomiasis in Brazil dates back to 1908, as documented by Pirajá da Silva (BRAZIL, 2014; NEVES, 2016). Currently, schistosomiasis is reported in 19 Federative Units distributed across all regions of the country, making it the largest endemic area in the Americas. However, almost all cases are concentrated in the Northeast and Southeast regions (Figure 2). The occurrence is directly related to the presence of transmitting mollusks. In 2015, the country recorded 459 deaths due to schistosomiasis, with the Northeast and Southeast regions accounting for the majority, with 300 and 147 deaths, respectively.

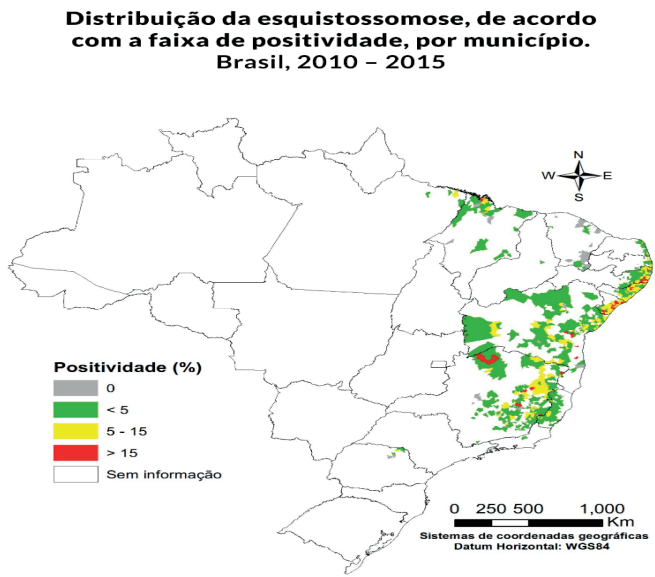

Figure 1 – Geographic distribution of schistosomiasis, according to the range of positivity, by municipality. Brazil, 2010-2015

Source: Secretaria de Vigilância em Saúde/MS

In the state of Maranhão, schistosomiasis has been known since 1920 (ALVIM, 1980, apud LIRA, 2017). According to the 2011 epidemiological situation report, the disease was considered endemic in 20 municipalities and focal in 29 of the 217 existing municipalities. The oldest and highest prevalence foci are found in the North Coast Zones and Baixada Maranhense. In 2010, the state's prevalence was 5.27% among 69,005 examined individuals. Between 2005 and 2010, there was an average of six hospitalizations and eight deaths per year, with a reduction in the mortality rate per 100,000 inhabitants from 0.20 in 2005 to 0.02 in 2010 (BRAZIL, 2011).

In 2007, 5,363 cases of schistosomiasis were reported in the endemic area of the state, a number that gradually decreased to 920 cases by 2016. For the non-endemic area, three cases were recorded in 2007, rising to 79 cases in 2010, and gradually decreasing to nine cases in 2016 (BRAZIL, 2018).

ETIOLOGICAL AGENT OF MANSONIC SCHISTOSOMIASIS

The causative agents of schistosomiasis are macroscopically visible schistosomes, with a cylindrical, whitish-gray body approximately 1 cm (male) to 1.5 cm (female) in length. Taxonomically, they belong to the phylum Platyhelminthes and the class Trematoda (GRYSEELS, 2012). The genus *Schistosoma* (schisto = fissure; soma = body) comprises dioecious individuals (separate sexes) with different developmental stages (adult worms, eggs, miracidia, sporocysts, cercariae, and schistosomules). In the adult stage, the male (which is smaller) houses the female in a kind of fissure in his body, known as the gynecophoral canal (SOUZA et al., 2011; BRAZIL, 2017). This groove is actually formed by the lateral edges of the male, which fold ventrally.

There are about 16 species within the genus, but only five of them can infect humans, divided into two major groups: parasites causing hepatic and intestinal diseases (*S. mansoni, S. japonicum, S. mekongi, S. intercalatum*) and parasites causing renal and bladder diseases (*S. haematobium*) (JAKA et al., 2014).

The species *S. mansoni* is the only one described in Brazil. The initial designation was given by Sambon in 1907, although Pirajá da Silva was also observing the species around the same time independently. This author confirmed that the *Schistosoma* producing eggs with lateral spines lived in the mesenteric veins and was a species distinct from those previously described. However, the species name was actually attributed to the first author (NEVES, 2016).

It is believed that this species was brought to the American continent through the slave trade from Africa, where it found favorable conditions for its development, including vertebrate (definitive) and invertebrate (intermediate) hosts, as well as a suitable environment (SOUZA et al., 2011).

S. mansoni lives in the bloodstream of vertebrate hosts, with an average lifespan of three to five years, but can reach up to 30 years. This is a notable evolutionary milestone achieved through an intrinsic mechanism of evasion of all forms of innate and acquired immunity (GRYSEELS, 2012). The helminth has two suckers: oral and ventral (acetabulum), located at the anterior region of the body and feeds on blood, ingesting about 300,000 erythrocytes per hour. It lacks a circulatory system. Its tegument is composed of a syncytial layer of anucleate cells, covered by a thick heptalamellar membrane, which is constantly renewed (PRATA, 2007, apud SOUZA et al., 2011). The male has tiny projections (tubercles) that give it a rough appearance, while the female has a smooth tegument (NEVES, 2016) (Figure 2).

Figure 2 – Photomicrographs of the adult form (male and female) and egg of *S. mansoni*

Source: Science Photo Library and CDC

The eggs of *S. mansoni* measure approximately 50 µm in length by 60 µm in width. They are oval-shaped, with a spine at their widest part, which is a specific characteristic of the species. Inside the egg is the miracidium, a larva with cilia that allows movement in aquatic environments. The cercaria, which originates from the miracidium after it penetrates the intermediate host, is a larval form consisting of two parts: a cercarial body measuring 190 by 70 µm and a bifurcated tail measuring 230 by 50 µm. It has an oral sucker and a ventral sucker, with the latter being the main structure the larva uses to attach to the host's skin during the penetration process (NEVES, 2016)

LIFE CYCLE

For the disease transmission to occur, the presence of humans as definitive hosts and aquatic snails of the genus *Biomphalaria* as intermediate hosts is essential. An infected human eliminates viable *S. mansoni* eggs through feces. When these eggs come into contact with water, they rupture, allowing the release of the ciliated larval form known as the miracidium. The miracidia penetrate the snail, where they multiply over a period of four to six weeks. After this period, the snails release cercariae, which are the infective larvae of *S. mansoni*. These cercariae penetrate humans through the skin and/or mucous membranes, more frequently through the feet and legs, as these are areas of the body that come into more contact with contaminated water (BRAZIL, 2008).

HOSTS INVOLVED IN THE PARASITE'S LIFE CYCLE

Intermediate Hosts

The biological cycle of *S. mansoni* depends on the presence of the intermediate host in the environment. The intermediate hosts are aquatic gastropod snails belonging to the family Planorbidae and the genus *Biomphalaria*. In these snails, the asexual reproduction of the helminth occurs (BRAZIL, 2017).

Biomphalaria snails have a planispiral shell, with a diameter varying between 7 mm and 40 mm in adult individuals, and a natural yellowish color. However, depending on the substances the snail contacts in its habitat, the shell color can vary from brown to black. They have two long, filamentous tentacles with eyes located at their base, a mouth surrounded by a T-shaped jaw when viewed from the front, an oblong foot, and a cephalic portion of the visceral mass. The mantle folds to form the pulmonary cavity, which is an important characteristic for the specific identification of the species *B. glabrata*, as it contains the renal crest (BRAZIL, 2008).

Biomphalaria snails have predominantly pulmonary respiration but can also respire in aquatic environments through the pseudobranch (main respiratory organ) and the skin in contact with the liquid medium. They are hermaphroditic, with cross-fertilization predominating over self-fertilization (BRAZIL, 2008).

Among the 11 species of *Biomphalaria* present in Brazil, only three are involved in the transmission of schistosomiasis: *Biomphalaria* glabrata Say, 1818, *Biomphalaria* straminea Dunker, 1848, and *Biomphalaria tenagophila* Orbigny, 1835. These are considered natural hosts of *S. mansoni*. Other species of the genus *Biomphalaria* are potential hosts, such as *Biomphalaria* amazonica Paraense, 1966, and *Biomphalaria* peregrina Orbigny, 1835. Of the three species of greatest epidemiological importance, at least one (*B. straminea*) has been reported in 24 of the 26 Brazilian states, in addition to the Federal District, according to data from the Ministry of Health (BRAZIL, 2008).

In a study on the geographic distribution of intermediate hosts of Schistosoma mansoni in Brazil, Carvalho et al. (2018) found that out of 429 municipalities selected for the study, *Biomphalaria* snails were found in 300 (70.2%) of them, distributed across states in the Northeast, Southeast, and South regions. The species *B. glabrata*, the most important in epidemiological terms, was reported in 16 Brazilian states, as well as in the Federal District, and in 806 municipalities, primarily concentrated in the Northeast and Southeast regions, with its distribution almost always associated with the distribution of schistosomiasis (Figure 3).

Figure 3 – Distribution of *B. glabrata* snail foci

Source: Carvalho et al. (2009)

The species *B. straminea* is found in almost the entire Brazilian territory, with the exception of the states of Amapá and Rondônia (Figure 4). These mollusks inhabit both permanent and temporary water bodies and are better adapted to the dry climate of the Northeast.

The species *B. tenagophila* has been reported in 603 municipalities across 10 Brazilian states, as well as in the Federal District. It has a more limited geographic distribution, being mostly restricted to the states in the Southeast and South regions, while also reaching southern Bahia (Figure 5) (BRAZIL, 2008; CARVALHO et al., 2009).

Figure 4 – Distribution of *B. straminea* snail foci

Source: Carvalho et al. (2009)

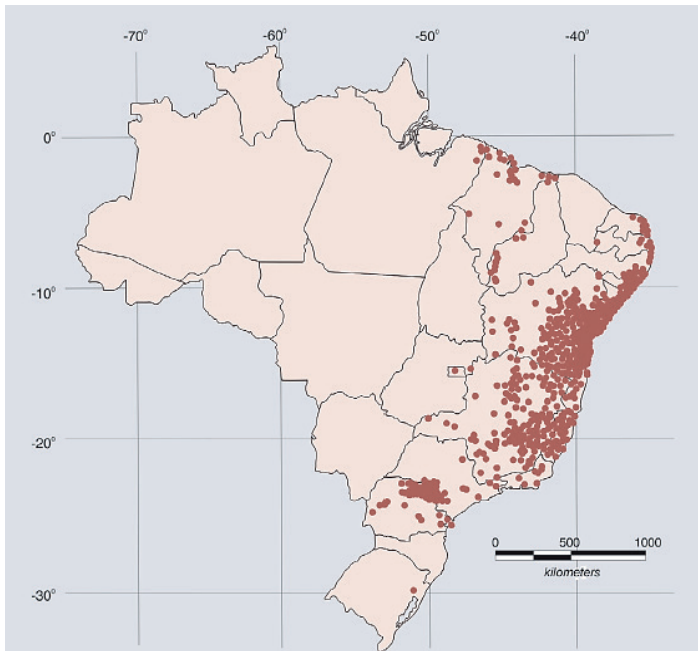

Figure 5 – Distribution of *B. tenagophila* snail foci

Source: Carvalho et al. (2009)

In the state of Maranhão, the species *B. glabrata* and *B. straminea* are predominantly found, mainly in the flooded fields of the Baixada Ocidental and the Northern Coast of the state. According to malacological surveys conducted by PCE-MA from 1997 to 2016, 67.40% of the captured mollusks were identified as *B. glabrata*, 28.36% as *B. straminea*, and 0.10% as *B. tenagophila*, the latter being restricted to the municipality of São Luís (BRAZIL, 2019).

The mollusks can colonize a wide variety of habitats, ranging from small puddles to streams and ponds. When located in urban areas, the transmission sites generally have similar ecological characteristics, being located near houses, in artificial water collections such as ditches, gutters, and drains (temporary breeding grounds) (GOMES et al., 2012). These communities, whether urban or rural, lack piped water, proper sanitation, and rainwater drainage, and are deprived of street cleaning services and garbage collection. The presence of vegetation along the margins of streams is essential both for the snails' food supply and for their shelter and egg-laying. These organisms are highly adaptable to various environmental changes, using several mechanisms to survive stressful situations such as anhydrobiosis, burial, diapause, and quiescence, in which snails reduce their biological activity until favorable conditions are available again (BRAZIL, 2008).

Definitive Hosts

On the other side of the schistosomiasis cycle, mammals act as the definitive hosts of the parasite. Primates, marsupials (opossums), ruminants, rodents, and lagomorphs (hares and rabbits) are considered permissive hosts or reservoirs; however, the role of these animals in the transmission and epidemiology of the disease is unclear, despite their ability to excrete eggs in their feces (BRAZIL, 2010).

In the Baixada Maranhense region, Bastos (1982) identified another definitive host in the transmission cycle besides humans: the wild rodent of the genus *Holochilus*. With rapid reproduction, this animal lives in constant contact with water bodies and is highly adapted to the region's environmental conditions, acting as a natural reservoir for the parasite. Schistosomiasis transmission is then enhanced by the presence of both definitive hosts in the same environment, establishing two parasite strains: the wild strain (carried by the rodent) and the human strain (LIRA et al., 2016).

Humans are considered the primary host due to their epidemiological importance. In them, the worm will complete its body development and sexual maturity. The reproduction of *S. mansoni* in the human body causes various symptoms characteristic of schistosomiasis mansoni, which vary depending on the stage of the disease (SOUZA, 2011).

In the acute phase, abdominal pain, nausea, diarrhea, and blood in the stool may occur. In more advanced stages of the disease, liver enlargement (due to the immune response caused by egg deposition), fluid accumulation in the peritoneal cavity, and hypertension of the mesenteric veins may occur, leading to the characteristic chronic condition of the parasitosis, known as "water belly" (NEVES, 2016).

DISEASE CONTROL

The first control program for schistosomiasis began in 1913 in Egypt, where both the local population and stationed soldiers were heavily infected. At that time, the approach used was the control of transmitting mollusks. In the 1930s, sanitation was incorporated into the program, such as the construction of latrines and piped water supply, but the results were still insufficient. With the progressive elucidation of the evolutionary cycle of Schistosoma spp., mollusk control and mass treatment became the model for strategy (USEH, 2012).

The WHO Expert Committee on Schistosomiasis Epidemiology and Control adopted a holistic approach to disease control and noted that "a comprehensive understanding of environmental, demographic, social, behavioral, and economic factors" in schistosomiasis is essential for the planning of successful long-term programs (USEH, 2012).

The first large-scale coproparasitological survey in Brazil was conducted only in 1950, when the existence of the disease was evidenced in 612 of the 877 localities surveyed in the Northeast region and the state of Minas Gerais (PELLON & TEIXEIRA, 1950), allowing knowledge of its national distribution (CARMO & BARRETO, 1994). In this survey, schoolchildren aged 7 to 14 years were examined, with priority given to localities with populations over 1,500 inhabitants.

In 1975, a specific control program for the disease was created in Brazil, the Special Schistosomiasis Control Program (PECE), under the then Superintendency of Public Health Campaigns (SUCAM). This was later replaced by the Schistosomiasis Control Program (PCE) in the 1980s. In the state of Maranhão, disease surveillance and control activities have existed since 1977 (CUTRIM, 1987).

In 1999, the Program was decentralized, with municipalities taking responsibility for epidemiological surveillance activities, vector control, and patient treatment (BRAZIL, 1999).

Currently, the World Health Organization suggests, as a control strategy, what is called an integrated approach, which includes the following efforts: mass chemotherapy; snail control, which involves the use of chemical and natural molluscicides; proper sewage treatment; adequate environmental engineering designs for the development of irrigation and hydroelectric systems that limit the viability of breeding sites for host snails; safe drinking water supply; and extensive health education and population mobilization to raise awareness about the control program (KING, 2009).

Therefore, the enormous morbidity associated with schistosomiasis, which is significantly close to malaria in terms of significance and public health impact, requires coordinated and sustainable means for disease control, involving the agreement of different sectors of the public power, research institutions, and society (USEH, 2012).

FACTORS RELATED TO THE OCCURRENCE OF SCHISTOSOMIASIS

As it is a waterborne disease, for the biological cycle of *S. mansoni* to be completed and the transmission of parasitosis to be established in a particular area, three conditions must necessarily be met: a) the existence of parasitized people; b) the existence of water bodies contaminated by feces and colonized by *Biomphalaria* snails; c) human contact with these water bodies.

The areas where these conditions are most commonly observed are rural regions and peri-urban areas of municipalities. The lack of basic sanitation, inadequate water supply, and lack of information are the factors that contribute most to this situation (BARBOSA et al., 2008; SAUCHA et al., 2015; FREEMAN et al., 2017).

Although in 2008 only 33 municipalities in Brazil did not have a water supply service, 2,495 municipalities (44.8% of Brazilian municipalities) remained without sewage collection coverage. This serious situation persists in much of the states of the Northeast and North regions of the country, with Bahia, Maranhão, Piauí, and Pará standing out (IBGE, 2011).

According to the 2008 National Basic Sanitation Survey, only 6.5% of municipalities in Maranhão had a sewage collection network (considering that at least one district, even if only part of it, had sewage treatment).

The natural conditions of such environments themselves favor the transmission of the disease. In a study on the importance of floods in the spread of schistosomiasis mansoni, Ramos (1970) pointed out that floods can contribute to the expansion of schistosomiasis by providing conditions for the establishment of new foci, favoring the increase in the proliferation of *Biomphalaria tenagophila*.

In Maranhão, the micro-region of Baixada Maranhense constitutes a peculiar environment for the transmission of schistosomiasis, as it combines both natural and socioeconomic conditions. This region is located in the transition area between the Amazon and the Northeast, in a low latitude zone, and is characterized by high rainfall rates. The Baixada is located in a region of low, flat, and floodable lands, characterized by fields, gallery forests, mangroves, and lacustrine basins. Its population is predominantly rural (FARIAS FILHO, 2013). The extensive engagement in activities related to this environment, such as fishing, washing clothes, or leisure, constitutes a high risk factor for the spread of the disease in this and other regions with similar characteristics, such as the rural and peri-urban areas of São Luís (Figure 6).

Figure 6 – Environmental characteristics of Baixada Maranhense

Source: Google Images

CONCLUSION

Schistosomiasis is the second most prevalent disease worldwide, second only to malaria. It belongs to a special group of diseases known as Neglected Tropical Diseases. This parasitic disease is of high relevance in the global health scenario, predominantly affecting poorer populations living in rural or vulnerable urban areas. Such environments gather conditions that contribute to the successful establishment of schistosomiasis, such as the absence or inadequacy of basic sanitation, the abundance of water collections, and the lack of information about the disease or how to prevent it.

In Brazil, the so-called Schistosomiasis Control Programs (PCE) have been striving and have, to some extent, managed to reduce prevalence rates in the states. However, the fact that this is already a neglected disease in itself means that these programs face difficulties in effectively carrying out their prevention and control actions in a satisfactory manner. Being a disease linked to underdevelopment, there is no doubt that to achieve the elimination of schistosomiasis and other infectious and parasitic diseases, governments will need to promote significant improvements in the socio-economic conditions of the population, coupled with a secure water supply and sanitary improvements in urban centers and rural areas.

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