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Clinical findings of schistosomotic myeloradiculopathy: a systematic review

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Abstract

Introduction: Schistosomiasis is caused by a helminth of the genus Schistosoma. Schistosomal myeloradiculopathy (SMR) is the main ectopic manifestation of this species. The diagnosis of SMR is based on neurological symptoms of spinal cord injury, tests that indicate infection by the agent, and exclusion of other causes. Using magnetic resonance imaging of the spinal cord, the diagnosis of this ectopic form of the disease was facilitated. **Objective:** This was to develop a systematic review to present the main clinical outcomes of the diagnosis and treatment of schistosomal myeloradiculopathy. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was conducted from January to February 2025 in the Scopus, Embase, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument, and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 124 articles were found. 22 articles were evaluated, and 16 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 38 studies with high risk of bias and 19 studies that did not meet GRADE. Most studies presented homogeneity in their results, with X^2=83.8% >50%. It was concluded that among the main manifestations of schistosomiasis, schistosomal myeloradiculopathy is the most severe ectopic form of the disease, and should be suspected in patients with low back pain, lower limb strength and/or sensitivity disorders, or urinary tract disorders. Early diagnosis and treatment should be performed to reduce severe neurological sequelae. Treatment includes anti-schistosomiasis medications, corticosteroids, and/or surgery that significantly impacts the overall quality of life of affected individuals, reinforcing the importance of efforts to control and eradicate this debilitating disease and suggesting that multidisciplinary clinical management of patients with schistosomiasis would be more appropriate and could potentially improve patient quality of life.

Keywords: Schistosomiasis. Schistosomal myeloradiculopathy. Diagnosis. Treatment.

Introduction

Schistosomiasis is caused by a helminth of the genus Schistosoma. Transmission of the disease depends on whether the infected person is the definitive host, whether the water collection system has inadequate sanitation, and whether a freshwater mollusk is the intermediate host. It is suggested that people living in non-endemic areas with little exposure to *Schistosoma mansoni* are more susceptible to developing myelitis caused by this parasite [1,2].

In this context, schistosomal myeloradiculopathy (SMR) is the main ectopic manifestation of this species. The diagnosis of SMR is based on neurological symptoms of spinal cord injury, tests that indicate infection by the agent, and exclusion of other causes [1]. SMR can be treated with schistosomicides, corticosteroids, and/or surgery, but there is no consensus on the efficacy of one over the other. Schistosomal killers destroy the adult worm and, consequently, interrupt egg production, reducing the inflammatory reaction in the central nervous system (CNS) [1-3].

SMR has an underestimated prevalence in endemic areas. Diagnosis depends on the presence of

thoracic/upper lumbar neurological symptoms, demonstration of *Schistosoma mansoni* infection by microscopic or serological techniques, and exclusion of other causes of transverse myelitis [1,4,5]. When treatment with antischistosomal drugs and corticosteroids is initiated early, the clinical response is significant, and patients who are not treated may die. There is no consensus on doses and duration of treatment, but studies suggest that when steroids are administered for at least 6 months, clinical improvement is increased [6,7].

Since the diagnosis of SMR is presumptive and treatment is essentially clinical, physicians should be aware of the disease, and more research is needed to increase the accuracy of diagnostic methods and therefore avoid routine laminectomy. Employing spinal cord magnetic resonance imaging, the diagnosis of this ectopic form of the disease has been facilitated. Consequently, the number of reported cases of schistosomal myelopathy is increasing rapidly [8].

Therefore, the present study aimed to develop a systematic review to present the main clinical outcomes of the diagnosis and treatment of schistosomal myeloradiculopathy.

Methods

Study Design

The present study followed an international systematic review model, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 02/14/2025. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 02/14/2025.

Data Sources and Research Strategy

The literature search process was carried out from January to February 2025 and developed based on Web of Science, Scopus, Embase, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (DeCS / MeSH Terms) were used: "Schistosomiasis. Schistosomal myeloradiculopathy. Diagnosis. Treatment", and using the Boolean "and" between the MeSH terms and "or" between the historical discoveries.

Study Quality and Risk of Bias

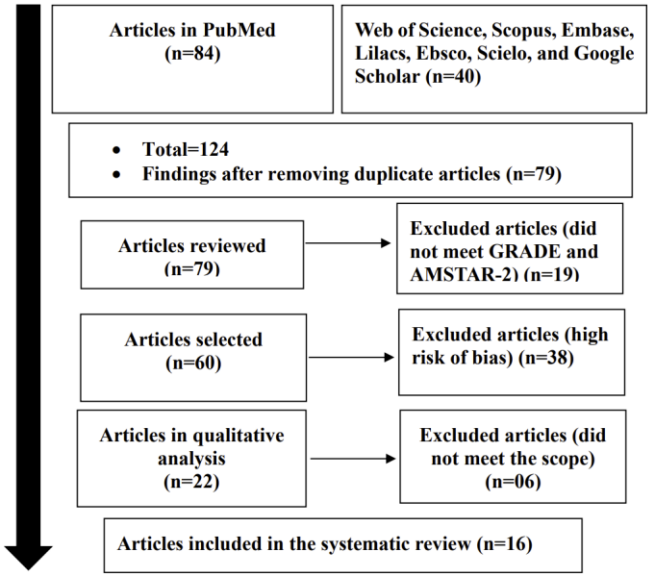
Quality was classified as high, moderate, low, or very low regarding risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. Risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

Results and Discussion

Summary of Findings

As a corollary of the literary search system, a total of 124 articles were found that were subjected to eligibility analysis, and, subsequently, 16 studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering in the first instance the level of scientific evidence of studies in types of study such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=83.8%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 38 studies with high risk of bias and 19 studies that did not meet GRADE and AMSTAR-2.

Figure 1. Screening the article selection process.

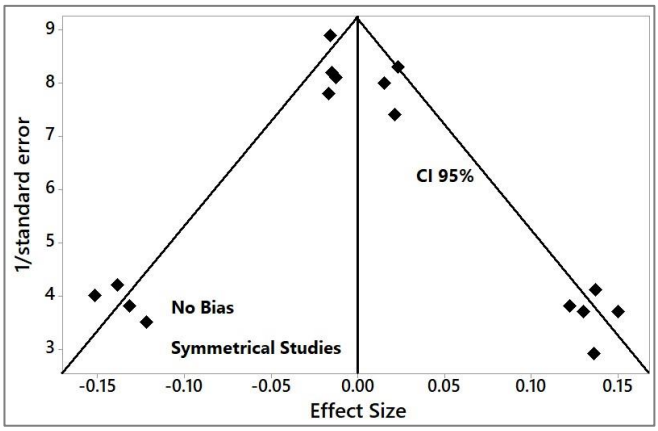


Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a

symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample size (lower precision) that are shown at the base of the graph and in studies with large sample size that are shown at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies with small sample sizes that are shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=16 studies).



Source: Own authorship.

Main Clinical Findings

Schistosomiasis is caused by a helminth of the Schistosoma family, with humans being the most important epidemiological host. *Schistosoma mansoni* is the most commonly associated with cases of myeloradiculopathy. Schistosomiasis can be divided into early and late stages. The early stage is subdivided into acute asymptomatic and symptomatic forms. The acute asymptomatic form usually occurs in childhood and may go unnoticed or be found in routine examinations (eosinophilia and *Schistosoma mansoni* eggs in the feces) [1,2].

The acute symptomatic form occurs 24 to 72 hours after infection, with the appearance of erythematous and pruritic micropapules, known as cercarial dermatitis [1]. The differential diagnosis with contact eczema and strobilar prurigo is difficult when considering the clinical and epidemiological histories. In the acute symptomatic form, symptoms such as lymphadenopathy, malaise, fever, loss of appetite, dry cough, sweating, myalgia, abdominal pain, hepatomegaly, splenomegaly, diarrhea, tachycardia, hypotension, headache and malaise may indicate a condition known as Takayama fever or a toxemic form [1-3].

Regarding the symptoms mentioned, their intensity depends on the parasite load and the patient's sensitivity, and when they worsen, it means that the egg-laying process (between the fifth and sixth week of infection) has already begun. The clinical signs and symptoms of the acute symptomatic phase may last for 90 days, which makes it appear as a fever of undetermined origin. Clinical diagnosis is made around 45 days after infection, through a stool sample or liver biopsy. Untreated clinical cases usually have spontaneous remission. In this phase, the disease rarely leads to death, and clinical improvement leads to normalization of body temperature and the disappearance of suggestive symptoms [1,8,9].

In the late phase, there are chronic forms, classified according to the organ most affected. Patients who respond well in the acute phase, that is, fewer inflammatory cells in the granuloma, develop the hepatic or hepatointestinal forms. Those who do not respond well continue to have a large granuloma and progress to the hepatosplenic form of the disease [9,10].

In the hepatointestinal form, frequent in endemic areas, there are no symptoms, and diagnosis becomes incidental with the parasitological examination of feces. When symptoms are present, they are nonspecific and difficult to differentiate from other parasites. On physical examination, there may be pain on abdominal palpation and hepatomegaly without splenomegaly. A liver biopsy usually does not provide information, but an intestinal biopsy may reveal viable eggs of *Schistosoma mansoni* [10,11].

In the hepatic form, the patient is asymptomatic or presents symptoms similar to the hepatointestinal form. There is hepatomegaly and liver fibrosis, but there is no splenomegaly or esophageal varices. Three main forms can be found in hepatosplenic schistosomiasis: compensated, decompensated, and complicated. The compensated form, associated with Symmer's fibrosis, presents with portal hypertension with or without digestive bleeding from esophageal varices. In children, there may be no portal hypertension. In the decompensated form, with decreased liver function, ascites, jaundice, and encephalopathy frequently occur. Finally, the complicated form is associated with other diseases, such as enterobacterial infections, other liver diseases, or other clinical forms of the disease. Ultrasonography improves the diagnostic accuracy of the hepatosplenic form, especially in endemic areas, where individuals may present with splenomegaly of other etiologies [1,2].

In addition, several other possible clinical forms, such as hypertensive and cyanotic vasculopulmonary disease, or pulmonary hypertension due to vascular obstruction caused by dead eggs or worms, or by immunocomplex pulmonary vasculitis. Another clinical feature is glomerulopathy, found in 10 to 15% of cases, and most commonly shown by nephrotic syndrome [1].

Neurological forms due to egg deposition and

granulomas in the CNS are also a possibility, with transverse myelitis being the most frequent lesion; the female genitals, testicles, skin, retina, thyroid, and heart are also related but uncommon sites. Pseudoneoplastic lesions, in which the tissue reaction suggests intestinal tumor formations and lymphoproliferative disease, characterized by nodular non-Hodgkin's splenic lymphomas and found in 0.9% of 863 splenectomies, are also related as clinical forms [1,4,7].

The central nervous system, especially the spinal cord, is the most commonly associated ectopic infection by *Schistosoma mansoni* [3]. SMR occurs more frequently in the acute and chronic intestinal forms of the worms and has a preference for males [4]. The movement of eggs and worms to the CNS can be explained by migration through the epidural venous plexus of Batson. This plexus connects the portal system and the vena cava to the veins of the spinal canal, reaching the CNS and causing myeloradiculopathy. The disease may initially present with a triad of low back pain, altered sensitivity of the lower limbs, and urinary disorders, progressing to weakness of the lower limbs and sexual impotence [4,6]. Clinical manifestations appear in acute or subacute forms and worsen in the second week [4].

The diagnosis is based on the neurological symptoms of spinal cord injury, tests that demonstrate infection by the agent, and the exclusion of other causes of myelopathy. Neurological examination shows areas of lesion in the affected spinal cord. Flaccid paraplegia associated with hyporeflexia, urinary retention, and reduced sensitivity demonstrates involvement of the conus medullaris and cauda equina. On the other hand, spasticity, altered sensitivity at the segmental level, and urinary incontinence demonstrate greater involvement of the spinal cord. Early recognition is essential to avoid irreversible neurological sequelae [4].

Schistosomiasis diagnostic methods can be differentiated into direct diagnostic methods, which detect the parasite or its parts; and indirect diagnostic methods, which identify indirect evidence of the parasite, which depend on biochemical or immunological markers [7]. The direct diagnostic method recommended by the Ministry of Health is the search for *Schistosoma mansoni* eggs in the feces, using the Kato-Katz technique that allows the visualization and counting of eggs in the sample, providing a simple and practical quantitative indicator [2,8]. In most reported cases of SMR, Schistosoma was found in stool, urine, or tissue samples, such as rectal mucosa [4].

Among the indirect methods, immunological tests are the most widely used, but they have limitations due to cross-reactions with other helminths. Furthermore, they do not define the intensity of the infection and may remain positive even after cure [4,7,9]. In this context, indirect immunoassays, that is, those that detect the host's immune response to the antigen, are the most widely used, mainly indirect hemagglutination, indirect immunofluorescence, and the enzyme-linked immunosorbent assay (ELISA) [7].

The indirect hemagglutination reaction is highly sensitive. However, due to cross-reactions with other helminths and inconsistent standardization of reagents, its reproducibility is impaired [7,9]. The indirect immunofluorescence reaction is based on the binding of immunoglobulins to parasite surfaces and fluorescein-labeled anti-human immunoglobulins, which become fluorescent under a microscope [7]. This method has proven to be practical, inexpensive, and has good sensitivity and specificity in detecting IgM antibodies in mild infections. Among the immunological techniques, the ELISA method is very stable and economical, and uses antigens or antibodies linked to enzymes that detect antibodies or antigens. This technique is the most widely used today, however, some authors have observed that the immunofluorescence technique demonstrated greater sensitivity, specificity, and predictive value when compared to ELISA [9].

It is also noted that Ferrari reported two cases in which the analysis of cerebrospinal fluid (CSF) from patients with SMR revealed nonspecific characteristics, a slight increase in proteins in 95% of cases, normal glucose levels, and pleocytosis with a predominance of lymphocytes in 91%. He also found eosinophils in 41% of cases, an alteration compatible with the patient's report. In addition, the identification of anti-Schistosoma antibodies by ELISA, indirect immunofluorescence, or hemagglutination techniques showed positive immunological reactions specific for schistosomiasis in 85 to 90% of the CSF tested [4]. Currently, the indirect immunofluorescence reaction is considered to have the best sensitivity and specificity for neuroschistosomiasis [11].

It has been found that magnetic resonance imaging (MRI) has demonstrated abnormalities in virtually all cases of SMR in which it has been used, even in cases where myelography or computed myelotomography did not reveal abnormalities. MRI has low specificity in differentiating between infectious, inflammatory, ischemic, tumoral, edematous, or gliotic etiologies. On the other hand, it has high sensitivity, which has strengthened the clinical diagnosis of SMR [6]. SMR can be treated with schistosomicides, corticosteroids, and/or surgery, but no study proves the superiority of one method over the other. In this context, schistosomicides, by destroying the adult worm, interrupt egg production and prevent the inflammatory reaction in the CNS [5].

The Brazilian Ministry of Health's SMR Manual recommends praziquantel as a schistosomicidal treatment, at a dose of 50 mg.kg-1 in adults and 60 mg.kg-1 in children up to 15 years of age, divided into two doses and associated with prolonged oral corticosteroid therapy [4]. There is no consensus in the literature regarding the duration of steroid treatment, but there is evidence that it should be given for more than two months and, if interrupted before six months, it increases the risk of recurrence of symptoms [4,12].

Badr et al. [12], in a report of 17 patients with SMR in Egypt, reported that among the patients who stopped corticosteroids early (less than 60 days of use), 75% presented recurrent symptoms of myelopathy. Andrade et al. [13], analyzing 16 patients with SMR treated with praziquantel 60 mg/kg/day for three days in combination with prednisone 100 mg/day, showed that improvement in symptoms was observed from the first two weeks of treatment. The speed of regression varied according to each patient.

Surgery should be reserved for patients with acute paraplegia and CSF blockage, and for those whose clinical condition worsens despite conservative treatment. It should be used less frequently for diagnostic purposes. SMR is a serious condition that presents a risk of significant neurological sequelae. However, it is underreported due to the difficulty of clinical recognition and the limitations of diagnostic tests [4].

Clinical characteristics associated with laboratory tests that suggest the presence of the causative agent and magnetic resonance imaging with suggestive images help to corroborate the diagnostic hypothesis of SMR. Early treatment of parasitic infections involving the CNS improves the prognosis and reduces morbidity and mortality [12]. It is noteworthy that the occurrence of SMR, unlike other severe forms of schistosomiasis, does not depend on high parasite loads. Patients with SMR generally have few eggs per gram of feces and often come from areas of low prevalence. These findings justify the implementation of epidemiological surveillance of SMR in all countries, even in non-endemic states [1].

A study reported a rare case of schistosomiasis of the upper thoracic spinal cord diagnosed by biopsy in an 18-year-old male migrant who presented to a spine and orthopedics center with complaints of upper back pain and associated symptoms of myeloradiculopathy. The initial suspicion of an intramedullary spinal cord tumor was made based on the MRI findings that justified the biopsy, which revealed Schistosoma spp. He was treated with anthelmintics and corticosteroids with a resolution of symptoms [14].

A case of spinal neuroschistosomiasis was presented in a patient who presented with low back pain, rapidly progressing to paraparesis with significant gait impairment. Magnetic resonance imaging findings revealed extensive spinal cord involvement from the conus to the level of the cervical spine. After ruling out other causes of myelopathy and considering the history, total anti-Schistosomal antibodies were tested and detected, confirming the diagnosis. Steroids and schistosomal antimicrobials were initiated, with remarkable clinical and imaging improvement. The patient regained normal muscle strength, gait, and functional independence over the next six months [15].

A study evaluated health-related quality of life (HRQoL) in patients with hepatosplenic schistosomiasis (HS) and SMR and healthy volunteers (HV) and determined whether clinical complications of the disease are associated with HRQoL scores. HRQoL was evaluated in 49 patients with HS, 22 patients with SMR, and 26 HV from an outpatient clinic of the University Hospital of the Federal University of Minas Gerais using the WHOQOL-BREF questionnaire. Patients with SMR and HS had significantly lower overall quality of life scores when compared to the HV control group ($p=0.003$ and $p=0.005$, respectively). The multivariate ordinal regression model adjusted for sex, age, and educational level indicated that patients with HS and SMR are three and five times more likely to have a lower quality of life than healthy volunteers (Odds Ratio 3.13 and 5.04, respectively). There was no association between complications of HS disease and quality of life scores. In contrast, a worse quality of life was observed in patients with SMR who presented with back or leg pain, leg paresthesia, and bladder dysfunction [16].

Conclusion

It was concluded that among the main manifestations of schistosomiasis, schistosomal myeloradiculopathy is the most severe ectopic form of the disease, and should be suspected in patients with low back pain, lower limb strength, and/or sensitivity disorders or urinary tract disorders. Early diagnosis and treatment should be performed to reduce severe neurological sequelae. Treatment includes schistosomiasis medications, corticosteroids, and/or surgery that significantly impact the overall quality of life of affected individuals, reinforcing the importance of efforts to control and eradicate this debilitating disease and suggesting that multidisciplinary clinical management of patients with schistosomiasis would be more appropriate and could potentially improve patient quality of life.

CRediT

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