

## Prognosis of Schistosomiasis Mansoni Patients Infected with Hepatitis B Virus

Maria José Conceição/<sup>+</sup>, Carlos Alberto Argento, Vera Lucia A Chagas\*,  
Christina M Takiya\*, Débora C Moura/<sup>++</sup>, Sonia CF Silva/<sup>++</sup>

Departamento de Medicina Preventiva, Serviço de Doenças Infecciosas e Parasitárias, Hospital Universitário Clementino Fraga Filho \*Departamento de Patologia, Serviço de Anatomia Patológica, Universidade Federal do Rio de Janeiro, Av. Brigadeiro Trompowsky s/nº, 21941-590 Rio de Janeiro, RJ, Brasil

*A clinical study on the evolution of patients with schistosomiasis mansoni has been conducted since 1983 at the outpatient clinic of the Infectious and Parasitic Disease Service in the Clementino Fraga Filho University Hospital in Rio de Janeiro, Brazil, comparing prevalence of positive tests for HBsAg, anti-HBsAg, and anti-HBc among patients infected with Schistosoma mansoni coming from various regions of Brazil and with different clinical forms of the disease. A non-significant predominance of HBsAg, anti-HBsAg, and anti-HBc was detected among patients with the hepatosplenic form of schistosomiasis, who presented a more severe clinical evolution with a higher frequency of hematemesis and/or melena, in addition to the development of macronodular cirrhosis and a worse prognosis as compared to patients with the toxemic form, schistosomiasis-infection and the hepatointestinal form.*

Key words: schistosomiasis mansoni - hepatitis B virus - associated infection

Schistosomiasis mansoni and hepatitis B are endemic in various regions of Brazil and have posed a persistent challenge to the public health system due to the difficulty in their control. Prevalence of schistosomiasis is some 10% of the total Brazilian population and has tended to remain high, due to erratic human migratory patterns, leading to the appearance of foci in previously unaffected areas (Neiva 1947). As for prevalence of hepatitis B, Wakimoto (1997) quotes data from the Brazilian Ministry of Health pointing to high rates in the western Amazon Region (states of Acre, Amazônia, Rondônia, and Roraima) as well as areas in the State of Espírito Santo, intermediate rates in the eastern Amazon (Amapá, Pará, and Tocantins), middle west (Goiás, Mato Grosso do Sul, and Federal District), and northeast, and low rates in the south and southeast.

The combination of schistosomiasis mansoni and hepatitis B has been reported by Andrade (1965), Prince (1970), Lyra et al. (1976), Bassily et al. (1979, 1983), among other authors. Gayoto (1984) performed a serological survey on the prevalence of HBsAg in different geographical

areas and detected positive rates ranging from 0.3 to 0.5%. However, Kamel et al. (1994) found no epidemiological association between the two infections when they studied 1,850 inhabitants of northern Egypt. Chieffi (1992) referred to both the interaction between the two infections and the risk of occurring a clinical evolution different from that expected, resulting from two main factors, i.e., persistent viremia and aggravated hepatopathy. According to Andrade and Andrade (1984), in individuals with asymptomatic *Schistosoma mansoni* infection, hepatic lesions are limited to the portal system. Coutinho (1979) emphasized the possibility of an aggravated course of infection in the hepatosplenic forms of the disease. Such forms attain prevalence rates of up to 10% in some areas of Brazil (Coutinho & Domingues 1988). Lyra et al. (1976) in Brazil and Bassily et al. (1979) in Egypt emphasized the high frequency of markers for hepatitis B infection in patients hospitalized with the uncontrolled hepatosplenic form. However, Pereira et al. (1994) suggested that in order to avoid bias, patient samples with severe chronic hepatic lesions not be included in studies.

Since the above was a controversial, medically relevant theme, the current study was planned with the objective of assessing blood markers for the hepatitis B virus in outpatients infected with *S. mansoni*, with different clinical forms of the disease and coming from various endemic areas of Brazil, in addition to assessing the prognosis for coinfecting patients.

<sup>+</sup>Corresponding author. Fax: +55-21-280.3740.

<sup>++</sup> Fellowship from the Department of Tropical Medicine, Instituto Oswaldo Cruz.

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### PATIENTS AND METHODS

The study included 398 outpatients, as well as 50 other patients in the control group, all treated at the Infectious and Parasitic Disease Service, Clementino Fraga Filho University Hospital, School of Medicine, Universidade Federal do Rio de Janeiro. Etiologic diagnosis of *S. mansoni* was based on up to six parasitological stool tests using the Kato method (1960), as modified by Katz et al. (1972) and/or rectal biopsy. Clinical classification was that proposed by Pessoa and Barros (1953), as modified by Barbosa (1966).

Sera from all patients were tested for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBsAg), and antibody to hepatitis B core antigen (anti-HBc), using enzyme-linked immunoassay (ELISA). Patient clinical data were identified beginning in 1983, emphasizing specific prior treatment for schistosomiasis mansoni (both parenteral and enteral), reports of previous surgery, blood transfusions, complaints of nausea, vomiting, abdominal pain, hematemesis and/or melena, bloody stools, choluria, acholia, jaundice, telangiectasis, palmar erythema, hepato- and/or splenomegaly, hypersplenism, ascites, edema, and signs and symptoms of somatic and/or sexual underdevelopment. Tests included aminotransferase, bilirubin, complete blood cell count, total protein, and protein electrophoresis. Statistical analysis of the data used the Fisher's exact test, considering a *p* value of 0.05 as significant.

Hepatic biopsies were obtained from patients with the hepatosplenic form during therapeutic ablation of spleen, and processed for routine diagnosis.

### RESULTS

Of the 398 patients infected with *S. mansoni*, 52.5% were females and 47.5% males. Age varied from 10 to 62 years (Table I). This same age bracket included 50 patients from the control group who were negative for *S. mansoni* infection and had normal aminotransferase levels. As for clinical forms in the 398 patients, 5.5% had the toxemic form, 56.8% schistosomiasis-infection, 24.6% hepatointestinal form, and 12.3% hepatosplenic form (Table II). Positive rates for HBsAg were 3.8% for the toxemic form, 7% for schistosomiasis-infection, 9.2% for the hepatointestinal form, and 12.2% for the hepatosplenic form (Table III). There was no statistical difference ( $p = 0.54$ ) between clinical forms.

Positive rates for anti-HBsAg and/or anti-HBc were nil in individuals with the toxemic form, 5.3% in schistosomiasis-infection, 6.1% in the hepatointestinal form, and 10.2% in the hepatosplenic

form ( $p < 0.05$ ) (Table IV). Of the 50 members of the control group, one was positive for HBsAg, while 6% (3/50) tested positive for anti-HBsAg and/or anti-HBc, data significant when compared with infected patients disregarding clinical forms.

TABLE I

Distribution of 398 patients with schistosomiasis mansoni according to the age evaluated by HBV markers positivity

Age	No.	%
10 - 20	95	23.9
21 - 40	121	30.2
> 40	183	45.9

TABLE II

Clinical forms of 398 patients with schistosomiasis mansoni

Clinical form	No.	%
Toxemic	26	5.5
Schistosomiasis-infection	226	56.8
Hepatointestinal	97	24.6
Hepatosplenic	49	12.3

TABLE III

Positivity of HBsAg according to the clinical forms of schistosomiasis mansoni

Clinical form	No.	Positive	%
Toxemic	26	1	3.8 <sup>a</sup>
Schistosomiasis-infection	226	16	7.0 <sup>a</sup>
Hepatointestinal	97	9	9.2 <sup>a</sup>
Hepatosplenic	49	6	12.2 <sup>a</sup>

*a*:  $p = 0.54$

TABLE IV

Positivity of anti-HBsAg and/or anti-HBc according to the clinical forms of schistosomiasis mansoni

Clinical form	No.	Positive	%
Toxemic	26	-	- <sup>a</sup>
Schistosomiasis-infection	226	12	5.3 <sup>a</sup>
Hepatointestinal	97	6	6.1 <sup>a</sup>
Hepatosplenic	49	5	10.2 <sup>a</sup>

*a*:  $p > 0.54$

## DISCUSSION

In this study, positive rates for HBV markers in patients infected with *S. mansoni* showed no significant differences between the toxemic, schistosomiasis-infection, hepatointestinal, and hepatosplenic forms. However, this difference did exist in relation to the control (non-infected) group, in which there was one positive case (HBsAg). Studies by Lyra et al. (1976), Bassily et al. (1979), and Madwar et al. (1989) emphasized the prevalence of HBV markers in the hepatosplenic form as compared to non-infected individuals. Larouze et al. (1987) found no association between *S. mansoni* and hepatitis B virus infection in patients from Egypt. Hyams et al. (1987) concluded that there was no correlation between *S. mansoni* infection, with or without hepatosplenomegaly and HBsAg positivity. The study of Serufo et al. (1997) in endemic area from Minas Gerais also did not show association between schistosomiasis and HBV. In Brazil, Guimarães (1975) recorded 4.4% of patients infected with hepatitis B virus among patients with hepatosplenic schistosomiasis (as compared to 1.5% in the hepatointestinal form and 0.6% in controls); Lyra (1976) found 7.8% of HBV markers in the hepatosplenic form of schistosomiasis (as compared to 1.5% in the hepatointestinal form and 1.3% in controls). Silva (1979) found 22.5% of patients with HBV markers in the hepatosplenic form (as compared to 0.9% in the hepatointestinal form and 0% in controls). Hammad et al. (1995) found positive HBsAg in 58% of children with schistosomiasis hepatic fibrosis and 2% in controls. Chieffi (1992) emphasized the relevance of coinfection and the risk of aggravating hepatic lesions during the course of schistosomiasis. According to Strauss and Lacet (1986), the risk increases as the infection becomes chronic.

In the current study, due to the low rate of HBV markers in the control group, it was not possible to determine whether the markers remained for a longer period in patients with the hepatosplenic form. However, this correlation has been described by Lyra et al. (1976) and Ghaffar et al. (1991). There is no clear definition for either the causes of HBV infection or its persistence in patients with the hepatosplenic form (Pereira et al. 1994). Ellner et al. (1980) cite T-cell dysfunction as a probable factor in these patients. Madwar et al. (1983) suggested that the principal cause is the absence of HBsAg clearance in hepatosplenic patients.

The current study found no association between positive HBsAg status and prior history of parenteral treatment for schistosomiasis. Bassily et al. (1983) also failed to find such a correlation. However, Madwar et al. (1989) observed a marker

rate twice as high in individuals who had received such treatment. Hyams et al. (1987) studied 1,234 Egyptians and concluded that parenteral therapy for schistosomiasis can be a risk factor for hepatitis B virus antigenemia. Despite the lack of a significant difference in HBV markers in patients with the hepatosplenic form of schistosomiasis, the group displayed more nausea, vomiting, abdominal pain, hematemesis and/or melena (in six patients), worse evolution of bilirubin and aminotransferase, and hypersplenism. Hepatic biopsy in this group showed macronodular cirrhosis, making the prognosis more somber as compared to patients with the toxemic, schistosomiasis-infection, and hepatointestinal forms. Follow-up has been maintained on the progression of these patients in an attempt to shed light on interrelations between the two infections.

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