

THE ASSOCIATION OF *SCHISTOSOMA MANSONI* INFECTION WITH HEPATOCELLULAR CARCINOMA*

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The association of Schistosoma mansoni infection with hepatocellular carcinoma (HCC) was studied in Espírito Santo State, Brazil. Schistosoma infection was diagnosed by stool examinations or by histological finding at autopsy. HCC was diagnosed by biopsy, laparoscopy and biopsy or at autopsy. Among 45 cases of HCC six had Schistosoma mansoni infection (13.04%). The occurrence of Schistosoma infection among HCC HBs Ag positive or negative was similar (13.33% and 13.63% respectively). The chi squared comparison showed no significant differences between the frequency of schistosomiasis in patients with HCC and the frequency of Schistosoma infection among people living in the Espírito Santo State (5.9% among children of elementary school from all the counties of the State and 6.7% in people that attended medical care in Vitoria, the capital of the State). Therefore, the authors believe that the association of schistosomiasis mansoni with HCC may be casual, specially in areas where the Schistosoma mansoni infection is frequent.

Key words: Schistosomiasis mansoni. Hepatocellular carcinoma.

A possible relationship between schistosomiasis mansoni and hepatocellular carcinoma (HCC) has been proposed by Mott¹², based on the occurrence of both diseases in some areas. In experimental studies, mice with *Schistosoma mansoni* infection were injected with 2-amino-5 azotoluen, a carcinogenic drug. The hepatomas appeared earlier and more frequently in infected animals than in uninfected controls³. Also, infected mice treated with a single dose of hycanthone, developed hepatomas, whereas uninfected mice, treated with the same dose, did not^{8 9}. These experimental observations, showing a possible cocarcinogenic effect of *Schistosoma mansoni* infection were not corroborated by other investigators¹⁷.

In the Espírito Santo State, Brazil, schistosomiasis mansoni is endemic and we found frequent cases of HCC among the autopsies performed in Vitoria, the capital of the State¹⁴.

In this communication we report our observations about the association of *Schistosoma mansoni* infection in 45 cases of HCC studied at the University

Hospital Cassiano Antonio Moraes, in Vitoria, Espírito Santo State.

MATERIALS AND METHODS

Among 45 cases of HCC, the presence of schistosomiasis was investigated by stool examination or by detection of granulomas in sections of liver or large bowel. The diagnosis of primary liver cell carcinoma was made by blind liver biopsy (9 cases), by laparoscopy and liver biopsy (12 cases) or by autopsy (24 cases). In all cases the HBs Ag was investigated by reverse passive haemagglutination (13 cases), by radioimmunoassay (12 cases) or in paraffin sections of the liver (20 cases), stained by the orcein method of Shikata et al¹⁶, as modified by Deodhar et al².

The frequency of schistosomiasis in patients with HCC was compared with the frequency of *Schistosoma mansoni* infection in people living in the Espírito Santo State. For this purpose we used: (a) the result of a stool survey performed by the Health Ministry among children of elementary school in all the counties of the State, and (b) the frequency of *Schistosoma mansoni* infection among patients that attended medical care in Vitoria. For comparison the chi squared test, with the Yates correction, was used.

RESULTS

In 45 cases of hepatocellular carcinoma, six had *Schistosoma mansoni* infection (13.04%). Nevertheless, none of the patients had the hepatosplenic

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form of the disease (Symmers' fibrosis). The frequency of schistosomiasis associated with HCC HBs Ag positive or negative was similar: three cases among 23

HCC HBs Ag positive (13.33%), and three cases among 22 HCC HBs Ag negative (13.6%). These results are summarized in Table 1.

Table 1 – Frequency of *Schistosoma mansoni* infection among patients with hepatocellular carcinoma and in two samples of population living in Espírito Santo State.

S. mansoni infection	Children of elementary school *	People who attended medical care in Vitoria**	Hepatocellular carcinoma diagnosed in Vitoria		
			Total	HBsAg+	HbsAg-
Positive	43650 (94,03%)	41025 (93,26%)	39 (86,96%)	20 (86,67%)	19 (86,37%)
Negative	2772 (5,97%)	2967 (6,74%)	6 (13,04%)	3 (13,33%)	3 (13,63%)
Total	464222	43992	45	23	22

* Result of a coprologic survey by direct stool examination performed by the Health Ministry (SUCAM-Regional E. Santo) among children (7-12- years old) during the period 1978-1980.

** Data obtained from one laboratory for stool examinations that used routinely the Kato-Katz method during the period 1979-1981 (personal communication of Dr. D.B. Pereira Jr.).

DISCUSSION

Schistosomiasis associated with HCC has been noted by some authors. Nkrumah¹³ found a liver cell carcinoma in a boy with schistosomiasis in Ghana, and Edington⁴ reported a similar finding in Nigeria. In Bahia State, Brazil, Cheever and Andrade¹ showed that HCC was more common in uninfected cases than in those with *Schistosoma mansoni* infection. Also Martinez-Maldonado¹¹ considered that schistosoma infection played no part in the etiology of hepatocarcinoma in Puerto Rico.

Our observations showed that 13.04% of HCC diagnosed in Vitoria, Espírito Santo State, were associated with *Schistosoma mansoni* infection. This frequency of schistosoma infection is not significantly different from that of schistosomiasis in people living in Espírito Santo. Stool examinations of children (7-12 year old) in different counties of the State showed that 5.9% had schistosoma infection, but 8 to 26% of infection were observed in the West counties (information obtained from SUCAM, Health Ministry, Section of Espírito Santo State). In Vitoria, the frequency of schistosoma infection among people who attend the health service, investigated by the Kato-Katz method, was 6.7% during the period 1979-1981 (personal communication of Dr. D.B. Pereira Jr.). The comparison of the frequency of schistosomiasis in patients with HCC with the frequency of *Schistosoma*

mansoni infection among these two samples of the population living in the Espírito Santo showed that the differences are not significant (Table 2). This observation is influenced by the great number of patients with HCC came from the West counties of the state, where the frequency of *Schistosoma mansoni* infection in the population is higher.

Table 2 – Chi squared comparison between the frequency of *S. mansoni* infection associated with hepatocellular carcinoma and in the general population living in the E. Santo State.

Hepatocellular carcinoma	Observed	Expected (a)	Expected (b)
with <i>S. mansoni</i>	6	2.69	3.03
without <i>S. mansoni</i>	39	42.31	41.97
chi squared values		3.19*	2.16*

(a) Children of elementary school
(b) People who attended medical care in Vitoria.
* p > 0.05

In the hepatosplenic form (Symmers' fibrosis) of schistosomiasis the hepatic lesions are severe and the association with persistent hepatitis B virus infection is frequent^{6 10}. Hepatitis B virus is considered one possible etiological factor of HCC⁷. Therefore, the association of HCC with the hepatosplenic

form of the schistosomiasis should be frequent. Nevertheless, we did not find cases of HCC associated with Symmers' fibrosis. On the other hand, HBs Ag is frequently associated with HCC in our county¹⁵, but in this series the occurrence of HBs Ag positive and negative HCC cases with schistosomiasis were similar. Therefore, we think that the association of HCC and schistosoma infection in endemic areas of schistosomiasis is casual. However, it would be interesting to study the occurrence of HCC in schistosoma infected patients treated with hycanthone, a hepatotoxic drug that can produce post-necrotic cirrhosis⁵ and with carcinogenic effects in laboratory animals^{8,9}.

SUMÁRIO

Foi estudada a associação de infecção pelo *Schistosoma mansoni* em pacientes portadores de carcinoma hepatocelular (CHC) diagnosticados no Espírito Santo. O diagnóstico de esquistossomose foi feito pelo exame parasitológico das fezes ou pelos achados histológicos à necrópsia. O diagnóstico de CHC foi feito por laparoscopia e biópsia, somente biópsia ou por necrópsia. Entre 45 casos de CHC, seis apresentavam infecção pelo *S. mansoni* (13,04%). A ocorrência de infecção esquistossomótica nos CHC HBsAg positivos ou negativos foi semelhante (13,33 e 13,63% respectivamente). A comparação pelo método do qui quadrado não mostrou diferença significativa entre a frequência de infecção esquistossomótica nos pacientes com CHC e a frequência de esquistossomose na população que vive no E. Santo (5,97% entre crianças do curso primário de todas as regiões do Estado e 6,75% entre a população que procura recursos médicos em Vitória, a capital do Estado). Desta forma os autores acreditam que a associação de infecção esquistossomótica e CHC deve ser casual, especialmente nas áreas onde a esquistossomose é frequente.

Palavras chaves: Esquistossomose mansônica. Carcinoma hepatocelular.

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