

# Very low prevalence of hepatitis C virus infection in rural communities of northeastern Brazil with a high prevalence of schistosomiasis mansoni

## Muito baixa prevalência de infecção pelo vírus da hepatite C em comunidade rural do nordeste brasileiro com elevada prevalência de esquistossomose mansônica

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### ABSTRACT

*The association of hepatitis C virus infection and the hepatosplenic form of schistosomiasis mansoni has been claimed to result in the concomitant evolution of the two pathologies, with a poor prognosis due to aggravated liver disease. Recently, however, some authors have begun to reject the hypothesis of a higher susceptibility of hepatosplenic schistosomal patients to HCV. The aim of the present transverse study carried out between July and August 1990 was to determine the possible association between SM and HCV markers in residents of Catolândia, Bahia State. Anti-HCV markers were assayed by ELISA-II and RIBA-II in serum samples obtained from 1,228 residents (85.8%). The anti-HCV antibody (ELISA-II) was positive in six (0.5%) individuals, eight (0.6%) cases were inconclusive and 1,214 (98.9%) were negative. However, only in one ELISA-positive serum sample (0.08%) were antibodies confirmed by RIBA-II, while two other samples assayed by RIBA-II were indeterminate. These three patients presented the hepatointestinal form of SM during the follow-up period (1976 to 1996). In conclusion, no association was observed between HCV and SM in the endemic area studied, especially among patients with the hepatosplenic form of the disease.*

**Key-words:** Schistosomiasis mansoni. Hepatitis C. Schistosoma mansoni. Brazil.

### RESUMO

*Alguns autores passaram a rejeitar a hipótese da maior susceptibilidade dos esquistossomóticos com a forma clínica hepatoplênica ao vírus da hepatite C, justificando que a associação foi descrita em pacientes hospitalizados ou acompanhados em serviços de saúde e, conseqüentemente, mais expostos à transmissão destes vírus, durante os procedimentos diagnóstico e/ou terapêuticos. Desse modo, o objetivo foi verificar se há ocorrência de associação da esquistossomose mansônica e marcador do VHC em moradores de Catolândia (Bahia, Brasil). Neste estudo transversal, os anticorpos anti-VHC foram pesquisados (ELISA-II) em 1.228 (85,8%) moradores, com os seguintes resultados: Seis (0,5%) soropositivos, oito (0,6%) inconclusivos e 1.214 (98,9%) soronegativos. Todavia, somente em um soro ELISA-positivo (0,08%) os anticorpos foram confirmados pelo RIBA-II e dois outros (ELISA-II positivos) apresentaram RIBA-II indeterminado – esses três casos, durante período de seguimento (1976 – 1996), sempre tiveram a forma hepatointestinal da esquistossomose mansônica. Em conclusão a hipótese de associação entre a esquistossomose mansônica e o VHC nesta área endêmica foi rejeitada, especialmente entre os portadores da esquistossomose mansônica com a forma clínica hepatoplênica.*

**Palavras-chaves:** Esquistossomose mansônica. Hepatite C. Schistosoma mansoni. Brasil.

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Several lines of evidence have favored an association between hepatitis B virus (HBV) infection and the hepatosplenic form of schistosomiasis mansoni (SM)<sup>26</sup>. More recently, however, this association has been revised<sup>6,24,29</sup>, with the conclusion that it is due to a greater exposure to HBV rather than to a higher susceptibility of individuals with SM to hepatotropic viruses, i.e., HBV and hepatitis C virus (HCV).

Despite phylogenetic differences between HBV and HCV, their mechanisms of transmission show some similarities<sup>11</sup>. Thus, one might speculate that HCV infection is associated with SM, especially among patients with the severe hepatosplenic form of the disease.

Before the HCV era, some patients with hepatosplenic schistosomiasis and a histopathology compatible with chronic viral hepatitis did not present HBV markers in serum or hepatic tissue<sup>16,17</sup>. Similar findings have been reported in Brazil by Andrade et al<sup>3,4</sup>.

After characterization of HCV by Choo et al<sup>7</sup> and the consequent possibility of detecting HCV markers in serum, Lins<sup>16</sup> showed that the frequency of individuals with anti-HCV antibodies does not differ between patients with the hepatointestinal form of SM and those with the hepatosplenic form.

Other authors<sup>1,2,5,8,10,12,13,14,15,31</sup> have provided evidence suggesting that the presence of anti-HCV antibodies is associated with schistosomiasis, but contradictory data exist. However, it should be noted that these authors used different serologic methods. In addition, these studies were conducted on patients recruited from referral centers and not from rural Brazilian communities where *Schistosoma mansoni* is endemic.

Based on the clinical and immunological peculiarities of SM and hepatitis C in Brazil, the aim of the present study was to determine the possible association between the two diseases in an area endemic for SM.

## MATERIAL AND METHODS

A cross-sectional population-based study was conducted on residents from an SM endemic area in the county of Catolândia<sup>29</sup>, which is located in the western region of the State of Bahia, Brazil (12°8' latitude South and 44°52' longitude West of Greenwich).

A longitudinal study on the morbidity of SM was started in the study area in 1976, and since then the clinical forms of the disease were classified according to the criteria of Prata<sup>22,24</sup>. In addition, the clinical involution of the hepatosplenic forms of SM after antiparasitic treatment was observed along the study<sup>24,30</sup>.

Anti-HCV antibodies were screened using a second-generation enzyme immunoassay kit (ELISA-II, Abbott®, Chicago, IL, USA)<sup>31</sup>. Anti-HCV-positive sera, those providing doubtful results were tested by a second-generation recombinant immunoblot method (Ortho Diagnostic Systems Inc®, Emerville-CA, USA).

Clinical examination of the patients was carried out without knowledge of the anti-HCV result.

## RESULTS

Of the 1,432 residents in the study region, 1,228 (88.9%) provided complete information and were tested for anti-HCV. Table 1 and Table 2 summarize the demographic characteristics (gender and age) and the frequency of different clinical forms of SM in this population.

**Table 1 - Demographic characteristics (gender and age) of the population from Catolândia, according to place of residence (rural or urban).**

Characteristic	Population				Statistics
	urban (n= 717)		rural (n=556)		
	n°	%	n°	%	
Gender					
male	348	48.5	280	50.4	$\chi^2_1=0.35$ p>0.54
female	369	51.5	276	49.6	
Age group					
0 — 7	162	22.6	102	18.3	$\chi^2_8=23.07$ p<0.003
8 — 15	181	25.2	148	26.6	
16 — 23	85	11.9	86	15.5	
24 — 31	75	10.0	45	8.1	
32 — 39	72	10.0	28	5.0	
40 — 47	45	6.3	45	8.1	
48 — 55	40	5.6	36	6.5	
56 — 63	19	2.7	20	3.6	
64 — 90	41	5.7	46	8.3	
Mean age ( $\mu \pm SD$ )	23.6 $\pm$ 19.6		25.7 $\pm$ 21.4		t=-1.78* p>0.07*

\* F test=1.20, p<0.002, degrees of freedom=1137.35.

**Table 2 - Distribution of the clinical forms of schistosomiasis mansoni in the population from Catolândia, according to gender, age and place of residence.**

Characteristic	Clinical form n (%)						Statistics
	hepatointestinal HI (n=1,165)		advanced HI AHI (n=66)		hepatosplenic HS (n=42)		
Gender							
male	585	93.8	20	3.1	23	3.7	$\chi^2=1.18^*$ p>0.26
female	580	89.9	46	7.1	19	3.0	
Mean age (m $\pm$ SD)	23.6 $\pm$ 20.4		33.4 $\pm$ 18.5		35.2 $\pm$ 17.4		**
Place of residence n(%)							
urban	640	89.3	41	5.7	36	5.0	$\chi^2=15.27^*$ p<0.0001
rural	625	94.4	25	4.5	6	1.1	

\* Mantel-Haenszel test; \*\* HI vs AHI: t=-3.79, p<0.0001 (F=1.22, p>0.29); HI vs HS: t=-3.62, p<0.0001 (F=1.39, p>0.18); AHI vs HS: t=-0.51, p>0.60 (F=1.13, p>0.67).

With respect to the presence of anti-HCV antibodies, six (0.5%) patients were positive, eight (0.6%) were inconclusive, and 1,214 (98.9%) were negative.

In only one sample of 14 tested (6 positive, 8 inconclusive) by ELISA-II commercial Kits (Boehringer-Germany) anti-HCV was confirmed by the RIBA-II test (Chiron, Emerville, CA®). Two (0.2%) individuals presented results classified as indeterminate by RIBA-II (both showing antibodies against the recombinant protein c100-3).

All six residents presenting anti-HCV antibodies, as well as the eight individuals with inconclusive results, as determined by ELISA-II, had the hepatointestinal form of SM, with the age of these patients ranging from 5 to 66 years (18.9  $\pm$  9.4).

## DISCUSSION

Despite massive anti schistosomal treatment and improved sanitary conditions, the frequency of schistosomal infection continues to be high in this area. Progressively higher frequencies of individuals excreting *S. mansoni* eggs among those seeking the Catolândia public health service were observed during the period from 1993 (35.8%) to 1996 (65.4%)<sup>29</sup>. Thus, SM was the main cause of morbidity and mortality in Catolândia until the mid-eighties<sup>30</sup>. The hepatosplenic form was diagnosed in 187 (8.3%) registered residents (n=2,241) during the study period from 1976 to 1996.

Although the population of Catolândia shows a reasonable geographic and cultural isolation<sup>27,28</sup>, temporary residence and/or occupation in other states are frequent; for example, during the study period 273 (12.2%) of the 2,241 individuals registered migrated<sup>28</sup>.

In the early eighties, residents from Catolândia commonly underwent medical treatment in some nearby capitals. Thus, a temporary migratory flow might have facilitated the introduction or increased dissemination of HCV in the region, where the lack of health services represents another characteristic predisposing to the use of parenteral medication under inadequate conditions, a fact that could also have contributed to the dissemination of HCV in many regions of Brazil.

Based on the fact that this region is hyperendemic for SM, with patients developing upper gastrointestinal bleeding by rupture of the esophageal varices and receiving blood transfusions when treated at larger centers, the introduction and dissemination of HCV can be expected in this region.

The finding of the present study of only one individual with anti-HCV and without a history of travel to or residence in other towns supports the hypothesis that in this endemic SM area the risk of transmission of HCV was not increased. In addition, the seroprevalence of anti-HCV antibodies observed for residents from Catolândia was lower than the 1.7% prevalence estimated for blood donor candidates from the metropolitan region of Salvador, capital of the State of Bahia (Santana et al, unpublished data).

Silva et al<sup>25</sup> observed a 1.2% prevalence of anti-HCV antibodies in individuals from the metropolitan region of Salvador, and a 0% prevalence of anti-HCV in a populational study carried out in the rural area of the State of Bahia, Northeast of Brazil. Other studies concerning the seroprevalence of HCV in the State of Bahia were carried out on populations at risk of acquiring HCV infection<sup>19,23</sup>, while there were no populational studies. However, the results reported by Silva et al indicate a very low prevalence of HCV among residents of rural communities also endemic for *S. mansoni* infection.

Based on these results we may also speculate that the *S. mansoni* occurring in the rural areas of the State of Bahia does not influence the transmission or dissemination of HCV. This finding contrasts with Egyptian studies that demonstrated high HCV prevalence in SM endemic areas probably due to parenteral treatment for *schistosomiasis* using non-disposal

material<sup>32</sup>. In Brazil, non-disposal needles were used in the past but it seems that this practice was concentrated in larger urban centers<sup>20</sup>.

With respect to reviews<sup>6,26</sup> proposing a possible association between the hepatosplenic form of SM and infection with hepatotropic viruses, notably HBV, one can also speculate that the same spurious association exists with HCV, i.e., the association reported between the hepatosplenic form and HBV<sup>26</sup> and, more recently, between the hepatosplenic form and HCV<sup>1,2,5,8,10,14,13,15,21,32</sup>, is more likely to be due to greater exposure to these viruses during diagnostic and/or therapeutic procedures at health services rather than to a higher susceptibility of hepatosplenic individuals to hepatotropic viruses.

Our results show that during the more than 20 years of the sentinel study in Catolândia co-infection with HCV was negligible in patients with SM<sup>29,30</sup>. In the only case with confirmed anti-HCV antibodies, hepatic biochemical tests, especially aminotransferases, were found to be normal. However, hepatic enzymes showed fluctuations in these individuals throughout the evaluation period, including periods of normality.

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