

High seroprevalence of hepatitis B and C markers in the upper Madeira River region, Porto Velho, Rondônia State, Brazil

Alta soroprevalência dos marcadores das hepatites B e C na região do alto rio Madeira, Porto Velho, Rondônia, Brasil

Alta seroprevalencia de los marcadores de las hepatitis B y C en la región del alto río Madeira, Porto Velho, Rondônia, Brasil

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ABSTRACT

A seroprevalence study on the serologic markers of hepatitis types B and C on the inhabitants of the upper Madeira River, between the communities of Santo Antonio and Abunã, in the Municipality of Porto Velho, Rondônia State, was conducted. This locality will be flooded by two new hydropower plants yet to be built in the Madeira River. Local population was estimated in 5 thousand individuals, according to *Instituto Brasileiro de Geografia e Estatística's* (Brazilian Institute of Geography and Statistics) census. A sample of 10% of the population was randomly selected. Five milliliters of peripheral venous blood were collected in Vacutainer® dry tubes, and the serum samples were maintained in a freezer at -20° C. ELISA serological tests (DiaSorin, Inc.) were performed according to the manufacturer's methodology for the following viral markers: total Anti-HBc, HBsAg, Anti-HBs and Anti-HCV. After the processing of 431 samples, the results were: 192 (44.5%) were positive for total Anti-HBc, 29 (6.7%) were positive for HBsAg, 230 (53.4%) were positive for Anti-HBs, and 32 (7.4%) were positive for Anti-HCV. We concluded that this region presented an intermediate and a high prevalence rate for hepatitis B and C, respectively, according to the World Health Organization. The high prevalence (more than 50%) of individuals immune to hepatitis B leads us to the conclusion that in the next decades problems related to that type of hepatitis tend to decrease, whereas the incidence of hepatitis C will probably increase. Migration of thousands of new inhabitants drawn by the implementation of the new hydropower plants in this region has the potential of worsening the public health issues related to these viral hepatitis infections.

Keywords: Hepatitis B; Hepatitis C; Serology; Enzyme-Linked Immunosorbent Assay; Cross-Sectional Studies.

INTRODUCTION

It is estimated that between 300 and 350 million people worldwide are carriers of hepatitis B⁸. The hepatitis B virus

(HBV) may cause severe fulminant disease with up to a 0.5% mortality in the acute phase and chronic infections that may result in serious complications, such as liver cirrhosis and hepatocellular carcinoma, in approximately 25% of patients^{16,10}.

Antibodies against the hepatitis C virus (HCV) are found in 2.5% to 4.9% of the Brazilian population; that is, approximately 3.9 to 7.6 million people are infected by this virus⁴. The risk of developing liver cirrhosis and/or cancer is high in this group^{4,18}.

The state of Rondônia in West Amazonia is an area with a high endemicity of hepatitis B and C, possibly due to past

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lapses in prenatal care and the low quality of blood transfusions in addition to other social or cultural factors, such as sexual promiscuity or sharing of personal hygiene products¹¹.

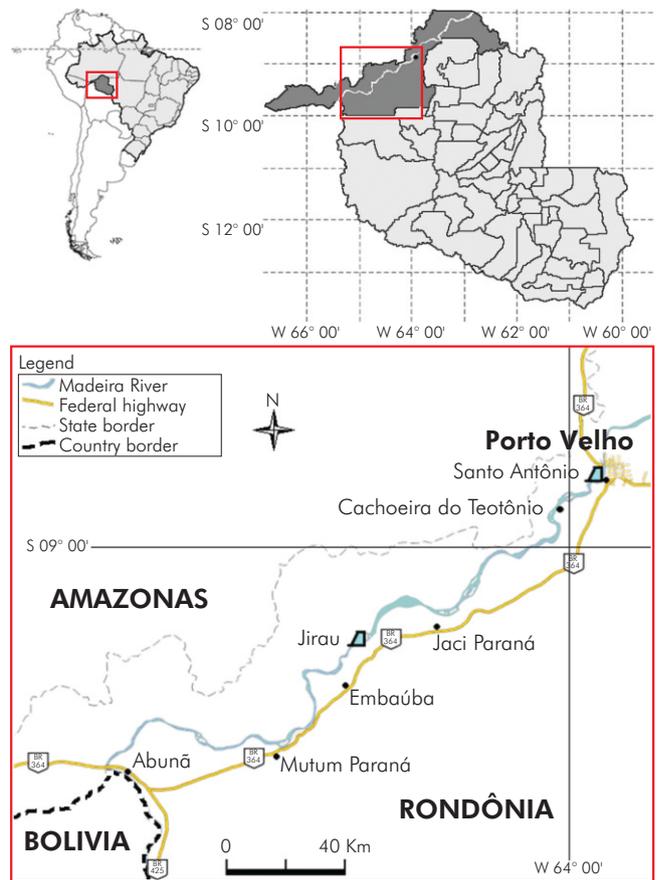
Previous studies performed in rural areas of Rondônia found a prevalence of 67.9% for anti-HBc total antibodies and 7.8% for HBsAg (Villalobos-Salcedo, personal communication).

In accordance with the local data on their high prevalence, this cross-sectional study aimed to confirm the prevalence of hepatitis B and C serum markers among the riverine population of the Municipality of Porto Velho, which mostly comprises native residents.

MATERIALS AND METHODS

STUDY POPULATION

This cross-sectional study was performed in the Municipality of Porto Velho, Rondônia State, between the communities of Santo Antônio and Abunã (Figure 1) from August 2004 to February 2005. This area equated to a population of 5,294 residents, according to the *Instituto Brasileiro de Geografia e Estatística-IBGE* (Brazilian Institute of Geography and Statistics). Initially, 1,662 dwellings were registered, of which 624 were vacant. A 10% sample of all the inhabited homes was randomly selected using the *EpilInfo®* software. When the house selected was vacant at the time of the visit, the next inhabited home was surveyed. Due to the extent of the area under study, it was divided into segments, which are described in table 1. Segments 1, 2, 3, and 4 corresponded to the population residing between the communities located on the riverside of the Madeira River (1 - Santo Antônio/Cachoeira do Teotônio, 2 - Cachoeira do Teotônio/Jaci Paraná, 3 - Jaci Paraná/Jirau, 4 - Jirau/Abunã), whereas segments 5, 6, 7, 8, and 9 corresponded to the population residing in the same area but along the federal highway BR 364 that runs along the Madeira River (5 - Santo Antônio, 6 - Jaci Paraná, 7 - Embaúba, 8 - Mutum Paraná, 9 - Abunã). These areas are located within the direct impact area of the Santo Antônio and Jirau Hydroelectric Power Plants (HPP) (Figure 1).



Source: LabEpi/IPEPATRO/CEPEM.
 Note: Santo Antônio and Jirau are the possible sites for the installation of the hydroelectric power plants. Jaci Paraná, Embaúba, Mutum Paraná, and Abunã are close to federal highway BR 364 in the direction Porto Velho (RO) – Rio Branco (AC).

Figure 1 – Map of the study area

HEPATITIS B AND C SERUM MARKERS – TOTAL ANTI-HBc, HBsAg, ANTI-HBs, AND ANTI-HCV

All participants were subjected to clinical interviews, and a 5 mL peripheral blood sample was collected using disposable syringes and needles and anticoagulant-free vacuum tubes. To evaluate HBV and HCV serum markers (total Anti-HBc, HBsAg, Anti-HBs, and Anti-HCV), enzyme-linked immunosorbent assays (ELISAs) were performed according to the manufacturer's instructions (DiaSorin, Inc.).

Table 1 – Distribution of hepatitis B and hepatitis C serum markers by investigated segment (2004-2005)

Segment	P	n	Hepatitis B						Hepatitis C	
			Total Anti-HBc		HBsAg		Anti-HBs		Anti-HCV	
			N	%	N	%	N	%	N	%
1 – Sto Antônio / Teotônio	423	76	28	36.8	9	11.8	35	46.1	4	5.3
2 – Teotônio / Jaci Paraná	333	87	43	49.4	8	9.2	43	49.4	13	14.9
3 – Jaci Paraná / Jirau	106	21	10	47.6	1	4.8	10	47.6	1	4.8
4 – Jirau / Abunã	100	24	10	41.7	–	–	12	50.0	2	8.3
5 – Santo Antônio	100	34	13	38.2	2	5.9	19	55.9	2	5.9
6 – Jaci Paraná	2,826	96	49	51.0	5	5.2	66	68.8	6	6.3
7 – Embaúba	100	4	1	25.0	–	–	3	75.0	–	–
8 – Mutum Paraná	613	39	22	56.4	1	2.6	20	51.3	3	7.7
9 - Abunã	693	50	16	32.0	3	6.0	22	44.0	1	2.0
Total	5,294	431	192	44.5	29	6.7	230	53.4	32	7.4
^{95%} CI			(39.9-49.3)		(4.7-9.5)		(48.6-58.0)		(5.3-10.3)	

P = resident population; n = number of participants in the study; N = number of individuals with positive serum markers; % = percentage of corresponding "n" in the same row; ^{95%} CI = confidence interval of "Total"; Employed conventional data: - numeric data equal to zero not resulting from rounding.

Note: Segments 1 to 4 are part of Madeira River flume (riverine population); for these segments, "P" stands for residents in the indicated locations. Segments 5 to 9 are located along federal highway BR 364.

DATA ANALYSIS

Positive results for hepatitis B serum markers, HBsAg or total Anti-HBc, were used to establish the prevalence of HBV infection. The prevalence of HBV and HCV chronic infection was established from the proportion of HBsAg-positive results for hepatitis B and Anti-HCV for hepatitis C. Positive results were defined as Anti-HCV serum levels at 2.5 times the cut-off point for the optic density established by the manufacturer, according to the recommendations by the *Programa Nacional de Hepatites Virais* (National Program for Viral Hepatitis). Prevalence was expressed in absolute values and the corresponding 95% confidence intervals ($_{95\%CI}$). Data were analyzed using the software EpiData Analysis® V2.2.1.171.

RESULTS

A total of 431 participants distributed among 116 dwellings were included. Samples were collected from residents of Santo Antônio, Cachoeira do Teotônio, Jaci Paraná, Jirau, Embaúba, Palmeiral, Mutum Paraná, and Abunã, including individuals up to 88 years of age who had lived in the area for 0.1 to 83.0 years (average = 21.6); the majority comprised natives from Rondônia (59.8%). This study was approved by the Research Ethics Committee of the *Centro de Pesquisa em Medicina Tropical* (Tropical Medicine Research Center) (CEP-CEPEM). All participants signed an informed consent form upon their inclusion.

Positive serum markers were distributed as follows: for total Anti-HBc 192 (44.5%; $_{95\%CI}$: 39.9-49.3), the highest percentage was found in segment 8 (Mutum Paraná); for HBsAg 29 (6.7%; $_{95\%CI}$: 4.7-9.5), the highest percentage was found in segment 1 (Santo Antônio/Teotônio); for Anti-HBs 230 (53.4%; $_{95\%CI}$: 48.6-58.0), the highest percentage was found in segment 7 (Embaúba); and for Anti-HVC 32 (7.2%; $_{95\%CI}$: 5.3-10.3), the highest percentage was found in segment 2 (Teotônio/Jaci Paraná) (Table 1).

Upon stratification by age range, the serum markers that exhibited the highest percentages were as follows: total Anti-HBc in ages less than 5 years old, HBsAg in the 30 to < 50 years age range, and Anti-HBs in the 5 to <15 years age range. The highest percentage of hepatitis C was found in the 5 to <15 years age range (Table 2).

Participants who carried chronic hepatitis B and who were immunized by contact, vaccinated, isolated and exhibited negative results for all tested serum markers are described in Table 3. Only one individual from the 5 to <15 year age range, who resided in segment 2, exhibited positive serum markers for hepatitis B and C (0.2%; $_{95\%CI}$: 0.0-1.3).

Among all investigated individuals, four concomitantly exhibited positive results for all three hepatitis B serum markers (total Anti-HBc, HBsAg, and Anti-HBs), but further testing could not be performed because they could not be located again.

Table 2 – Distribution of hepatitis B and hepatitis C serum markers by age range and sex (2004-2005)

Age range (years)	Individuos				Hepatitis B						Hepatitis C	
	M	F	T	%* ($_{95\%CI}$)	Total Anti-HBc		HBsAg		Anti-HBs		Anti-HCV	
					N	%	N	%	N	%	N	%
< 5	7	6	13	3.0 (1.8-5.1)	7	53,8	1	7.7	2	15.4	1	7.7
5 to < 15	63	52	115	26.7 (22.7-31.1)	52	45,2	6	5.2	60	52.2	14	12.2
15 to < 30	46	61	107	24.8 (21.0-29.1)	52	48,6	6	5.6	64	59.8	10	9.3
30 to < 50	57	55	112	26.0 (22.1-30.3)	54	48,2	10	8.9	58	51.8	5	4.5
> 50	55	29	84	19.5 (16.0-23.5)	27	32,1	6	7.1	46	54.8	2	2.4
Total	228	203	431	100.0	192	44,5	29	6.7	230	53.4	32	7.4

M = male; F = female; T = total; N = number of individuals with positive results to analyzed parameter; * = percentage of total participants in the study; % = percentage regarding "T".

Table 3 – Distribution of the hepatitis B serologic profiles of the 431 residents from the study area (2004-2005)

Age range (years)	n	VAC		ISO		HEA		CHR		SUC		PSM	
		N	%	N	%	N	%	N	%	N	%	N	%
		< 5	13	-	-	4	30.8	2	15.4	1	7.7	6	46.2
5 to < 15	115	24	20.9	10	8.7	36	31.3	6	5.2	39	33.9	-	-
15 to < 30	107	30	28.0	13	12.1	33	30.8	5	4.7	25	23.4	1	0.9
30 to < 50	112	20	17.9	7	6.3	37	20.2	9	8.0	38	33.9	1	0.9
> 50	84	27	32.1	5	6.0	17	29.0	3	3.6	30	35.7	2	2.4
Total	431	101	23.4	39	9.0	125	29.0	24	5.6	138	32.0	4	0.9
$_{95\%CI}$			19.7-27.7		6.7-12.1		24.9-33.5		3.8-8.2		27.8-36.6		0.4-2.4

n = number of participants; VAC = individuals with a serologic profile suggesting immunization by vaccination; ISO = individuals with a total Anti-HBc + isolated serologic profile; HEA = individuals with a serologic profile suggesting a healed infection; CHR = individuals with a chronic carrier serologic profile; SUC = individuals with a susceptible serologic profile; PSM = individuals with positive total Anti-HBc, HBsAg, and Anti-HBs; (%) = percentage of "n" in the same row; $_{95\%CI}$ = confidence interval of "Total"; Employed conventional data: - numeric data equal to zero not resulting from rounding.

DISCUSSION

The geographical area investigated in this study was chosen to be the site of two new HPPs that will be built at the upper Madeira River, specifically in the communities of Santo Antônio and Jirau. Together with the onset of actual construction, approximately 100 thousand new inhabitants, attracted by trade and job openings, are expected. However, there is no basic sanitary system in this area, and the small towns close to the implicated area have poor health care facilities.

The prevalence rates found for both HBV and HCV are high according to the classification system by the World Health Organization (WHO)¹⁸.

In Brazil, the extent of HBV infection is highly variable and is related to the area under investigation. Prevalence rates as high as 82.9% were found among northern Mato Grosso miners¹⁷, whereas in Rio de Janeiro, the rate was 40%¹⁰. Some studies point to low prevalence rates in Bolivia, which borders Rondônia; however, updated research is needed to confirm these rates. High migration rates and the early onset of sexual activity, among other factors, might explain the high prevalence of hepatitis in Rondônia. This migration was mainly observed during the 1970s and 1980s when agriculture settlements were established and the federal highway BR 364 was opened, in addition to the local mining activity.

The prevalence of HBV carriers among the Rondônia indigenous populations varies between 3.4% and 9.7%, whereas the prevalence of a past infection varies between 35.3% and 54.5%^{6,2}. In Lábrea, Amazonas State, which is close to Porto Velho, the prevalence for HBsAg was found to be 3.3% and 49.9% for total Anti-HBc³. The proximity of indigenous reservations to the area of influence of the HPPs certainly increases the risk of transmission.

Vertical and perinatal transmission has been characterized to be of little significance in the Amazon Region by some authors⁷. However, many studies point to the Northern Region as exhibiting the highest hepatitis B prevalence^{2,7,5}, and it is currently known that adult carriers were contaminated when they were newborns or before 5 years of age. In Mato Grosso State, an epidemic affecting new settlers was detected in 1995, and the same study demonstrated the importance of vaccination campaigns among the stable and migrant populations. It was further observed that most of the population was composed of migrants from Rondônia and that the variables associated with the infection were sexual activity, use of alcohol, contact with hepatitis carriers, and having lived in a mining area.^{17,1}

In rural areas in São Paulo State, the prevalence found for one or more hepatitis B serum markers was 7.7%, whereas among the 0 to 15 years age range, it was 4.7%; it was further observed that the prevalence was higher among rural populations compared with urban populations¹⁴.

The prevalence rate was found to be 6.7% for HBV carriers in this study, which classifies Rondônia as a high endemicity area. The high prevalence of Anti-HBs (53.4%) shows that most of the population is immunized, either naturally or actively, against hepatitis B. When considering individuals with positive results for Anti-HBs and negative results for total Anti-HBc (102) to be immunized by means of vaccination, it is noteworthy that 63.7% of these individuals belong to the 0 to 14 years age range. This result indicates that probably only 23.7% of participants in this study were vaccinated against hepatitis B.

Considering the aforementioned set of data, the World Health Organization would classify Rondônia as an area with an intermediate endemicity for hepatitis B¹⁸. Thus, more efforts should be devoted to active immunization, which should become a permanent policy in areas that are subjected to the effects of the HPPs. Indeed, the communities exhibiting the highest prevalence of both hepatitis B and C are very close to the sites designated for the new HPPs.

The use of injected drugs and blood derivatives plays an important role in HCV transmission. In developed countries, this rate can reach up to 12.6%¹⁵. In Brazil, the anti-HCV prevalence was reported to be from 1.0% to 3.0%, and the main risk factors were the use of injected drugs, blood transfusions, and tattoos^{4,12}.

According to data supplied by the Ministry of Health, 1,831 cases of hepatitis C were confirmed in the Northern Region between 1999 and 2005, of which 400 (21.8%) occurred in Rondônia¹³. Analysis of these data shows that the incidence of hepatitis C was 2.7/100,000 inhabitants in 1999 and 5.8/100,000 in 2005, thus representing more than a 100% increase in this period. This study showed alarming rates for the prevalence of hepatitis C, although the sample does not represent the state as a whole. For this reason, further studies are needed that better represent this area.

Data available from the Rondônia State Secretary of Health do not agree with the data from the Brazilian Ministry of Health; therefore, a precise statistical analysis is difficult. Nevertheless, the Federal Government reports a gradual increase of confirmed cases throughout the country. In this regard, the data show that among the Northern States, the rates in Rondônia are second only to Acre for reported cases¹³.

CONCLUSION

According to the developers, it is estimated that the area around the HPP construction sites along the Madeira River in Santo Antônio and Jirau will attract approximately 100 thousand new inhabitants, comprising workers directly or indirectly involved with the construction. However, the local health authorities are not engaged in any educational or preventative campaigns. The large number of susceptible individuals found in this study

confirms this fact. The high prevalence of hepatitis B and C serum markers found in this study indicates that measures must be urgently enacted to control and treat existing cases, as well as to prevent the transmission and appearance of new cases by the use of vaccination campaigns and educational programs.

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Alta soroprevalência dos marcadores das hepatites B e C na região do alto rio Madeira, Porto Velho, Rondônia, Brasil

RESUMO

Foi realizado um estudo de soroprevalência de marcadores sorológicos de hepatites B e C na população residente no alto rio Madeira, entre as localidades de Santo Antônio e Abunã, no Município de Porto Velho, Rondônia, local previsto para ser inundado pelas novas hidrelétricas do Madeira. A população local foi estimada em 5 mil pessoas, segundo o censo do Instituto Brasileiro de Geografia e Estatística, e uma amostra populacional de 10% foi selecionada de modo aleatório. Coletaram-se 5 mL de sangue periférico por punção venosa em tubo seco e o soro foi conservado em freezer a -20° C. Os exames sorológicos tipo ELISA foram realizados seguindo a metodologia do fabricante, para os seguintes marcadores virais: Anti-HBc Total, HBsAg, Anti-HBs e Anti-HCV. Foram processadas 431 amostras, das quais foram obtidos os seguintes resultados: 192 positivas para Anti-HBc Total (44,5%), 29 positivas para HBsAg (6,7%), 230 positivas para Anti-HBsAg (53,4%), 32 positivas para Anti-HCV (7,4%). Concluímos que a região estudada estaria classificada, segundo a Organização Mundial da Saúde, como de prevalência intermediária para hepatite B, e alta para hepatite C. Se considerarmos a alta prevalência de pessoas imunes contra hepatite B (superior a 50%), podemos concluir que, nas próximas décadas, o problema de saúde pública relacionado com a hepatite B tenderá a diminuir. A migração de milhares de novos habitantes para a região sem a devida atenção das autoridades sanitárias para prevenção, vacinação e educação em saúde da população, pode agravar a situação na região em relação a estas hepatites virais.

Palavras-chave: Hepatite B; Hepatite C; Serologia; ELISA; Estudos Transversais.

Alta seroprevalencia de los marcadores de las hepatitis B y C en la región del alto río Madeira, Porto Velho, Rondônia, Brasil

RESUMEN

Fue realizado un estudio de seroprevalencia de marcadores serológicos de hepatitis B y C en la población residente en el alto río Madeira, entre las localidades de Santo Antônio y Abunã, en el Municipio de Porto Velho, Rondônia, local previsto para ser inundado por las nuevas hidroeléctricas del Madeira. La población local fue estimada en 5 mil personas, según el censo del *Instituto Brasileiro de Geografia e Estatística* (Instituto Brasileño de Geografía y Estadística), y una muestra poblacional de 10% fue seleccionada de modo aleatorio. Se colectaron 5 mL de sangre periférica por punción venosa en tubo seco y el suero fue conservado en congelador a -20° C. Los análisis serológicos de tipo ELISA (DiaSorin, Inc) se realizaron siguiendo la metodología del fabricante, para los siguientes marcadores virales: Anti-HBc Total, HBsAg, Anti-HBs y Anti-HCV. Se procesaron 431 muestras, de las cuales se obtuvieron los siguientes resultados: 192 positivas para Anti-HBc Total (44,5%), 29 positivas para HBsAg (6,7%), 230 positivas para Anti-HBsAg (53,4%), 32 positivas para Anti-HCV (7,4%). Concluimos que la región estudiada estaría clasificada, según la Organización Mundial de Salud, como de prevalencia intermedia para hepatitis B, y alta para hepatitis C. Si consideramos la alta prevalencia de personas inmunes contra hepatitis B (superior a 50%), podemos concluir que, en las próximas décadas, el problema de salud pública relacionado a la hepatitis B tenderá a disminuir, mientras que, el relacionado a la hepatitis C, probablemente, aumentará. La migración de miles de nuevos habitantes atraídos por las obras civiles de las hidroeléctricas tiene la potencial capacidad de empeorar la situación de salud pública asociada a estas hepatitis virales.

Palabras clave: Hepatitis B; Hepatitis C; Serology; Prueba ELISA; Estudios Transversales.



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