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INFECTION WITH HEPATITIS C VIRUS AMONG HEALTH CARE WORKERS IN THE BRAZILIAN WESTERN AMAZON REGION (RIO BRANCO, STATE OF ACRE)

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Abstract. Clinical and epidemiologic studies on the hepatitis C virus (HCV) in the western Brazilian Amazon region are scarce. However, reports of clinical cases of hepatitis or pathologies associated to the HCV infection are frequent. In the state of Acre, there have been no studies on the population with the greatest exposure to parenteral transmission of virus infection. The objective of this study was to determine the prevalence of HCV infection among health care workers (HCWs) in this region. Of 2,338 HCWs, 646 were randomly selected for this study. The presence of antibody to HCV was determined. If these persons were antibody positive, they were tested for HCV RNA and the viral genotype was determined. The seroprevalence of antibody to HCV was 4.8% (31 of 646), and 3.7% (24 of 646) of those tested had detectable HCV RNA. Among these 24 viremic cases, HCV genotype 1 was most common (n = 16), followed by genotypes 3 (n = 6), 2 (n = 1), and an unidentified genotype. Infection with HCV (identified by a polymerase chain reaction) was more frequent among those with lower educational levels and lower incomes, those who lived for a longer period in the city of Rio Branco, those who reported intravenous use of vitamin complexes, those with a history of dental treatment, those with alcoholism, and women with history of caesarian parturition. The high prevalence of patients with HCV observed among HCWs in the city of Rio Branco and risk factors indicate the need for prevention and control programs, in addition to assistance programs, because this region is also hyperendemic for hepatitis B virus and hepatitis D virus.

INTRODUCTION

It is estimated that more than 170 million people are infected with the hepatitis C virus (HCV) worldwide. Infection with HCV is the most common cause of patients requiring liver transplants in the Western Hemisphere.[1] In Brazil among potential blood donors, the prevalence of HCV carriers ranges from 0.4% to 3% with distinct regional differences.[2] Transmission of HCV occurs mainly by contact with contaminated blood.[3]

In Brazil, the groups most exposed to the HCV infection are patients who had blood transfusions before 1994, intravenous drugs users, patients undergoing hemodialysis, and those who have used non-disposable syringes.[4] Among other forms of transmission not extensively investigated in Brazil are nosocomial and intrafamilial transmission and transmission through inadequate tattooing procedures.[5] Among health care workers (HCWs) in Brazil, there are no studies on HCV transmission. In the Brazilian Amazon region, a high prevalence of infection with two other hepatotropic viruses (hepatitis B virus and hepatitis D virus) is observed, and a study also reported that this region is hyperendemic for HCV.[7] However, there are no population studies on the prevalence or incidence of the HCV infection in the State of Acre, despite the high frequency of patients with chronic hepatitis C, liver cancer, or extra-hepatic pathologies associated with the HCV infection in health units of the city of Rio Branco. A hospital study in Rio Branco detected HCV in 7 (20.6%) of 34 patients with hemophilia A and in 9 (18.4%) of 49 patients with chronic kidney disease undergoing hemodialysis, and a high prevalence of HCV genotype 1 (Lobato C, unpublished data).

This epidemiologic situation encouraged the investigation of the prevalence of HCV infection among HCWs in the city of Rio Branco in the Western Brazilian Amazon region, where the health units have no HCV infection prevention programs and the hospital infection control services are not satisfactory.

MATERIALS AND METHODS

This study was performed in the city of Rio Branco, State of Acre, from November 20, 2003 to February 28, 2004. Participants were HCWs (physicians, biomedical sciences professionals, nurses, dentists, nursery technicians, laboratory technicians, and cleanness and laundry personnel) who worked at the State of Acre Central Laboratory and at four hospitals: the Emergency Hospital of Rio Branco, the State of Acre General Hospital Foundation, the State of Acre Mental Health Hospital, and the Bárbara Heliodora Maternity Hospital Complex and Children's Hospital. A list of HCWs was requested from each health unit. After exclusion of those involved in administrative activities, the reference population was 2,338 employees. The sample size was defined based on 95% confidence intervals ($P < 0.05$) and on an expected HCV infection prevalence of 2%. A sequential number was added to each name. Numbers were obtained using Epi-Info version 6.0 software (Centers for Disease Control and Prevention, Atlanta, GA). A total of 659 people were then randomly selected to participate and only those who agreed to participate were included. The study was reviewed and approved by the Ethic Research Committee of the State of Acre General Hospital Foundation. Subjects who refused to participate in this study were replaced by subjects from the same health unit and area and with the closest registration number.

Subjects provided demographic and clinical epidemiologic data using a previously tested questionnaire.[8] Venous blood samples were collected, centrifuged (2, 500 × g for 10 min-

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utes), and aliquots of serum were stored at –20°C until used. Antibodies to HCV were detected using enzyme-linked immunosorbent assay kits (Roche, Basel, Switzerland). HCV RNA was detected in seropositive samples with an Amplicor kit (Roche). Genotyping was conducted in samples positive for HCV RNA using Innolipa kits from Innogenetic (Ghent, Belgium).

Results were analyzed by parametric and nonparametric tests according to the type and distribution of variables. The continuous variable in univariate analysis was the mean + SD and it was analyzed with the Mann-Whitney test, the *t*-test, or the Tukey test (one-way analysis of variance *post hoc* test). Categorical variables, which were expressed as proportions, were analyzed with the chi-square test (with or without Yates' correction) or with the Fischer exact test. Odds ratios and their respective 95% confidence intervals were calculated whenever necessary. Variables ($P < 0.25$) associated with HCV infection in univariate analysis were included in a multiple logistic regression model. Data were analyzed using SPSS version 9.0 software (SPSS Inc., Chicago, IL). Results were considered significant if P was ≤ 0.05.

RESULTS

The prevalence of antibody to HCV was 4.8% (31 of 646); 3.7% (24 of 646) were also positive for HCV RNA. Of these 24 cases with HCV RNA, genotype 1 was found in 16 (66.7%), genotype 3 in 6 (25%), and genotype 2 in 1 (8.3%), and an undetermined genotype in 1 (8.3%). We analyzed only patients with viremia because of the low optical density cutoff value observed in non-viremic individuals, which strongly favors false-positive results. In addition, we did not perform a recombinant immunoblot assay confirmatory test. The HCWs were studied in the five health units in Rio Branco. The highest frequency of patients with HCV (4.5%) was observed in HCWs from the Emergency Hospital of Rio Branco, and the lowest frequency (2.1%) was observed in HCWs from the Maternity Hospital Complex and Children's Hospital. However, no statistically significant difference was observed ($\chi^2 = 1.42$, $P > 0.23$) (Table 1).

In all health units, males showed a higher prevalence of HCV ($P < 0.01$), but no differences were observed between persons 20–40 years of age and those more than 41 years of age (Table 2). All persons with viremia (n = 24) were more than 30 years of age (median = 42.5 years, range = 31–59 years, mean ± SD age = 43.4 ± 6.3 years), which was similar ($P > 0.51$) to the age of non-viremic persons (n = 622, mean ± SD = 42.5 ± 9.3 years). The proportion of viremic persons who were Caucasian (2.8%, 11 of 399) was similar ($P > 0.10$) to that in non-Caucasians (5.3%, 13 of 247), which included African and Amerindian descendents. No statistically significant difference was observed ($P > 0.07$) in the frequency of viremia in single (4.5%, 6 of 133) and married (3.5%, 18 of 513) persons. Persons born in the State of Acre (4.2%, 22 of 528) and those born in other states or countries (1.7%, 2 of 118) showed no statistically significant differences for the presence of HCV RNA. Among 646 persons studied, those who lived in Rio Branco for ≤ 20 years (0.6%, 1 of 159) were 7.8 times less likely to test positive for HCV than persons who lived in Rio Branco for > 20 years (4.7%, 23 of 487) ($\chi^2 = 5.62$, $P < 0.02$). Among 275 persons < 40 years of age, HCV RNA was found in 9 (4.4%) of 206 persons who lived in Rio Branco for ≥ 20 years. In persons > 41 years of age, viremia was not related to the time of residence in Rio Branco (1.1%, 1 of 90 for ≤ 20 years versus 5.0%, 14 of 281 for > 20 years) ($P > 0.18$).

Family incomes of the study group ranged from U.S. $100 to U.S. $5.000 (median = U.S. $250, mean = U.S. $350. Persons positive for HCV (5.5%, 18 of 327, mean rank = 235.13) had significantly lower incomes than persons negative for HCV (1.9%, 6 of 319, mean rank = 326.91) ($\chi^2 = 5.93$, $P < 0.02$, by Mann-Whitney test). Those with lower levels of education (did not finish high school or less education) had a significantly higher frequency of HCV positivity (6.8%, 15 of 221) than those with higher levels of education (finished high school or college) (2.1%, 9 of 425) ($\chi^2 = 8.86$, $P < 0.004$). This difference was even more significant ($P < 0.009$) when years spent in school were analyzed by the Mann-Whitney test (HCV carriers, mean rank = of 231.81 versus non-HCV carriers, mean rank = 327.04). The number of people who live in the same dwelling as the HCV carriers and non-HCV carriers was similar (means ranks = 378.06 and 321.39, respectively, $P > 0.13$, by Mann-Whitney test) (variation = 1–12 residents, median and mean = 4 persons). If median values were analyzed (≤ 4 persons versus > 4 persons), the proportion of HCV carriers was similar in both groups (3.3%, 14 of 426 for ≤ 4 persons versus 1.5%, 10 of 220 for > 4 persons; $\chi^2 = 0.64$, $P > 0.42$).

The HCV carriers were stratified by education level and individual income (range = U.S. $100–U.S. $5,000, median = U.S. $400) (Table 3). Among those with low family incomes less than the median and basic levels of education, a higher frequency of HCV carriers was observed than in those with a higher level of education (7.2% versus 2.5%; $P < 0.05$).

TABLE 1
Gender, age and HCV RNA distribution among health care workers from health units of Rio Branco, Brazil*

Health unit	No.	Female No. (%)	Age (years)		HCV RNA by PCR No. (%)
			Mean ± SD	Range	
FUNDHACRE	154	86.4 (133)	40.7 ± 8.7	22–65	3.9 (6)
LACEN	70	87.4 (61)	42.0 ± 9.1	22–66	4.3 (3)
HOSMAC	79	83.5 (66)	45.1 ± 10.6	26–67	3.8 (3)
HUERB	200	72.0 (144)	42.5 ± 8.5	24–63	4.5 (9)
MBH and HC	143	89.5 (128)	43.2 ± 9.7	20–66	2.1 (3)
Total	646	82.4 (532)	42.5 ± 9.2	20–67	3.7 (24)

* HCV = hepatitis C virus; PCR = polymerase chain reaction.
FUNDHACRE, State of Acre General Hospital Foundation; LACEN, State of Acre Central Laboratory; HOSMAC, State of Acre Mental Health Hospital; HUERB, Emergency Hospital of Rio Branco; MBH and HC, Bárbara Heliodora Maternity Hospital Complex and Children's Hospital.

TABLE 2
Frequency of HCV carriers (HCV RNA) by polymerase chain reaction, according to gender stratified by age range*

Gender	Age range (years)	% (no./total)	P†
Female		2.4 (13/532)	A
	20–40	0.9 (2/210)	> 0.07
	41–67	3.4 (11/322)	
Male		9.6 (11/114)	B
	20–40	10.8 (7/65)	> 0.64
	41–67	8.2 (4/49)	
Total		3.7 (24/646)	
	20–40	3.3 (9/275)	> 0.60
	41–67	4.0 (15/371)	

* HCV = hepatitis C virus.
† A versus B: χ^2 with Yates correction = 11.69, $p < 0.001$.

TABLE 3
HCV viremia according to income and educational level*

Income	Educational level	Total	% HCV RNA positive (n)	P
Low (≤ R$800.00)	Basic (A) (if senior high school or college (B))	180 160	7.2 (13) 2.5 (4)	< 0.05
Intermediate (> R$800.00)	Basic (C) (if senior high school or college (D))	41 265	4.9 (2) 1.9 (5)	> 0.52†

* HCV = hepatitis C virus.
† A versus C: χ^2 with Yates correction = 0.04, $P > 0.84$; B versus D; $\chi^2 = 0.01$, $P > 0.93$.

Among those with intermediate family incomes greater than or equal to the median, similar frequencies of HCV carries were observed between this group and those with a higher level of education (4.9% versus 1.9%; $P > 0.52$).

Of the 646 persons studied, only one had a history of organ transplantation (kidney). Univariate analyses showed that following variables were not associated with HCV infection: type of healthcare activity, a blood transfusion before or after 1995, acupuncture treatment, immunization with vaccination pistols, manicures, sharing of nail clippers, use of nondisposable blade in barbershops, use of nondisposable blades for hair removal, sharing of toothbrushes with relatives or friends; ≥ 2 tooth extractions, history of kidney disease with treatment by hemodialysis, previous diagnosis of diabetes mellitus, history of malaria, history of surgery, number of teeth extracted, sex before 16 years of age, number of sexual partners in the last 12 months (0–1 versus 2–20), homosexuality or bisexuality, anal intercourse, sex with transfused people, sex with intravenous drug users, sex with sex professionals (male and/or female), sex with people who have had hepatitis, use of illicit drugs of any type, use of drugs with sharing of syringe with other users, use of cocaine in any form, use of a straw to inhale drugs, tattooing, and body piercing ($P > 0.25$).

Table 4 shows that a history of dental treatment by people not certified in dentistry ($P < 0.0001$), a history of alcoholism ($P < 0.007$), and injection of intravenous vitamin complexes with a non-disposable syringe ($P < 0.0001$) were associated with HCV positivity. Other risk factors associated with HCV infection were an accident at work or a history of surgery. Multivariate analysis (Table 5) in the final model of multiple logistic regression showed that time of residence in Rio Branco, dental treatment by people not certified in dentistry, history of alcoholism, and use of intravenous vitamin complexes (95% confidence interval of the odds ratio = 2.5–9.4, $P < 0.05$) were associate with HCV positivity.

DISCUSSION

This study showed a high prevalence (3.7%) of HCV carriers among HCWs health in Rio Branco in the western Brazilian Amazon region. Although there have been no population studies of this region, studies conducted in other Brazilian regions report HCV prevalences between 1.0% and 1.5%.[9] Furthermore, information from blood banks in this area indicates that the prevalence of antibodies to HCV among potential blood donors is1.5–2.0%. The distribution of the HCV genotype 1 in this sample was similar to that reported for the northeastern area of Brazil: a predominance of genotype 1, followed by genotype 3.[10] Other investigators reported similar results, which suggests a homogeneous distribution of HCV genotypes in the several regions of Brazil, despite racial and cultural differences.[11]

The design adopted in this study was similar to that of Proietti and others in Italy.[12] They evaluated 1,086 HCWs care workers and reported that 2.1% were HCV carriers. In their study, risk factors most commonly associated with the carrier state among these workers was the type of activity and an age range > 45 years. Also, similar to what was observed in our study, they reported a high number of patients with hepatitis C, who despite being HCWs, did not know that they were seropositive. Another study conducted in Italy by Sulotto and others reported a prevalence of HCV carriers of approximately 1.9% in 4,517 HCWs.[13] The risk factor most commonly associated with HCV infection was an age > 45 years. However, no association between report of an perforating accident and seroprevalence was observed. In our study, no association was observed between a reported perforating accident and seroprevalence. Sulotto and others postulated that seroprevalence among HCWs was similar to that expected in the general population, and HCW showed no greater risk of developing hepatitis C.[13] In contrast to our study, Ozsoy and others reported a seroprevalence of antibody to HCV of 0.3% in 702 HCWs in Turkey.[14]

The high prevalence of HCV infection among HCWs in Rio Branco indicates that occupational risk, as well as the risk of nosocomial transmission through medical procedures performed by infected professionals, can result in infection with HCV. Even in developed countries with a better health system structure, accidents with surgically medical objects among HCWs are common. Continued and repeated exposure may increase the seroprevalence of HCV infection in this group of workers.[15] Another factor that supports our results is that HCWs are not well informed about HCV transmission and prevention, even in more developed countries. In our study, the low level of education and less access to information have been associated with the risk for HCV infection in HCWs. In Brazil, although official education, prevention, and control programs on parenteral transmission of viruses have been implemented, logistic problems make preventive actions difficult to initiate. Hospital infection control services must play an important role in informing professionals from each

TABLE 4
Hepatitis C virus carriers distribution according to possible risk factors*

Exposure factor	% (Yes/total)	% PCR positive (no./total)		P
		Yes	No	
Any type of surgical treatment	78.0 (504/646)	2.8 (14/504)	7.0 (10/142)	< 0.02
Among the 532 women: caesarian parturition	53.0 (282/532)	1.4 (4/282)	3.6 (9/250)	> 0.10
Dental treatment conducted by people not certified in dentistry	24.4 (157/643)†	8.9 (14/157)	2.1 (10/486)	< 0.0001
Report of two or more tooth extractions	93.8 (606/646)	3.2 (19/606)	14.3 (5/40)	< 0.009
History of alcoholism	36.2 (234/646)	6.4 (15/234)	2.2 (9/412)	< 0.007
Accident with surgical-medical devices contaminated with blood from patient	40.1 (256/638)†	5.5 (14/256)	2.6 10/382)	> 0.06
Men: anal sex in the active or passive condition?‡	46.4 (51/110)	5.9 (3/51)	13.6 (8/59)	> 0.18
Sex with menstruating women?‡	47.5 (307/646)	2.3 (7/307)	5.0 (17/339)	> 0.06
History of sexually transmissible diseases?‡	8.2 (53/646)†	7.6 (4/53)	3.4 (20/593)	> 0.24§
Use of intravenous vitamin complex use with non-disposable material	48.3 (312/646)	7.2 (21/312)	0.9 (3/331)	< 0.0001
Number of sex partners (0–2 vs. 3–150 partners)	17.0¶ (109/642)†	7.3¶ (8/109)	3.0# (16/533)	> 0.05
Use of illicit intravenous drugs	0.6 (4/646)	25.0 (1/4)	3.6 (23/642)	> 0.14§
Imprisonment	2.3 (15/646)	13.3 (2/13)	3.5 (22/631)	> 0.19**

* PCR = polymerase chain reaction.
† Cases with no information.
‡ Excluding 4 cases with no history of sex.
§ χ^2 with Yates correction.
¶ 3–150 partners.
# 0–1 partners.
** By Fisher exact test.

health unit, but many HCWs are not aware of this serious public health problem. Although programs emphasize antibiotic resistance, they do not face adequately address preventive actions regarding parenterally transmitted viruses. In hospital practice, many HCWs are not aware of parenteral transmission of viruses, and many are not involved in preventive programs even after having a work-related accident with a high risk of exposure to such virus infections.[16] These aspects, plus the fact that most cases of hepatitis C have no clinical symptoms, lead to an underestimation of the diagnosis of acute infection. Thus, many patients are not given antiviral treatment, which increases their progression to the carrier state.

The participation of health staff in the HCV transmission in hemodialysis units has been suggested by some investigators.[17] In addition, physicians and other HCWs involved in dialysis procedures can transmit HCV to their patients. Ross and others reported HCV transmission from an infected physician to his patient during gynecologic procedures.[18] Although we are not aware of additional data on hemodialysis units and the spread of HCV in Brazil, Santana and others reported showed a high seroprevalence (> 23%) of HCV in 395 individuals who underwent hemodialysis in Salvador in northeastern Brazil.[19] In this study, the age of the dialysis unit was strongly correlated with HCV prevalence. This suggests that older units may have had less biosafety control compared with newer ones, which were implemented in more recent times when prevention of parenteral transmission of virus was emphasized. In patients undergoing hemodialysis in Rio Branco, the frequency of viremic patients for HCV (all with genotype 1) was of 18.4% (9 of 49) (Ministry of Health, unpublished data). Furthermore, HCWs are exposed to other infections through contact with body fluids of patients. This contact is often imperceptible or believed to be a possible source of parenteral transmission of virus.[20] This characteristic makes tracking of acute infections among HCWs even more difficult, as well as understanding the risk factors involved in HCV transmission. In addition, these health professionals are also exposed to the same risk factors as the general population, including those associated with cultural and socioeconomic characteristics.

In Brazil, there is evidence associating tattooing with HCV transmission.[21] Another factor also evaluated in this study was the abusive use of intravenous vitamin complexes. This practice was more frequent in the 1970s and 1980s because these complexes were believed to stimulate sexual or athletic performance. Many of these injections were given with used non-disposable syringes that were available in drugstores, especially to young males.[22] Therefore, HCWs, who had greater access to these complexes, may also have had greater exposure to HCV compared with the general population.

TABLE 5
Final model of the multiple logistics regression analysis for risk factors for HCV infection*

Variable	β	EP (β)	P	OR	95% CI of the OR
Time of residence in Rio Branco	2.2399	1.0399	≤ 0.004†	9.4	1.2236–72.0990
Dental treatment	1.2822	0.4481	≤ 0.005†	3.6	1.4976–8.6756
Cesarean parturition	–1.2950	0.5714	≤ 0.02†	0.27	0.0894–0.8394
History of alcoholism	0.9218	0.4541	≤ 0.04†	2.5	1.0322–6.1220
Use of intravenous vitamin complex with non-disposable material	1.8429	0.6344	≤ 0.0007†	6.3	1.8212–21.8965
Constant	–7.0688	1.2055	≤ 0.00001‡	–	–

* Homer and Lemeshow adjustment test (χ^2 = 2.73, degrees of freedom = 7, P = 0.91). HCV = hepatitis C virus; OR = odds ratio; CI = confidence interval.
† By likelihood ratio test.
‡ By Wald test.

Our results show a high prevalence of HCV in HCWs in the western Brazilian Amazon region. These results also reinforce the probable influence of the long-term exposure to HCV because this type of infection was more frequent in persons more than 40 years of age and in those who lived in Rio Branco for a longer time. These results also demonstrate the need for development of educational, tracking, and prevention programs to prevent HCV transmission in HCWs in Brazil.

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