Hepatitis C in prisoners and non-prisoners in Colatina, Espírito Santo, Brazil

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The aim of the present work was to compare hepatitis C prevalence, genotypes, and risk factors between prisoners and non-prisoners in the city of Colatina, Espírito Santo, Brazil. This cross-sectional study involved approximately 1,600 residents and 730 prisoners, all of whom were living in Colatina. The percentage of individuals who tested positive for anti-HCV was 0.1% (2/1,600) in the non-prisoner group and 1.0% (7/730) in the prisoner group, confirming a higher risk of hepatitis C in the latter group. The percentage of subjects who progressed to HCV-RNA negative was 11.1% (1/9), confirming the high probability of evolution to chronicity. Genotype 1 was the most predominant genotype found. Factors associated with increased risk of hepatitis C were being male, being institutionalized, having an income of less than three minimum wages, having low educational attainment, and using injected drugs. Alcohol use, pain in the liver, migraine, and reported history of hepatitis were markedly associated with hepatitis C. The prison population tested positive for anti-HCV at a higher rate than the non-prison population.

Uniterms: Hepatitis C/prevalence. Hepatitis C/genotypes. Hepatitis C/risk factors. Hepatitis C/symptoms. Anti-HCV. Prison population/risks evaluation.

O objetivo do presente trabalho foi comparar a prevalência, os genótipos e fatores de risco da hepatite C entre a população em geral e os presos na cidade de Colatina, Espírito Santo, Brasil. O presente estudo é transversal e comparou cerca de 1.600 moradores e 730 prisioneiros, todos eles vivendo em Colatina. A prevalência de anticorpos anti-HCV positivo foi de 0,1% (2/1.600), na população em geral, e de 1,0% (7/730) entre os presos, o que confirma o elevado risco nesse grupo. A percentagem de indivíduos que apresentam RNA-HCV negativo foi de 11,1% (1/9), confirmando a alta taxa de evolução para a cronicidade. O genótipo predominante foi o I. Fatores associados ao aumento do risco de hepatite C foram do sexo masculino, sendo institucionalizado, com renda de até três salários mínimos, baixa escolaridade e uso de drogas injetáveis. O uso de álcool, dor no fígado, enxaqueca e relato de histórias de hepatite apresentaram associação significativa com a hepatite C. A população carcerária teve maiores taxas de positividade para o anti-HCV do que a população não-prisional pesquisada.

Unitermos: Hepatite C./prevalência. Hepatite C./genótipos. Hepatite C./fatores de risco. Hepatitis C/sintomas. Anti-HCV. População carcerária/avaliação de riscos.

INTRODUCTION

Viral hepatitis C, isolated from viral RNA, is a relatively recent discovery (Choo *et al*., 1989). It has been cited often as a major determinant of chronic liver disease (Martins, Schiavon, Schiavon, 2011) and as a worldwide public health concern (Sy, Jamal, 2006). In Brazil, certain infectious diseases must be reported to the government, which is responsible for the diagnosis and treatment of these conditions. The high rates of morbidity and mortality associated with hepatitis B and C create the need for large investments by the government (Rantala, Laar, 2008).

According to the World Health Organization, approximately 3% of the world's population (ranging

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from 2.5 to 4.99% in the surveyed countries) is infected with HCV (Hepatitis C) (WHO, 2003). In Brazil, according to a 2010 study conducted in Brazilian state capitals by the Ministry of Health, the average prevalence of HCV is 1.6% in patients between 20 and 69 years of age (Brazil, 2011).

Most estimates of the prevalence of hepatitis C in Brazil are drawn from studies of specific populations, such as blood donors.

Prison populations are disproportionately affected by HCV, with higher incidence and prevalence observed in certain risk groups (Rantala, Laar, 2008; Cornberg *et al.*, 2011). However, differences between the prison surveillance systems of different countries makes the comparison of epidemiological characteristics and trends difficult, which delays the collection of information useful for establishing hepatitis C prevention and control strategies.

In Brazil, despite the uniformity of the surveillance system, data collection is hampered by the large cultural and social differences in different regions, the difficulty of accessing health services (Ferreira, Silveira, 2004), and the frequent absence of symptoms in the early phase of the disease (WHO, 2003).

It is possible to detect the virus by ELISA at 49 to 70 days following infection (Brazil, 2008). There are 11 known genotypes in the world, of which I and III are the most common, and there are several subtypes. The existence of various genotypes and subtypes has little impact on the virulence and pathogenicity of the virus, but it does affect how the virus responds to treatment with interferon and ribavirin (WHO, 2003).

A major barrier to the primary prevention of hepatitis C is the absence of an effective vaccine or post-exposure prophylaxis, which limits basic preventive care to avoiding contact with the virus (Brazil, 2001).

The constant mutation of the viral genome sequence may be the reason for the existence of numerous quasispecies. Mutation enables the virus to evade the immune system and the innate immunity of the host, leading to the development of chronic hepatitis C in most patients, as well as cirrhosis (20%) and hepatocellular carcinoma (1-4%) (Chen, Morgan, 2006). Worldwide, 27% of cases of cirrhosis and 25% of cases of hepatocellular carcinoma are attributable to the hepatitis C virus (Perz *et al.*, 2006).

As stated in Passos *et al.* (2012), the epidemiologic profile and risk factors for HCV in the population are of substantial importance for the establishment and evaluation of health policy programs. This work has the merit of being the first study to simultaneously establish the prevalence of hepatitis C in a high risk population (inmates) and in the non-prisoner population in the city of Colatina, ES, Brazil.

MATERIAL AND METHODS

This is a cross-sectional, descriptive, comparative, and population-based study involving 1,600 city residents of both sexes chosen from the general population and 730 prisoners of both sexes from the three prisons (which have a total of 896 inmates) in the city of Colatina, Espírito Santo. All participants were over 18 years of age. Resident sample size (calculated sample size = 1,101) was calculated based on defined and acceptable standard error around the estimated prevalence of HCV. The sample was probabilistic, through cluster sampling, with the 22 basic health institutions as the unit sample. The researchers approached patients at the 22 Health United centers independently of their comorbidities. All persons included in the present study signed an informed consent document.

In the two male prisons (PSMECOL – Penitenciaria de segurança media de Colatina and CDPCOL - Centro de Detenção Provisória Colatina), data collection occurred between January and February of 2010; in the female prison (PRFCOL - Presídio Regional Feminino de Colatina), data collection occurred between July and August of 2010.

Due to the greater degree of difficulty of access to the prison population and the desire to avoid the need for new collection, blood was collected by finger prick lancets with a disposable paper filter for the "Dry Spot" (dried blood) testing technique. The samples were dried at ambient air temperature for 30 minutes or until the blood was completely dry and then sealed in foil-lined envelopes containing silica. They were then sent to the Genome Center for serological and molecular tests (GENOME CENTER, 2005). The samples were analyzed for anti-HCV antibodies using the enzyme immunoassay method (HCV Rapid Test Bioeasy ®). Indeterminate results were considered positive for the purposes of indicating molecular testing confirmation.

Blood was collected from the non-prisoner population from May to June of 2010 in 22 districts located within the municipality. It was decided that data collection in the non-prisoner population would follow the same male-female ratio as the prison population sample. Blood samples were collected at the municipal health facilities of the government of Colatina, according to a schedule that was proposed, accepted, and disseminated to the population by community health workers.

Following the administration of the interview, the participants, all older than 18 years of age, signed an informed consent document before sample collection.

The test used was the HCV Rapid Test Bioeasy®, qualitative immunoassay (immunochromatography 3rd generation) for detection of IgG antibodies specific to HCV, where the recombinant HCV Core (framework region capsid core of the genome of HCV), NS3 (the non- structural - protease / helicase - HCV genome), NS4 (non-structural region - the membrane binding - the HCV genome) and NS5 (non-structural region - polymerase - HCV genome) were used as capture agents and detectors. Blood was collected by fingerstick with a disposable lancet, and manufacturer procedures were followed, with the results evaluated after 15 to 20 minutes. Participants who tested positive received post-test counseling and were invited to undergo a second blood test in the laboratory. A portion of blood from this sample was separated, mixed with the anticoagulant EDTA (Ethylene Diamine Tetra-acetic Acid) serum was separated and sent to the Genome Center for confirmatory tests.

The confirmation of positive results for both the prisoner and non-prisoner populations was performed at the Genome Center by analyzing the blood sample for evidence of qualitative HCV-RNA using Real Time Polymerase Chain Reaction (RT-PCR) and TaqMan (which are probes that increase the specificity of the PCR), assessing HCV viral load using RT-PCR and TaqMan (both of which have a detection limit of 50 UI/mL), and genotyping using RT-PCR. Biopsies, genotyping, and viral load counts were conducted for all participants who were HCV-RNA positive. The biopsy was analyzed for grade and stage of liver injury using the Ishak scoring system (Ishak *et al*., 1995). The extent of necroinflammatory activity defined the grade, while the extent of fibrosis or the presence of cirrhosis determined the stage.

All participants were guaranteed the confidentiality of information obtained through this study, as well as access to specialized medical care and free treatment by the Unified Health System, according to the "Clinical Protocol and Therapeutic Guidelines for Viral Hepatitis C Coinfection" and the Brazilian Ministry of Health (Brazil, 2011).

Epi-Info (version 3.5.1) is free software that enables users to generate questionnaires, manage data, and conduct subsequent statistical analyses. It was chosen because it was well-known, easy to use, reliable, free, and already widely used in epidemiological research, as described by Xia *et al*. (2008) and Cruz *et al*. (2009), among others. Questions that were considered important in the literature were entered into the program to create the questionnaire. The questionnaire was administered to all participants, and their responses were entered into an Epi-Info database.

Responses were collected from more than 1,600 people. The program was used to conduct statistical analysis. The percent frequencies of socio-demographic variables were determined. To analyze the association between positive HCV and potential risk factors, the prevalence ratio and associated 95% confidence interval were calculated.

The study was approved by the Ethics Committee (CEP) (CEP Hospital South, No. 04-30-2009) and authorized by the State Department of Justice (Official Letter 03/2010).

RESULTS

Colatina is a county in the state of Espírito Santo, Brazil. It has a population of 111,788 residents and is located between coordinates -40.63º and -19.53º, with a total land area of 1.417 km^2 (IBGE, 2013).

Among all study participants, the prevalence of anti-HCV positivity was 0.4% (09/2,330), and that of HCV-RNA positivity was 0.3% (08/2,330), with the highest frequencies observed for genotypes 1 (87.5%) and 3 (12.5%). No other genotype was found.

Five patients (three females and two males) had indeterminate results, and all were HCV-RNA negative.

In the prison population, the prevalence of HCV RNA-positivity was 0.8% (6/730), and for anti-HCV positivity, it was 1.0% (7/730). In the non-prisoner population, the prevalence of HCV-RNA and anti-HCV positivity was 0.1% (2/1,600).

The six biopsies revealed different degrees of fibrosis: one had grade 3 fibrosis (16.7%), three had grade 2 fibrosis (50%), and two had grade 1 fibrosis (33.3%). Two additional biopsies were not performed due to the transfer of prisoners to semi-open prisons located in other municipalities.

Of the four cases in which biopsy indicated grade 2 or 3 fibrosis (66.7%), two came from participants incarcerated in PSMECOL, and two came from the non-prisoner population. Immediate treatment was indicated by the results, and they were referred to specialized medical support (SAE-Hepatitis).

Hepatitis diagnosis was strongly associated with male sex (77.7%), monthly income of less than three minimum wages (100.0%), and low educational attainment (77.8% with four years of school or less). The combination of the three features together was 35.1%. The mean age of hepatitis diagnosis was 40.6 ± 6.4 years. Associations were also present between hepatitis C infection and injected drug use (p = 0.00), alcohol use (p = 0.01), migraine (p = 0.01), pain in the liver (p = 0.02), and institutionalization (p = 0.00), although it is not possible to generalize these results to the broader population (Table I).

TABLE I - Correlation of risk factors and factors associated with hepatitis C

Variable	Anti-HCV positive					Anti-HCV negative					p
	prisoners		non-prisoners		Total	prisoners		non-prisoners		Total	
	n	%	n	%		n	%	n	%		
anti-HBc	6	0.8	2	0.2	8	722	99.2	1598	99.8	2320	
injected drugs	3	0.4	1	0.1	4	40	5.8	2	0.2	42	0.00
inhaled drugs	3	0.4	1	0.1	4	403	58.5	49	4.1	452	0.09
tattoo	4	0.6	0	0.0	4	395	57.3	107	9.0	502	0.14
blood transfusion	2	0.3	0	0.0	2	70	10.2	145	12.2	215	0.23
piercing	5	0.7	0	0.0	5	470	68.2	518	43.5	988	0.48
homosexual	1	0.1	0	0.0	1	89	12.9	30	2.5	119	0.53
alcohol	6	0.9	2	0.2	8	492	71.4	379	31.8	871	0.01
previous hepatitis	3	0.4	1	0.1	4	41	6.0	111	9.3	152	0.01
migraine	5	0.7	1	0.1	6	266	38.6	311	26.1	577	0.01
hepatic pain	3	0.4	0	0.0	3	75	10.9	148	12.4	223	0.02
mental confusion	3	0.4	0	0.0	3	137	19.9	153	12.9	290	0.07
flu	2	0.3	1	0.1	3	108	15.7	176	14.8	284	0.08
depression	3	0.4	1	0.1	4	256	37.2	354	29.7	610	0.28
lack of appetite	3	0.4	0	0.0	3	219	31.8	203	17.1	422	0.28
diabetes	0	0.0	0	0.0	0	10	1.5	108	9.1	118	0.46
muscular pain	3	0.4	1	0.1	4	253	36.7	613	51.5	422	0.89

Injected drug use and institutionalization were the factors most strongly associated with hepatitis C.

DISCUSSION

In Brazil, information about hepatitis C has become more accessible following the publication of several studies (Paltanim, Reiche, 2002; Zarife *et al*., 2006; Strazza *et al*., 2007; Fagundes *et al*., 2008; Gabe, Lara, 2008; Coelho *et al*., 2009; Ferrao *et al.,* 2009; Mousquer, Castro, 2009; Silva *et al*., 2010; Oliveira-Filho *et al*., 2010; Santos *et al*., 2011). Fagundes *et al*. (2008) found that 2.2% (10/457) of adults in Criciúma (Santa Catarina) were anti-HCV positive and that 1.53% (7/457) were HCV RNA-positive, but the study did not identify the HCV genotype (16). Zarife *et al*. (2006) found a prevalence of 1.5% (20/1,308) in Salvador, with genotype 3 (53.3%) predominating, followed by genotype 1 (40%). Ferrao *et al*. (2009) studied the population of the district of Bebedouro, SP, and found a HCV RNA-positive prevalence of 8.8% (31/353). The results of this study differ from those studies, which may be explained by the location and associated risk factors.

Studies of specific populations also differ from the results of this study. In a study by Silva *et al*. (2010), seroprevalence for injected drug users (IDUs) was 35.6%;

for ex-IDUs, 29.8%; and for non-IDUs, 5.3%, with predominance of genotype 1 (76.5%). A study conducted by Strazza *et al*. (2007) of inmates in São Paulo found a prevalence of 16.2%, with injectable drug use and a larger number of sexual partners as prevalent risk factors. A study conducted by Lopes *et al*. (2009) with 691 drug users in Goiania and Campo Grande revealed a prevalence of 6.9%, with the greatest frequency of genotypes 1 (80.5%) and 3 (19.5%). Oliveira-Filho *et al*. (2010) studied 256 blood donors in Pará, finding a prevalence of 45.3%, with unsafe injections, dental treatment, and sharing of razors as risk factors.

Paltanim and Reiche (2002) found a seroprevalence of 0.9% (88/10,990) anti-HCV positive in blood donors from Paraná, but only 0.1% (11/10,990) were HCV-RNA positive, 0.13% (14/10,990) exhibited indeterminate results, and 0.003% (38/10,990) exhibited negative results. In 0.28% (25/88) of participants, confirmatory testing was not performed.

In the prison population of Campo Grande (MS), Mousquer and Castro (2009) evaluated 409 inmates of both sexes and found a prevalence of 4.9% (20/409) of confirmed cases of hepatitis C, much higher than the 0.8% prevalence found in this study (6/730). In Aracaju, Santos *et al*. (2011) found that 3.1% (13/422) of participants

were Ac-HCV positive (11/422), with confirmed viremia by PCR and a predominance of genotype 1 (90.9%). In another study involving prison populations, Coelho *et al.* (2009) found a prevalence of 8.7% of anti-HCV positive in a prison in Ribeirão Preto. In a female prison in Rio Grande do Sul, Gabe and Lara (2008) found 9.21% (7/76) anti-HCV positive. These studies revealed higher rates of anti-HCV positive in prison populations than in the non-prison population, which was confirmed in this study. The present study, showed that the prevalence in the prison population was eight times higher than in the non-prison population, although this value (0.8%) is also well below those found in other prisons. It is important to mention that the prevalence rates in the present study are much lower than those cited in the literature review. This fact may be explained by the municipality's size and its location within the state, or perhaps its distance from the main drug trafficking routes, but the difference in prevalence between the prisoner and non-prisoner groups remained very high, indicating that institutionalization is a substantial factor in the concentration of the virus.

Data published by the Ministry of Health show a detection rate of anti-HCV from 1999 to 2010 of 5.3:100,000 in Brazil, and in the state of Espírito Santo, 2.2:100,000, which is the lowest detection rate in the Southeast Region (Brazil, 2011). In Brazil, the reporting of chronic diseases such as hepatitis C are mandatory through the SINAM (Information System for Notifiable Diseases - Chronic Diseases) of the Ministry of Health, which reported 57 cases in Espírito Santo in 2010: 11 cases in the capital, Vitória, and 46 within the other 71 municipalities in the state. From 1999 to 2010, there were 561 total cases in Espírito Santo (Brazil, 2011). In 2010, eight cases of HCV-RNA positive were reported to SINAM. Although this seems to represent a higher prevalence of cases in Colatina than in the state, it only demonstrates the importance of disclosure and availability of tests by the government.

In Zambia, a study by Kapembwa *et al.* (2011) showed a HCV prevalence of 1.2% among 323 HIV-positive individuals studied. In Mexico, Burquete *et al.* (2011) reported a 1.5% prevalence, with 60.9% associated with blood transfusions and 25.2% associated with tattoos or piercings. The present study confirms tattooing as a risk factor as well (p = 0.049). In a study conducted with immigrants in Sicily, Tramuto *et al.* (2011) found a 4.0% positivity rate for anti-HCV (22/393). Thornton *et al.* (2011) found an average prevalence of 0.5 to 1.2% in Ireland, with a strong association (80%) with drug use, and Flisiak *et al.* (2011) also showed strong association with drug use and male gender in Poland.

Mohtasham *et al.* (2007) found a 45.4% prevalence in injected drug user inmates in Iran, and Mahfoud *et al.* (2010) found a prevalence of 3.4% in prisoners in Lebanon, with strong associations with injected drug use and tattoos. Adjei *et al.* (2007) found associations with injected drug use and unprotected sex as the risk factors most strongly associated with prisoners in Ghana, Africa. Pellegrini, Barbanera and Gonçalves (2007) found a 64.8% prevalence of HCV in patients with infectious diseases in São Bernardo do Campo.

Descriptive epidemiological observations have provided important clues for understanding the relationship between HCV and previously unknown risk factors. However, those studies are not representative of the entire population but instead are meant as indicators for potential risk factors that may contribute to improve the public health service.

Of the HCV risk factors that were evaluated in this study, a correlation between hepatitis C and injected drug use (p = 0.00) was observed. A Polish study found a higher prevalence in the non-prison population (1.92%) than among health professionals (1.42%). In Nigeria, Obienu *et al.* (2011) observed a prevalence of 4.7%, without any associated risk factors, which differs from the findings of the present work, in which risk factors such as injected drug use, alcohol consumption, and tattoos were strongly associated with hepatitis C in the prison population. Although the use of alcoholic beverages is not a risk factor for hepatitis C, alcohol use by patients with liver disease may facilitate the progression of hepatitis C. This characteristic was found in 88.8% (p=0.01) of anti HCV-positive participants.

The identification of symptoms associated with hepatitis C is also quite controversial. Research by Leyendecker *et al.* (1989) showed that fatigue and gastrointestinal symptoms have some correlation with the degree of liver damage in acute forms of the disease. MacDonald *et al.* (2002) studied patients with chronic hepatitis C and found a correlation between hepatitis C infection and fatigue, depression, anxiety, and hostility, while Iwasaki *et al.* (2002) noted the absence of specific symptoms. In 2007, Kallman *et al.* demonstrated that fatigue is an important factor impacting the quality of life in those with chronic liver disease, and Henderson (2009) confirmed fatigue and abdominal pain as symptoms associated with hepatitis C in children. Kershenobich *et al.* (2011) defined genotype 1 as predominant in Latin America, with a prevalence of 1% to 2.3%. This study also involved a comparatively large number of diagnosed and treated patients. It is noteworthy that in Brazil, there is no discrimination between free persons and detainees in

relation to the availability of treatment. Treatment criteria are defined in the Ministry of Health's "Clinical Protocol and Therapeutic Guidelines for Viral Hepatitis C and Coinfection." The prison health care system provides the diagnosis and treatment of inmates. However, treatment requires the availability of diagnostic and screening tests. Regular screening, regardless of whether requested by medical professionals, could be a strategy to reduce the prevalence rate of hepatitis C.

CONCLUSION

It was possible to establish the prevalence of hepatitis C in the population at risk (prison inmates, 0.8%) and in the non-prison population in the town of Colatina (0.1%), revealing that the prison population has higher rates of positivity for anti-HCV than the non-prison population. The data from the present study may not be representative for the entire population of Espírito Santo, but the present study includes data from more participants than comparable studies.

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