

Epidemiology of HIV/HCV coinfection in patients cared for at the Tropical Medicine Foundation of Amazonas

ABSTRACT

The association of HIV infection and hepatitis C virus (HCV) infection often occurs because both viruses share the same transmission routes, increasing the possibility of HIV/HCV coinfection. World prevalence greater than 30% of coinfecting cases is estimated, and it can reach 90% depending on the transmission route. With the aim of determining the frequency and profile of HIV/HCV coinfecting patients, a descriptive analysis was carried out with patients with HIV/AIDS whose serology was positive for hepatitis C virus (HCV), cared for at the Fundação de Medicina Tropical do Amazonas from 2000 to 2007. In the present study, of the 2,653 AIDS cases notified in SINAN, 1,582 patients underwent serology test for hepatitis C, and a frequency of 4.42% ($n = 70$) of HIV/HCV coinfecting patients was identified in the period studied. The most frequent infection route was sexual transmission (84.3%), 68.6% among heterosexual individuals. Most patients were males (72.9%), aged between 25 and 40 years (60.1%), of low income (50% earning up to one minimum wage), and low educational level (80% had completed only middle school). A high percentage of deaths were observed during the study (34.3%). The results indicate a low seroprevalence of HIV/HCV coinfection in this population, in which sexual transmission, characterized by sexual promiscuity among heterosexual individuals, is the major transmission route of the virus rather than the use of injection drugs, as shown in world statistics.

Keywords: coinfection, hepatitis C, HIV, epidemiology, transmission.

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INTRODUCTION

Hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections are among the ten major causes of death due to infectious diseases worldwide.¹ Nowadays, there are more than 40 million HIV-infected individuals, 30% of whom are estimated to be also infected by HCV, representing a growing public health problem worldwide.^{2,3}

Coinfection rates range from 4% to 90%, depending on the type of exposure. Studies carried out in Brazil have shown a coinfection prevalence of 40%, which varies according to region, geographic differences, age, and efficiency of exposure.^{1,3,4,5}

The HCV and HIV have similar transmission modalities, but the efficacy of the transmission of each virus differs, and several factors influence that coinfection. For both, blood exposure and injection drug use are efficient transmission forms. However, the risk of vertical and perinatal transmissions is high for

HIV and relatively low for HCV, although the risk increases twice when the mother is HIV positive.^{6,7}

The sexual transmission of HCV is inefficient, and the exact risk related to different types of sexual activity is unknown; nevertheless, it has been increasing among HIV-infected men who have sex with men (MSM).⁸

The introduction of highly active antiretroviral therapy (HAART) has significantly improved life expectancy of HIV-infected patients; however, the consequences of hepatitis C have become more apparent, as a result either of decompensated cirrhosis or hepatotoxicity due to HAART.^{9,10,11}

The interaction of those viruses has been the object of great concern, being considered one of the most important public health problems faced by health professionals and authorities worldwide.¹²

The present study aimed at determining the frequency of hepatitis C marker (anti-HCV) in a population of HIV patients notified in the

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SINAM database and cared for at the Fundação de Medicina Tropical do Amazonas (FMTAM) from 2000 to 2007. In addition, it also aimed at better knowing the profile and behavior of this population, since epidemiological studies on HIV/HCV coinfection in the state of Amazonas are scarce.

MATERIAL AND METHODS

Description of the study area

This study was developed at FMTAM, a state reference center for the follow-up of HIV patients in the city of Manaus, home to approximately 1.71 million people of the 2.8 million inhabitants of the state of Amazonas, 71.4% of whom are in urban areas and 28.6% in rural area.¹³

The FMTAM is one of the 20 testing and counseling centers of the state of Amazonas. It comprises specialized outpatient clinics, a hospitalization unit, and laboratories equipped for diagnosing infectious diseases.

To identify the HIV and HCV coinfecting population cared for at FMTAM from 2000 to 2007, the following databases were used: the SINAN (Sistema de Informações de Agravos de Notificação) database; the database of the Coordination of Sexually Transmitted Diseases/AIDS of the state of Amazonas, and the database of the Virology Unit of FMTAM.

We chose to start the study in the year 2000 due to the lack of available data on viral hepatitis prior to that year. It is worth noting that, over the study period, the institution has undergone modernization of its outpatient clinics and laboratories, such as digitalization of patients' data from 2005, and integration with the information network of the Ministry of Health for AIDS cases.

Study design

This is a descriptive study of a case series of patients with AIDS coinfecting with HCV cared for at the FMTAM during the study period. After database cross-referencing and patients' selection, medical records were sought for information referring to patients' identification, demographic data, socioeconomic and cultural profiles, as well as risk factors for the acquisition of the diseases in question. Those data were registered in a clinical-epidemiological form elaborated for the study.

Seventy patients were included in the study according to the following criteria: age over 12 years, both sexes, and positive serology for HIV (anti-HIV) and for HCV (anti-HCV). Patients with a positive marker for hepatitis B virus (HBsAg) and/or hepatitis D virus (anti-HD) and those who did not agree to participate in the study or sign the written informed consent were excluded.

This study has been approved by the Committee on Ethics in Research with Human Beings of FMTAM, under protocol 2857/2007, in accordance with Resolution CNS 196/96 of the National Health Council of the Ministry of Health.

Statistical analysis

The sample used for analysis comprised 70 HIV/HCV coinfecting patients cared for at FMTAM from 2000 to 2007.

Data were presented using tables and graphs of simple, absolute, and relative frequencies. In the analysis of quantitative variables, mean and standard deviation (SD) were calculated. Data analysis used the Epi-Info software, version 3.5 for Windows, developed and distributed by CDC (www.cdc.gov/epiinfo). The 95% confidence interval (CI) was adopted.

RESULTS

Origin of the coinfecting population

According to SINAN, from 2000 to 2007, the total number of AIDS cases accumulated in Brazil corresponded to 209,975 cases.¹⁴ In the Northern Region of Brazil, there were 8,903 cases, and in the state of Amazonas, 2,653 cases, representing 1.3% of the total number of cases in the country.¹⁴

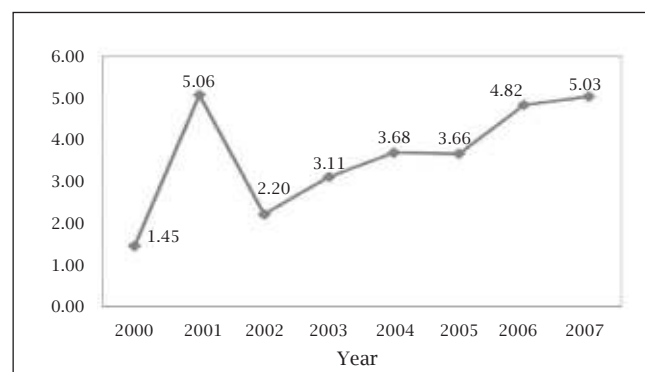
In terms of AIDS incidence, in the Brazilian northern region, the state of Amazonas is second only to the state of Pará. That population has a man to woman ratio of 2:1, a tendency that has been kept since 1999 in the state of Amazonas, while in Brazil the current ratio is 1.5:1.¹⁴

During the period studied, 2,653 cases of AIDS were notified at SINAN. Of those, only 1,582 patients had undergone the serologic test for hepatitis C, 70 of which tested positive, representing a frequency of 4.42% of HIV/HCV coinfecting patients cared for at FMTAM during this period.

The HBV/HCV double infection was identified in two patients, and the HBV/HCV/HDV triple infection was identified in only one patient. These three patients were excluded from the study.

In Figure 1, the annual curve shows an increase in coinfection cases, from 1.45% in the year 2000 to 5.03% in 2007.

Figure 1: Annual distribution according to the frequency of HIV/HCV coinfecting patients cared for at FMTAM from 2000 to 2007.



Demographic data

Regarding the gender of HIV/HCV coinfecting population ($n=70$), men ($n = 51, 72.9\%$) represented the majority. In this population, age ranged from 20 to 67 years (mean age, 38.5 ± 10.2 years), with the age bracket of 30-35 years being the most populous ($n = 20, 28.6\%$). Regarding the population educational level, 80% ($n = 56$) had completed middle school, and 4.2% ($n = 3$) were illiterate. Regarding monthly income, 50% ($n = 35$) of the patients received up to one national minimum wage and 20% ($n = 14$) were unemployed.

Among the HIV/HCV coinfecting patients, the place of birth of most patients ($n = 39, 55.7\%$) was the city of Manaus, followed by the inner Amazonas state ($n = 15, 21.4\%$), and other states ($n = 16, 22.9\%$). Regarding the site of origin, 94.3% ($n = 66$) came from the city of Manaus, only 5.7% ($n = 4$) from the inner Amazonas state, and nobody came from other states (Table 1).

Sexual orientation and risk factors

According to the sexual orientation of the patients studied, 48 (68.6%) patients were heterosexual, 16 (22.8%) were homosexual, and six (8.6%) were bisexual. Fifty-nine (84.3%) patients have reported sexual promiscuity, that is, more than two partners in six months, and that was the major risk factor analyzed. Other risk factors were as follows: acquisition of sexually transmitted diseases (STD), reported by 33 (47.1%) patients; sex partner known to have HIV infection, reported by 24 (34.3%) patients; and, in a lower proportion, use of injection drugs, reported by 15 patients (21.4%).

Some patients had more than one risk factor associated at the same time (Table 2).

Evolution of coinfecting patients

The coinfecting patients detected in the period studied showed a high death rate ($n = 24, 34.3\%$), with most deaths occurring between the years 2000 and 2003, and 46 (65.7%) patients were alive by the end of the study in December 2007 (Table 2).

DISCUSSION

The epidemiology of AIDS has changed over the years in Brazil. This epidemic has shown its strength by spreading from the southeastern region to other regions in the country. In the northern region of Brazil, especially in the state of Amazonas, the epidemic has shown social, cultural, and geographic peculiarities.¹⁵

Almost five years after its discovery, AIDS appeared in the state of Amazonas, and the first notification of the disease occurred in April 1986, when the notification of AIDS cases in Brazil became compulsory.¹⁶ From 1986 to 1990, AIDS was restricted to the municipality of Manaus, and, from 1991, it spread to the inner state, but the city of Manaus still has the greatest number of notified cases.¹⁴

Table 1. Distribution of HIV/HCV coinfecting patients cared for at FMTAM from 2000 to 2007, according to demographic, socioeconomic, and cultural data

Variables (n = 70)	n	%
Gender		
Male	51	72.9
Female	19	27.1
Age (years)		
20 --- 25	2	2.8
25 --- 30	9	12.9
30 --- 35	20	28.6
35 --- 40	13	18.6
40 --- 45	6	8.6
45 --- 50	8	11.4
50 --- 55	4	5.7
55 --- 60	6	8.6
≥ 65	2	2.8
Mean ± SD	38.5 ± 10.2	
Range	0 - 6	
Educational level		
Illiterate	3	4.3
Complete middle school	6	80.0
Complete high school	9	12.8
Complete university	2	2.9
Income (minimum wages)		
Unemployed	14	20.0
≤ 1	35	50.0
2 to 3	16	22.9
4 to 6	5	7.1
Place of birth		
City of Manaus	39	55.7
Inner Amazonas state	15	21.4
Other states	16	22.9
Origin		
City of Manaus	66	94.3
Inner Amazonas state	4	5.7

Table 2. Distribution of HIV/HCV coinfecting patients cared for at FMTAM from 2000 to 2007, according to sexual orientation, risk factors for coinfection, and outcome

Variables (n = 70)	n	%
Sexual orientation		
Heterosexual	48	68.6
Homosexual	16	22.8
Bisexual	6	8.6
Partner with HIV infection	24	34.3
STDs	33	47.1
Use of injection drugs	15	21.4
> 2 partners in the past 6 months	59	84.3
Death	24	34.3

According to data from the Ministry of Health, the epidemic in the state of Amazonas seems to have had a tendency to increase with a progressive incidence rate until 1999, and stabilization from 2000 to 2003. It began to increase again from 2004, when an improvement in epidemiological surveillance was observed with the restructuration of the State Coordination of STD/AIDS Program in the state of Amazonas.^{14,15}

Nevertheless, the AIDS Epidemiological Surveillance system still suffers from sub-notification of cases and delay in notifications.^{17,18} This may be one of the plausible justifications for the discrepancy observed between the cases notified in the state of Amazonas and the actual magnitude of the epidemic, as compared to the rest of the country.

In the population studied, a predominance of the male gender (72.9%) is observed, and this significant difference between men and women is in accordance with the findings of other studies carried out in Brazil,^{4,12,17,19} despite the tendency of AIDS to increase among women.^{14,20}

The population affected is young, at productive age, 60.1% aged between 25 and 40 years, but already showing an increase in the age bracket as compared with the cases at the beginning of the AIDS epidemic.¹⁴ Our data are in accordance with the study by Pottes *et al.* (2007),¹⁷ who have also reported a large number of individuals (89.2%) with AIDS at that age bracket.

The educational level expresses differences between individuals in terms of access to information, and some parameters to reach better quality in prevention and health assistance are undeniably directly linked to the socioeconomic level of the population, whose better indicators are educational level, income, and occupation.¹⁷

In Brazil, there was a tendency towards AIDS patients having a higher educational level. In 1982, almost all cases were among individuals with university level or complete high school level, while only 24% of the cases were among illiterate individuals. An inversion in this trend has been observed since 2000, with 74% of the cases informing the educational level were illiterate or had completed only middle school.²¹

These data are consistent with those presented in our study, in which 80% of the patients included have only completed middle school, representing a low-income population, 50% of whom receive up to one minimum wage, 20% are unemployed, and have a low educational level.

In our study, most of the patients were born and came from the capital of the state of Amazonas, the city of Manaus, where the quality of life and access to information regarding disease prevention is directly related to the educational and socioeconomic level, essential factors involved in reducing the rates of the diseases in question, especially HIV infection.

The HIV/HCV coinfection rate of patients cared for at FMTAM was 2.6% (n = 70), and the world estimates, according to some authors, have ranged from 4% to 90%, depending on transmission route.²²

In Brazil, the National Program of Control and Prevention of Viral Hepatitis has estimated, based on studies already carried out in the country that the prevalence of HIV/HCV coinfection ranges from 17% to 36% of the cases, varying in different regions.²³

Monteiro *et al.* (2004),²⁴ studying 406 HIV-infected individuals in the city of Belém, in the state of Pará, have reported a 16% prevalence of HCV infection. Carvalho *et al.* (2009)²⁵ in the city of Recife, in the state of Pernambuco, studying the HIV/HCV coinfection have reported a low prevalence (4.1%) as compared with other studies in the literature, possibly due to differences in risk factors for acquiring HCV.

The high variability depends not only on the risk factors to which the population are exposed to, but also on the methods of HCV detection.²⁶

In the present study, the major risk factor found was sexual transmission, characterized by sexual promiscuity (84.3%), and STD acquisition (47.1%) between heterosexual patients. This is in accordance with the studies by Szwarcwald (2000)²⁷ and Amaral *et al.* (2007),⁴ who have also shown the predominance of coinfection among patients having heterosexual intercourse (68.6%) as compared with men having sex with men (MSM) (22.8%).

The transmission modalities of HCV and HIV are known to be similar, but the transmission efficiency of each virus differs. HCV transmission is more efficient through exposure to contaminated blood or blood products, especially through the use of injection drugs.²⁸ In certain high risk populations, such as users of injection drugs, coinfection is present in 72% to 95% of them.^{6,29,30}

Similarly to the northeastern region of the country, in the northern region, the major drugs known to be used are cannabis and cocaine.^{12,17} The United Nations has reported Brazil as the second country with the highest number of individuals with HIV among drug users in Latin America, in addition to being one of the major cocaine traffic routes.³¹

A recent study carried out in the state of Pernambuco, in the northeastern region of Brazil, confirms our study, also showing a low prevalence of coinfecting individuals in this state.²⁵ The authors have reported that only 8.4% of the patients acquire HIV infection through the use of injection drugs, differently from the southeastern and southern regions, whose rates are 25.8% and 30.7%, respectively. They have not found a positive relation between coinfection and the use of injection drugs, in accordance with our study, in which the drug-injection use rate was only 21.4%.²⁵

Despite the small number of HIV/HCV coinfecting patients (4.42%) in our study, the annual distribution according to the frequency showed an ascending curve, ranging from 1.45% in the year 2000 to 5.03% in 2007.

Such findings emphasize the possibility that gradual increase results from the improvement in notification of AIDS

cases, from the investigation of hepatitis cases in those patients over the years, and from the longer survival of AIDS patients due to the use of the HAART regimen introduced in 1996.

It is worth noting that the deaths in our study (34.3%) occurred mainly between the years 2000 and 2003, when the cause of death could not be attributed to the presence of HCV.

Our study can have underestimated the actual prevalence of coinfection in the population studied due to the existence of floatation in the serologic status and even seroconversion (the anti-HCV turns negative), which are 2.5 times more frequent among HIV/HCV coinfecting patients as compared with HCV mono-infected patients.³²

In anti-HCV positive immunosuppressed patients, HCV RNA should be investigated, and its presence confirms the diagnosis; however, a negative result does not exclude HCV infection, and, whenever suspicion is high, a new investigation should be performed in six months.^{33,34}

However, in some active HCV infections, HCV RNA cannot be detected. This can occur in individuals whose anti-HCV antibody levels are high, and RNA levels are low.³⁵ Thus, HCV RNA cannot be detected in certain individuals in the acute phase of hepatitis C, but such findings are transient and a chronic infection can develop.³⁶

The low HIV/HCV coinfection rate (4.42%) found in our study as compared to that of other regions can be attributed not only to the small size of the sample, but also to the fact that HCV infection and diagnosis are still increasing in the region.

On the other hand, serological tests are known to have lower sensitivity in the immunodeficiency scenario, and polymerase chain reaction (PCR) is required for confirming the diagnosis.

The present study suggests that larger studies are required for better assessing the profile of this population and the prevalence of HIV/HCV coinfection in the state of Amazonas. The present study also stresses the need for early investigation of hepatitis C in HIV patients by using both serologic and molecular methods, because the literature emphasizes the impact of HIV in patients with HCV, regarding the rapid liver disease progression and evolution to death.

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