ARTIGO/ARTICLE

Low prevalence of hepatitis B virus, hepatitis D virus and hepatitis C virus among patients with human immunodeficiency virus or acquired immunodeficiency syndrome in the Brazilian Amazon basin

Baixa prevalência do vírus da hepatite B, vírus da hepatite D e vírus da hepatite C entre pacientes com o vírus da imunodeficiência humana ou síndrome da imunodeficiência adquirida na Amazônia Brasileira

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ABSTRACT

Comorbidities in human immunodeficiency virus infection are of great interest due to their association with unfavorable outcomes and failure of antiretroviral therapy. This study evaluated the prevalence of coinfection by human immunodeficiency virus and viral hepatitis in an endemic area for hepatitis B in the Western Amazon basin. Serological markers for hepatitis B virus, hepatitis C virus and hepatitis D virus were tested in a consecutive sample of all patients referred for treatment of human immunodeficiency virus or acquired immunodeficiency syndrome. The variables sex, age, origin and exposure category were obtained from medical records and from the sexually transmitted diseases and acquired immunodeficiency syndrome surveillance database. Among 704 subjects, the prevalence of chronic hepatitis B carriage was 6.4% and past infection 40.2%. The presence of hepatitis B was associated with birth in hyperendemic areas of the Amazon basin, male sex and illegal drug use. The overall prevalence of hepatitis C was 5% and was associated with illegal drug use. The prevalence of hepatitis B and C among human immunodeficiency virus or acquired immunodeficiency syndrome patients in the Western Amazon basin was lower than seen elsewhere and is probably associated with the local epidemiology of these viruses and the degree of overlap of their shared risk factors. An opportunity presents itself to evaluate the prevention of hepatitis C through harm reduction policies and hepatitis B through vaccination programs among human immunodeficiency virus or acquired immunodeficiency syndrome patients.

Key-words: *HIV-1. Amazon basin. Co-infection. Viral hepatitis.*

RESUMO

Co-morbidades na infecção pelo vírus da imunodeficiência humana são de grande interesse devido à associação com desfechos desfavoráveis e falhas na terapia anti-retroviral. Este estudo avalia a prevalência de co-infecção entre o vírus da imunodeficiência humana e hepatites virais, em uma área endêmica de hepatite B, na Amazônia Ocidental. Marcadores sorológicos para o Vírus da hepatite B, Vírus da hepatite C e vírus da hepatite D foram testados em uma amostra de pacientes referenciado para o tratamento em ambulatório para pacientes com infecção pelo vírus da imunodeficiência humana ou síndrome da imunodeficiência adquirida. As variáveis: sexo, idade, origem e categoria de exposição, foram obtidas dos prontuários médicos e do banco de dados da Coordenação Estadual de Doenças sexualmente transmissíveis. Entre os 704 indivíduos incluídos, a prevalência de portador crônico do vírus da hepatite B foi 6,4% e de infecção passada 40,2%. O vírus da hepatite B esteve associado com o local de nascimento em áreas hiperendêmicas da Amazônia, sexo masculino e uso de drogas ilícitas. A prevalência de hepatite C foi 5%, estando associada com uso de drogas ilícitas. A prevalência dos vírus da hepatite B e C, entre indivíduos vivendo com o vírus da imunodeficiência humana e síndrome da imunodeficiência adquirida, na Amazônia ocidental, foi mais baixa que as observadas em estudos com populações de outras regiões. Provavelmente, estes resultados estão associados à epidemiologia local destes vírus, e ao grau de superposição dos fatores de risco associados à infecção na população estudada. O estudo apresenta oportunidade de avaliar a prevenção da hepatite C e B, através de medidas de redução de danos e programa de vacinação em indivíduos vivendo com vírus da imunodeficiência humana e síndrome da imunodeficiência adquirida.

Palavras-chaves: *HIV-1. Amazônia. Co-infecção. Hepatites virais*

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Co-infections with viral hepatitis in individuals living with human immunodeficiency virus or acquired immunodeficiency syndrome (HIV/AIDS) are of great interest due to their association with unfavorable outcomes and failure of antiretroviral therapy[12 13 20 21]. Clinical studies conducted in Europe[21] and in the United States[4] among patients coinfected with the hepatitis B virus (HBV) indicate inadequate response to antiretroviral drugs and the development of liver disease. The latter occurs particularly in cases of hepatitis C virus (HCV) co-infection, which is probably related to changes in the natural history of HCV infection within coinfected individuals[8 13 26].

The Western Amazon basin has long been known to have one of the world's highest prevalences of HBV and hepatitis D virus (HDV) infection[1 2 3 6 24]. Although universal childhood HBV vaccination was introduced in 1989, the prevalence of chronic HBV infection may still be as high as 10% and past infection over 80%[7]. HDV is present in up to 30% of HBsAg carriers associated with severe forms of liver failure (the Lábrea *black fever*), early evolution to cirrhosis, and liver cancer[2 3 5 11]. The prevalence of HCV in populations in the Western Amazon basin is unknown. Coinfection with HCV in Europe, USA and Australia ranges from 30% to 50% overall and up to 90% among persons acquiring human immunodeficiency virus (HIV) parenterally[14 21].

No data are available on the prevalence of coinfection in the Western Amazon basin. Since all these viruses share transmission mechanisms, high rates of coinfection are expected in this region. We therefore sought to estimate the prevalence of coinfection of HIV with HBV, HDV and HCV using data from routine screening of patients in the region's only referral clinic for HIV/AIDS and viral hepatitis, in Manaus, State of Amazonas.

MATERIAL AND METHODS

Patients. We studied HIV/AIDS patients seen at the only reference center in the State of Amazonas, which cares for nearly 100% of the AIDS cases notified. It is also a referral facility for the management of viral hepatitis in the North of Brazil and, since May 1998, it has been routinely performing serological tests for viral hepatitis in HIV/AIDS patients. The present study included patients whose test results were available up to 2003. Results were available for 78% of all HIV/AIDS patients; 22% did not have results due to hemolyzed blood or loss of specimen. The study protocol was approved by the Research Ethics Committee of the Fundação de Medicina Tropical do Amazonas (590/2002-FMT/IMT-AM).

Measurements. Information was collected from existing medical records and from the HIV/AIDS surveillance database of the State's STD/AIDS Coordination Office. The variables studied included sex, age, place of birth, HIV exposure category, and results from HBV, HCV or HDV tests. Individuals whose medical charts reported AIDS-defining symptoms[17] were considered to be AIDS patients. Place of birth was classified as regions outside of the Western Amazon basin, Manaus and areas of high HBV endemicity.

Laboratory methods. Tests were performed using the enzyme-linked immunosorbent assay (ELISA), in accordance with the manufacturer's recommendations. Samples were first tested for HBsAg (BioMérieux, Boxtel, Netherlands) and then confirmed with a second ELISA. All samples available were also tested for anti-HBc IgG (BioMérieux, Boxtel, Netherlands), Specimens with confirmed HBsAg+ or anti-HBc IgG+ were tested with anti-HDV (DiaSorin, Vercelli, Italy). All specimens were tested with a single anti-HCV ELISA (DiaSorin, Vercelli, Italy).

Data analysis. HIV/AIDS patients were classified with regard to coinfection as follows: chronic HBV carriers (HBsAg+), past infection (anti-HBc+ alone) and HCV coinfection (anti-HCV+). Associations with coinfection were evaluated using the chi-square and Fisher's exact tests, with 5% as the level for defining statistical significance, using Epi-Info[10].

RESULTS

Among 704 HIV/AIDS patients, 45 tested positive for HBsAg, yielding a 6.4% prevalence of chronic HBV carriers (Table 1). Among the 701 patients with preserved specimens, 282 tested positive for anti-HBc IgG alone, yielding a 40.2% prevalence of past HBV infection (Table 1). Among the 211 patients who tested positive for any HBV marker with the available specimens, anti-HDV IgG was detected in four, yielding a minimum prevalence of 1.9% overall, and 9.4% among HBsAg carriers. Anti-HCV was detected in 35 patients, giving an overall prevalence of 5% (Table 1).

Chronic HBV infection was associated with birth in a hyperendemic area of the Western Amazon and illegal drug use. The prevalence of chronic HBV infection was 17.3% among persons born in a hyperendemic area and 11.5% among strictly heterosexual males, 5.1% among men who have sex with men (MSM), 5% among heterosexual women, and 42.9% among male drug users (Table 1). Past HBV infection was associated with male sex (46.9%), age over 30 (42.2%) years, and origin in endemic HBV areas (45.2%). HCV infection was only associated with illegal drug use, and the prevalence was 28.6% (Table 1).

Table 1. Prevalence and associations with chronic HBV infection, past HBV infection and HCV infection among HIV/AIDS patients, in Manaus, Amazonas, 1998-2003.

	Chronic HBV infection				Past HBV infection				HCV infection			
Variable	N	HBsAg+	prevalence (95% CI)	p	N	anti-HBc T	prevalence (95% CI)	p	N	anti-HCV	prevalence (95% CI)	p
Total	704	45	6.4 (4.7-8.5)		701	282	40.2(36.6-44.0)		701	35	5.0 (3.6-6.9)	
Sex				0.17				<0.001				0.77
male	458	34	7.4 (5.3-10.3)		456	214	46.9 (42.3-51.6)		455	24	5.3 (3.5-7.9)	
female	246	11	4.5 (2.3-7.9)		245	68	27.8 (22.2-33.8)		246	11	4.5 (2.3-7.9)	
Age				0.81				<0.001				0.39
Up to 30	298	18	6.0 (3.6-9.4)		296	85	28.7 (23.6-34.2)		297	12	4.0 (2.1-7.0)	
31-49	359	23	6.4 (4.2-9.6)		358	170	47.5 (42.2-52.8)		357	19	5.3 (3.3-8.3)	
≥50	47	4	8.5 (2.4-20.4)		47	27	57.4 (42.2-71.7)		47	4	8.5 (2.4-20.4)	
Exposure												
Men				<0.001				0.10				0.001
MSM	253	13	5.1 (2,8-8.6)		253	113	44.7 (38.4-51.0)		252	10	4.0 (1.9-7.2)	
hetero	122	14	11.5 (6.4-18.5)		120	63	52.5 (43.2-61.7)		120	9	7.5 (3.5-13.8)	
IDU	14	6	42.9 (17.7-71.7)		14	10	71.4 (41.9-91.6)		14	4	28.6 (8.4-58.1)	
transf	1	0	-		1	0	0,0		1	0	0,0	
Women								0.78				0.57
sexual	199	10	5.0 (2.5-9.3)	-	198	56	28.2 (22.2-35.4)		199	10	5.0 (2.5-9.3)	
IDU	8	0	-		8	3	37.5 (8.5-79.5)		8	1	12.5 (0.3-52.7)	
Birth				<0.001				<0.001				0.08
1	169	5	3.0 (1.1-6.8)		168	75	44.6 (37.0-52,0)		169	12	7.1 (3.7-12.1)	
2	437	23	5.3 (3.4-7.9)		436	153	35.1 (30.6-39.8)		435	15	3.4 (2.0-5.8)	
3	98	17	17.3 (10.4-26.3)		97	54	56.7 (45.2-65.8)		97	8	8.2 (3.6-15.6)	

HBsAg, HBV surface antigen; anti-HBc T, antibody against HBV core antigen; anti-HCV, antibody against HCV; N, number of patients; 95%CI, 95% confidence interval; p, statistical significance; MSM, men who have sex with men; hetero, heterosexual men; transf., history of blood transfusion; IDU, Ilegal drugs users; 1-Patients born in other Brazilian regions; 2-Patients born in Manaus; 3-Patients born in HBV endemic areas, the Western Amazon.

DISCUSSION

In a group of patients living with HIV/AIDS, in the Brazilian Amazon basin, we were able to find both common and unique epidemiological aspects of coinfection with HBV, HCV and/or HDV. To our knowledge, this is the first study to estimate the prevalence of coinfection between HIV and these viruses in the Western Amazon basin. The study population comprised nearly all the known HIV-infected persons in the region. The prevalence rates for HIV and hepatitis B, C and D virus coinfection found in this specific investigation were much lower than those reported elsewhere. This was probably associated with the local epidemiology of these viruses, due to differences in the degree of overlap of risk factors for infection with these viruses, which is believed to be the major determinant of coinfection with viral hepatitis among persons living with HIV/AIDS.

The prevalence of HCV coinfection was lower than in many other areas of Brazil and the world. This low prevalence rate is first of all the result of the low proportion of HIV/AIDS cases that are drug users, and particularly injection drug users, in this region. However, even among drug users, the HCV prevalence was lower than expected. Other studies have reported rates of 36% in Santos[23] and 53.8% in Campinas[22], in southeastern Brazil, and over 30% in Spain[13], regions where the use of injected drugs contributes significantly towards the dissemination of HIV. In the present study, only 22% of those who reported drug use or blood transfusions tested positive for anti-HCV, thus differing from other studies, which showed rates above 50% within scenarios in which parenteral transmission of HIV plays an important role[9 16 19 22 23 28].

The HBV-HIV co-infection rates in the present study were surprisingly similar to those found in other Brazilian regions[16 18 25 28] and to those reported in developed areas, including Europe[9 21], Australia[14], and North America[27], regions where the prevalence of HBV described within the general population is much lower than what is found in the Amazon basin[15 16 21]. HDV was detected in four subjects only. Nevertheless, all four showed signs of chronic hepatitis, thus confirming the role of the HDV/HBV association in the development of chronic liver disease in the region[11]. In hyperendemic areas, primary HBV infection is likely to occur during childhood. However, our population of HIV/AIDS patients included a mixture of individuals from different regions.

Unfortunately, we were unable to collect information on the timing of migration to the Western Amazon basin, timing of HIV versus HBV infection and vaccination status.

We recognize other limitations to our study. First, the study population represented only those in care. While the clinic includes the vast majority of persons in care, it does not include those who are outside of care or unaware of their HIV infection. Second, specimens were missing in some instances. However, the sex and age of the patients with missing specimens did not differ significantly from those examined.

Despite potential limitations, our data signal important public health issues. They reveal an excellent opportunity for the implementation and evaluation of HCV prevention

programs among HIV/AIDS drug users through harm reduction policies. Although universal childhood HBV vaccination was implemented 15 years ago, there still remains a large adult population at risk, for instance, persons living with HIV/AIDS. Specific programs are needed to reach them.

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