

HEPATITIS B, C AND HIV CO-INFECTIONS SEROPREVALENCE IN A NORTHEAST BRAZILIAN CENTER

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ABSTRACT – Context - The occurrence of HIV and hepatitis B (HBV) and C (HCV) virus associations is of great concern since co-infected patients respond poorly to antiviral treatment and usually progress to chronic and more complicated hepatic disease. In Brazil, these co-infections prevalence is not well known since published data are few and sometimes demonstrate conflicting results. Also, a significant number of co-infected individuals are HBV/HCV asymptomatic carriers, leading to under notification. **Objectives** - The present study aimed to determine the prevalence of the HBV and HCV infection in a recently diagnosed HIV population in the state of Ceará/Brazil. **Methods** - Retrospective cohort, with >18yo patients diagnosed HIV+ from 2008-2010. First year medical attention information was collected. **Results** - A total of 1.291 HIV+ patients were included. HBV serologies were collected in 52% (23% had previous hepatitis B, 3.7% were co-infected) and HCV in 25.4% (1.5% had previous hepatitis C, 5.4% co-infection). The majority of HBV/HIV patients referred multiple sexual partners/year, 28% homosexuality and 20% bisexuality. In the HCV/HIV group 38.8% individuals had > one sexual partner/year and 22.2% used intravenous drugs. **Conclusion** - The study reinforces the need for better training healthcare workers and providing laboratory support for a prompt hepatitis diagnosis and adequate medical management to avoid complications and decrease viral spread.

HEADINGS – AIDS-Related Opportunistic Infections. Hepatitis B virus. Hepatitis C. Chronic hepatitis.

INTRODUCTION

In Brazil, since 1996, the HIV/AIDS program delivers antiretroviral therapy to eligible individuals based on a national guideline⁽³⁾. This current practice has caused a significant decrease on AIDS related mortality, which led to prolonged survival expectancy and, as a consequence, increased vulnerability to other infections. The HIV, hepatitis B (HBV) and C (HCV) viruses have coincident mechanisms of transmission. In fact, concomitant infections involving these associations became quite common nowadays. The hepatitis viruses (B and C)/HIV co-infections are major clinical problems, since these patients usually respond poorly to antiviral treatment, being more susceptible to progress to chronic and more complicated hepatic disease^(1, 12). Therefore, the knowledge of Hepatitis B/C and HIV co-infection status becomes

an important issue in order to determine adequate strategies for prevention and treatment of this specific population.

In Brazil, hepatitis B and C seroprevalence varies according to both geographic and population risk factors. In Brazilian North-Northeast regions, 0.2% to 0.6% of the individuals with ages ranging from 13 to 69 years is HBsAg positive⁽¹⁰⁾. This prevalence is particularly elevated in high risk populations, such as drug addicted individuals (27,3%)⁽⁸⁾. An overall HCV prevalence of 2.5% to 10% has been estimated by the WHO in Brazil⁽¹⁸⁾. In contrast, some national studies results point toward a lower prevalence, at least in the Northeast region: 0.5%-5%^(2, 9).

In Brazil, hepatitis viruses (B and C) and HIV co-infections prevalence is not well known since published data are few and sometimes demonstrate conflicting results. Also a significant number of co-

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infected individuals are asymptomatic carriers of hepatitis viruses, which leads to a delayed diagnosis and under notification. In Brazilian studies, HBV/HIV prevalence ranges from 2.8% to 4.8%, whereas HCV/HIV co-infection rates vary from 4.4% to 36.2%^(6, 14, 15, 17, 19).

The present study aimed to determine the prevalence of the HBV and HCV infection in a recently diagnosed HIV population in the state of Ceará - Brazil. The authors also investigate other relevant epidemiological aspects related to this condition.

METHODS

This retrospective cohort included adult (>18 years old) patients, diagnosed HIV positives from 2008-2010. Medical records were reviewed and data on the first year of regular follow-up visits were collected. All patients attended medical treatment at Hospital São José of Infectious Diseases, a reference in infectious disease care in the state of Ceará, Brazil. Demographic data, the occurrence of risk factors for HIV, HBV and HCV infection and serologic results from the first year of medical attention were collected. Definitive HIV diagnosis was

considered with the presence of, at least, two positive serologic tests, with one of them being a specific method (Western blot, Immunoblot or indirect immunofluorescence). Patients were considered HBV carrier only if they were HBsAg positive. The occurrence of a positive total anti-HBc with a negative HBsAg was considered previous hepatitis B infection. Positivity of both anti-HCV and RNA-PCR for HCV was needed for the diagnosis of HCV infection. A positive anti-HCV with negative HCV RNA-PCR was considered previous contact with HCV. The study was approved by the hospital Ethical Research Committee (document n°007/2010). Epi Info 3.5.3 version was used for statistical analysis.

RESULTS

A total of 1,291 HIV positive patients were followed. In the first year, 671 (52%) of them collected HBV serologic tests: 23% (154 patients) had previous hepatitis B and 3.7% (25 patients) were co-infected. Only 329 (25.4%) had undergone serologic tests for HCV: 1.5% (5 patients) had previous hepatitis C and 5.4% (18 patients) were co-infected. Table 1 shows descriptive data.

TABLE 1. Hepatitis B, C and HIV co-infected patients in Ceará-Brazil, 2008-2010: descriptive data

Variables	HIV/HBV co-infected	HIV/HCV co-infected
Gender (%):		
Male	23 (92)	14 (77.8)
Female	02 (8)	04 (22.2)
Mean age in years (standard deviation)	37.4 (+/- 9.1)	39.7(+/-7.7)
Educational degree (%):		
Incomplete second degree	06 (24)	06 (33.4)
Complete second degree	05 (20)	04 (22.2)
University degree	03 (12)	02 (11.1)
Ignored	11 (44)	06 (33.3)
Sexual practice (%):		
Bisexualism	05 (20)	05 (27.8)
Heterosexualism	06 (24)	08 (44.4)
Homosexualism	07 (28)	-
Ignored	07 (28)	05 (27.8)
N° of sexual partners/year (%):		
>3	10 (40)	05 (27.7)
2-3	03 (12)	02 (11.1)
Monogamic	-	02 (11.1)
Ignored	12 (48)	09 (50)
IV drug use (%):		
Yes	02 (9.1)	04 (22.2)
No	15 (68.2)	12 (66.7)
Ignored	05 (22.7)	02 (11.1)
Alcohol use (%):		
Yes	09 (36)	08 (44.4)
No	06 (24)	04 (22.2)
Ignored	10 (40)	06 (33.3)
Mean CD ₄ count: cels/dL (Standard deviation)	400 (+/- 375.9)	402 (+/-226.2)
Mean HIV viral load: copies/dL (Standard deviation)	9,443 (+/- 1,649)	99,578 (+/- 26,299)
Total	25	18

Male gender was predominant in both groups, 92% (23/25) in HBV/HIV and 77.8% (14/18) of the HCV/HIV, and mean age was 37.4 and 39.7 years respectively. Regarding educational level, 24% (6/25) of the HBV/HIV and 33.4% (6/18) of the HCV/HIV patients did not complete middle school.

Among HBV/HIV patients, 52% (13/25) referred multiple sexual partners/year. Two of them had a HBV infected sexual partner and three had a known HIV positive partner. Homosexualism (MSM – men who have sex with men) and bisexualism were present in 28% (7/25) and 20% (5/25) respectively. Seven (28%) patients were adept to condom, but only one of them used it regularly. In the HCV/HIV group 38.8% (7/18) individuals have reported more than one sexual partner/year and 44.4% (8/18) were heterosexual. None of them had a known HCV positive sexual partner and only one referred an HIV positive partner. Two patients referred occasional condom use.

Intravenous drug use (IVDU) was reported by 22.2% (4/18) of the HCV/HIV studied population and in 9.1% (2/25) of the HBV/HIV group. Three patients in each group also referred the use of inhaled cocaine. Alcohol use was present in both groups: 36% (9/25) of the HBV/HIV group and 44.4% (8/18) of the HVC/HIV one. Only one patient of the HCV/HIV group had a risky occupation (nursing assistant). There was no history of occupational accident. A tattoo was present in two patients in the HCV/HIV group (11.1%) and in three (12%) HBV/HIV co-infected individuals. None of the studied patients were on hemodialysis treatment nor had been submitted to hemotransfusion prior to the co-infection diagnosis.

Only 5/20 HBV/HIV patients had $CD_4 < 200$ cells/dL compared to 3/11 patients in the HVC/HIV group. The former showed a mean CD_4 count of 400 cells/dL (standard deviation ± 375.9 ; variation: 19-1,607 cells/dL) and the latter 402 cells/dL (standard deviation ± 226.2 ; variation: 84-790 cells/dL). Mean HIV viral load was one log higher in the latter group: 9,443 copies/mL ($\pm 1,649$) in HBV/HIV individuals and 99,578 ($\pm 26,299$) in the HVC/HIV ones.

DISCUSSION

In our data, only 52% and 25.4% of the newly diagnosed HIV positive patients had known serologic status to HBV and HCV infection in the first year of medical care. This is of great concern since all these patients are receiving medical attention in an infectious disease reference center. Other studies report the same difficulty in testing patients for hepatitis. Tovo et al. found that only 58.4% (343/587) of the HIV patients on medical follow-up in a tertiary unit in south Brazil were tested for either HBV or HVC serologies⁽¹⁵⁾. Other authors, however, report successful experiences, which led to better results. The UK collaborative HIV cohort (UK CHIC) study showed that they were able to gradually increase the proportion of HIV patients tested for HCV over time (9.2% in 1996 to 79.9% in 2007)⁽¹⁶⁾. This improvement in screening coverage reflected a change in national management guidelines, since there was a clear instruction that all HIV positive patients should be screened for HCV since at least 2004⁽⁵⁾.

HBV/HIV and HCV/HIV prevalences were 3.7% and 5.4% respectively. These are in accordance with other Brazilian published data, in which values ranged from 2.8%-4.6% for HBV/HIV co-infection^(7,15,19) and 4%-6.4% for HCV/HIV association^(6,7,17). Similar to our study, these researches tested HIV patients who were in medical follow-up in infectious disease centers in four distinct Brazilian cities: São Paulo, Porto Alegre, Amazonas and Vitória. However, some authors have found quite different results in studying the prevalence of these co-infections in special populations such as IV drug users (84.8% HCV/HIV association)^(13,14). The mode of HCV transmission could explain this high prevalence.

Co-infected patients were mainly of the male gender in productive age, with a mean age of 37.4 and 39.7 years for HBV and HVC infections respectively. Other studies also reported a higher frequency of these co-infections among men and most of them describe the age interval of 35 - 40 years as the most prevalent^(11,15,17,19,20).

A considerable percentage of patients referred to have multiple sexual partner/year. However, bisexualism and homosexualism were more common in the HBV/HIV group. The HBV sexual transmission mode is well documented but the predominance in MSM is not the rule. Although some authors describe the same predominance^(12,14), others found different prevalent risk, such as IVDU⁽¹⁸⁾. It is possible that there was a high frequency of MSM in the HIV positive population on follow-up in the studied center, which could explain this result.

Interestingly there was a small frequency of IVDU in the HCV/HIV group (22.2%). It is possible that the number of IVDU, a key risk factor for this co-infection, is lower in our region than in other Brazilian urban centers⁽⁴⁾.

In our study most of the patients were diagnosed co-infected with CD_4 counts higher than 200 cells/dL. The small study sample and the presence of missing values possibly caused bias in this result.

The study limitations were the difficulty in collecting reliable data from secondary source (medical records) and the small sample. These could compromise some of the study results. Besides that, some of the study results are of great concern since a low percentage of the HIV infected individual under medical care were tested for viral hepatitis serology in the first year of follow-up, despite the vast literature showing the negative impact of HIV in the HBV and HVC liver disease progression. This reinforces the need for better training healthcare workers and providing laboratory support for a prompt hepatitis infection diagnosis. Routine hepatitis tests are essential for identifying infected people in order to facilitate adequate medical management to avoid complications and to decrease the spread of these diseases. In the same way, the accomplishment of educational programs for the population, providing information about HVB/HVC/HIV risk of transmission to others and HBV vaccination, in an effort to reduce viral spread, are very important issue. The study also suggests that larger prevalence studies are necessary for a better understanding of the HBV/HCV/HIV co-infection epidemiology in Ceará.

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RESUMO – Contexto - A ocorrência da associação de HIV com a hepatite por vírus B (HVB) e C (HVC) é preocupante visto que os pacientes coinfectados tendem a ter uma resposta pior à terapia antiviral e uma chance maior de progredirem para a cronicidade da doença hepática e suas complicações. No Brasil, os estudos publicados sobre a prevalência dessas coinfeções ainda são escassos e, muitos deles, com resultados conflitantes entre si. Além disso, muitos pacientes coinfectados são portadores assintomáticos dos vírus das hepatites o que causa um atraso no seu diagnóstico, com consequente subnotificação de casos. **Objetivos** - Este estudo objetiva determinar a prevalência da infecção pelo HVB e HVC em pacientes recém-diagnosticados com HIV no Ceará/Brasil. **Métodos** - Coorte retrospectivo com pacientes >18 anos, diagnosticados HIV+ de 2008-2010. Foram coletados dados referentes ao primeiro ano de acompanhamento desses pacientes através de revisão de prontuário: fatores de risco para HIV, HBV e HCV e resultados de provas sorológicas para esses vírus. **Resultados** - Foram acompanhados 1291 pacientes HIV+. Testes sorológicos para HBV foram realizados em 52% dos casos: 23% apresentavam hepatite B prévia e 3,7% eram coinfectados. Apenas 25,4% tinham testes sorológicos para HCV: 1,5% tinham hepatite C prévia e 5,4% eram coinfectados. A maioria dos pacientes HBV/HIV referia ter múltiplos parceiros sexuais em um ano. Homossexualismo e bissexualismo estavam presentes em 28% e 20% respectivamente. No grupo HCV/HIV 38,8% referia múltiplos parceiros sexuais em um ano e o uso de drogas endovenosas ocorreu em 22,2% dos casos. **Conclusão** - O estudo reforça a necessidade de um treinamento dos profissionais de saúde e de facilitação do acesso do paciente ao suporte laboratorial para que seja possível o diagnóstico rápido e precoce das hepatites virais, o que levaria a um adequado manejo clínico desses pacientes e a uma redução da disseminação dessas doenças. O estudo sugere também a necessidade de realização de campanhas educacionais para a população, abordando os riscos de transmissão desses vírus e incentivando a vacinação para o HBV, com o intuito de diminuir a propagação dessas doenças.

DESCRITORES - Infecções Oportunistas Relacionadas com a AIDS. Vírus da hepatite B. Hepatite C. Hepatite crônica.

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