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# Epidemiological analysis of serological markers of hepatitis B in HIV+ patients from Curitiba and metropolitan region

## *Análise epidemiológica de marcadores sorológicos de hepatite B em pacientes HIV+ de Curitiba e região metropolitana*

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### ABSTRACT

**Introduction:** The presence of hepatitis B virus (HBV) in patients infected by the human immunodeficiency virus (HIV) leads to a higher incidence of liver disorders due to persistence and recurrence of HBV infection in addition to increased morbidity and mortality. **Objective:** To determine the prevalence of serological markers for hepatitis B in patients infected by HIV followed at Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR). **Methods:** The clinical and epidemiological data were collected through a questionnaire applied to the patients, as well as a retrospective analysis of medical records. Serum levels of total hepatitis B core antibody (anti-HBc) and surface antigen of the hepatitis B virus (HBsAg) were evaluated through chemiluminescent microparticle immunoassay. Among the 297 HIV+ patients, 49.8% were seropositive only for anti-HBc, and 2.6 % were positive for both markers. **Results and discussion:** The prevalence of hepatitis B markers was significantly associated with HIV infection when compared with the prevalence observed in the general population from the same geographical area (anti-HBc+ HBsAg+: 0.14% vs. 2.6%, OR: 18.82, 95% CI 2.34-151.19,  $p = 0.00052$ ). Concerning the associated risks to acquire HIV/HBV infection, 44.87% of the patients reported having been infected through sexual contact. A total of 16.66% HIV/HBV positive patients were in the age group 18-30 years, 62.82% were between 31-50 years and 16.66% were over 60 years old. **Conclusion:** The findings of the present study corroborate the need to investigate systematically the presence of markers for HBV in HIV+ patients from different regions of the country.

**Key words:** coinfection; HBV/Aids; Paraná; serological markers.

### INTRODUCTION

The human immunodeficiency virus (HIV) affects approximately 35 million people in the world; approximately 8.6% of them are coinfecting by the hepatitis B virus (HBV)<sup>(1)</sup>. The HIV/HBV coinfection rates vary according to the origin of the studied population and the geographic position, among other factors<sup>(2, 3)</sup>, what illustrates the importance of epidemiological studies in different populations. In North America and Europe, more than half of the men who have sex with HIV+ men have already had contact with HBV, and 5%-10% suffer from chronic hepatitis B<sup>(2, 4)</sup>.

HBV infection in HIV+ patients is of clinical importance because it confers a poor prognosis for patients, and it may exert interference in the results of the provided treatments<sup>(1, 5)</sup>. Among HIV+ individuals chronically coinfecting by HBV, higher occurrence of progressive hepatic fibrosis, cirrhosis, and hepatocellular carcinoma is observed. Besides, persistence and relapse of HBV infection may occur. As a result, morbidity and mortality from hepatic diseases are significantly higher in HIV carriers<sup>(2, 3)</sup>.

In Brazil there are scarce epidemiological data on HIV/HBV coinfection relating risk factors for the acquisition of the virus to its seroprevalence. Studies carried out mainly in the South and Southeast regions, the most developed and populous parts

of the country, report the prevalence of HIV/HBV coinfection ranging from 5.3% to 38.6%<sup>(6-11)</sup>. HIV/HBV coinfection is strongly associated with exposure to infected blood or materials, such as sharps, needles, syringes, during transfusions, hemodialysis, tattoos and sexual intercourse<sup>(9)</sup>. The South and Southeast regions are known to concentrate the highest mortality rates of acquired immunodeficiency syndrome (Aids)/HIV in Brazil, with 9.4 and 7.1/100 thousand inhabitants, respectively<sup>(12)</sup>. Paraná occupies the third place among those states. It is important to highlight that around 60% of the HIV/Aids cases of the state of Paraná are concentrated in the city of Curitiba and its metropolitan region; the outpatient department of infectious and parasitic diseases of Hospital de Clínicas da Universidade Federal do Paraná (HC-UFRP) treats approximately 40% of them.

Although the determination of serological markers of HBV in HIV-infected individuals has clinical relevance and public health importance, it had not been assessed in a systematic way among patients followed at HC-UFRP. Thus, this study aimed to establish the prevalence and analyze the epidemiological factors of serological markers of HBV associated with HIV+ patients followed at HC-UFRP, a regional reference in the treatment of HIV/Aids, with around 2,500 registered patients to the date of the present study.

## METHODS

### Participants and clinical data

The study population comprised 297 individuals – 148 (49.8%) males and 149 (50.2%) females –, treated at the outpatient clinic of parasitic and infectious diseases of HC-UFRP from April 2008 to March 2009. In order to obtain clinical epidemiological data, besides consultation and interview, a retrospective analysis of medical records was conducted. Also, for each participant, a standardized questionnaire was applied, containing questions about demographic and socioeconomic variables, and risk factors for HBV and HIV/Aids acquisition. The following variables were analyzed: age, sex, injection drug use (IDU), history of transfusion of blood and/or blood products, number of transfusions (one, between two and five, or more than five), date of the first positive HIV serology test, and other risk factors associated with HIV acquisition.

### Blood collection and laboratory analysis

Patients were verbally informed about the study. After signing the consent form, each individual had 5 ml of blood collected

by venipuncture without anticoagulant. In the next step, blood was centrifuged and the serum was aliquoted and stored at -70° until use. Total hepatitis B core antibody (anti-HBc) and surface antigen of the hepatitis B virus (HBsAg) were detected by chemiluminescent microparticle immunoassay (Bioelisa colour Architect - Abbott, Illinois, USA), at the central laboratory of HC-FRP. The study was approved by the Human Research Ethics Committee of HC-UFRP.

## Statistical analysis

The acquired data about HIV+ were inserted at an Excel spreadsheet and analyzed according to the variables, using chi-squared test with Yates' correction or two-tailed Fisher test, aiming to find associations between possible risk factors and the presence of serological markers of hepatitis B. These data were compared with those obtained at a previous study<sup>(13)</sup> in a population of 681 healthy (HIV-) individuals from the same geographic region. When applicable, odds ratio (OR) was calculated, with a 95% confidence interval (CI). The *p*-value for statistical significance was *p* < 0.05.

## RESULTS

### Prevalence of HIV and HBV markers

The obtained results showed that among the 297 HIV+ patients, 148 (49.8%) were positive for anti-HBc. When comparing this result with the observed in 681 healthy individuals from the same geographic region, 42 (6.26%) presented positivity for this marker alone (148/49.8% vs. 42/6.26%, OR = 15.11; CI 95% = 10.27-22.23; *p* < 0.01) as shown in **Table 1**.

Another important piece of data is the association of both serological markers anti-HBc and HBsAg with HIV infection in patients from Curitiba and metropolitan region. Results demonstrated that among the 297 assessed HIV+ patients, eight

**TABLE 1 – HIV+ patients and controls that tested positive for anti-HBc**

	n° of patients	Anti-HBc	Reference
Healthy	681	42 (6.26%)*	13
HIV+	297	148 (49.8%)*	This study
OR (CI 95%)		15.11	
<i>P</i> -value		<i>p</i> < 0.05	

\*Statistically significant values.

HIV: human immunodeficiency virus; OR: odds ratio; CI: confidence interval.

(2.6%) were seropositive for both markers. When comparing this result with that observed in 681 healthy individuals from the same geographic region, where one (0.14%) tested positive for HBsAg and anti-HBc<sup>(13)</sup>, a statistically significant association was observed between the cited HBV markers and HIV infection (1/0.14% versus 8/2.6%. OR: 18.82, CI 95%: 2.34-151,  $p = 0.00052$ ).

### Demographic data and risk of contracting infections

Concerning the probable time of HIV infection, a time of progression to Aids longer than 10 years was observed in 49 (31.4%) of the HIV+ HBV+ patients, and in 59 (41.8%) of the HIV+ HBV- patients. Among the patients who presented time to progression shorter than 10 years, 96 (61.5%) and 76 (53.9%) were HIV+ HBV+ and HIV+ HBV-, respectively. There was no statistically significant difference ( $p = ns$  [non significant]) when the groups HIV+ HBV+ and HIV+ HBV- were compared.

Considering the probable modes of HIV transmission, the most prevalent for the groups HIV+ HBV+ versus HIV+ HBV- were: sexual, 62/156 (39.74%) versus 60/141 (42.55%); blood transfusion, 6/156 (3.85%) versus 12/141 (8.52%); IDU, 4/156 (2.56%) versus 8/141 (5.68%), respectively. A total of 62/156 (39.74%) among HIV+ HBV+ and 47/141 (33.33%) among HIV+ HBV- individuals did not know or did not inform the probable mode of transmission. There was no statistically significant difference among the cited modes of transmission ( $p = ns$ ).

Data analysis of age distribution showed that among HIV+ HBV+ patients 26 (16.66%) were aged 18-30 years, 98 (66.21%) were aged 31-50 years, 26 (16.66%) were over 50 years, and six (4.05%) did not inform age. Among the group of HIV+ HBV- patients, 26/141 (18.44%) were aged 18-30 years, 83/141 (58.87%) were aged 31-50 years, 23/141 (6.31%) were over 50 years, and nine (6.38%) did not inform age. There was no statistically significant difference among the analyzed age groups in both groups of patients ( $p = ns$ ).

## DISCUSSION

In Brazil there are scant data on the prevalence of serological markers of HBV in HIV+ individuals. Epidemiological studies about HIV/HBV coinfection are even scarcer in the state of Paraná, which holds an important position in the context of viral coinfections in Brazil, according to other studies<sup>(14)</sup>. Therefore, estimating the regional prevalence of these diseases by means

of an initial screening of serological markers, including anti-HBc and HBsAg, is extremely important, as coinfecting patients (HIV/HBV) have significantly lower HIV treatment success rates<sup>(15)</sup>. Also, because HIV/HBV coinfection can modify the course of hepatitis B, being related to morbidity and mortality increase, accelerating the disease progression to fibrosis and hepatocellular carcinoma<sup>(16,17)</sup>.

The data presented in this study reveal high prevalence of HBV markers in HIV patients treated at the reference hospital in Curitiba, and this prevalence is statistically significant in relation to the general population from the same geographic area and economic class. With regard to anti-HBc positivity, which characterizes previous contact with the virus, a risk of OR = 15.11 was observed in individuals infected by HIV. This association HIV/HBV remained significant when comparing the concomitant presence of HBsAg and anti-HBc markers, associated with an OR risk of 18.82. Consequently, these data reinforce the information of high prevalence of HIV/HBV coinfection in the investigated patients. It is worth remembering that the items of information reported here show coherence and correlations among themselves, because HIV/HBV coinfection presents sexual contact as the main infection/transmission mode; the main transmission mode cited in this study is one of the possible explanations for the high HIV/HBV coinfection rate.

The prevalence of anti-HBc in the present study was higher than those of other states in the country, such as Bahia<sup>(18)</sup>, Ceará<sup>(19)</sup> and Santa Catarina<sup>(10)</sup> (**Table 2**).

Curitiba presented one of the lowest HBsAg rates in comparison with the other states (Table 2), but with very high rates when in comparison with the general population not infected by HIV or HBV. Other studies in Brazil show high rates of HIV/HBV coinfection, such as that by Oliveira *et al.* (2013)<sup>(20)</sup>, in the state of Piauí, with a 6% rate, and that by Zago *et al.* (2007)<sup>(21)</sup>, who reported a 3.8% rate in Espírito Santo.

**TABLE 2 – Prevalence of markers of HBV infection in HIV+ patients reported in different Brazilian populations**

Place	n° of patients	Anti-HBc+	HBsAg+	Year	Reference
Ribeirão Preto (SP)	401	39.7%	8.5%	2002	8
Campinas (SP)	232	44.2%	5.3%	1995	10
Salvador (BA)	200	21.5%	0.5%	2013	19
Ceará (CE)	1.291	23	3.7	2010	20
São Paulo (SP)	1.693	38.6%	5.7%	1996	12
Curitiba (PR)	297	49.8%	2.6%	2009	Present study

HBV: hepatitis B virus; HIV: human immunodeficiency virus.

The differences between the coinfection rates found worldwide and in Brazil arise because of the different risk factors of transmission that the studied population is exposed to. In addition, one must consider the different methods employed in each study. The present investigation used a state-of-the-art method for the detection of these markers (chemoluminescence), whose sensitivity is much greater than that of the rapid tests (dot-blot assays) and other enzyme tests also used for patient screening.

The findings of the present study confirm the necessity of investigating, in a systematic way, the presence of HBV markers in

HIV+ patients from the different regions of Brazil. They are also an important instrument of alert to subsidize interventions in the health system and in epidemiological surveillance. In short, the presence of HBV markers was significantly high in HIV/Aids patients compared with the healthy population from the same geographic region, confirming HIV infection as an important risk factor for the acquisition of HBV. Still, no statistically significant association was observed between the presence of serological markers of HBV and HIV, and gender, patients' age group, progression time to HIV/Aids, and other risk factors for the acquisition of HIV.

## RESUMO

**Introdução:** A presença do vírus da hepatite B (HBV) em indivíduos infectados pelo vírus da imunodeficiência humana (HIV) está associada ao significativo aumento da morbimortalidade nos pacientes afetados. **Objetivo:** Estabelecer a prevalência de marcadores sorológicos de HBV e dos fatores epidemiológicos associados em pacientes HIV+ acompanhados pelo Hospital de Clínicas da Universidade Federal do Paraná (HC-UFPR). **Métodos:** Os dados clínicoepidemiológicos foram coletados por meio de análise retrospectiva dos prontuários e de aplicação de um questionário. Os marcadores anti-HBc total e o antígeno HbsAg foram avaliados pela quimioluminescência por micropartículas. **Resultados e discussão:** Dos 297 pacientes HIV+, 49,8% apresentaram sorologia positiva somente para anti-HBc e 2,6%, para anti-HBc e HbsAg. A prevalência de marcadores de hepatite B foi significativamente associada à infecção pelo HIV quando comparada com a prevalência observada na população geral da mesma área geográfica (anti-HBc+/HbsAg+: 0,14% vs. 2,6%, odds ratio (OR): 18,82, intervalo de confiança (IC) 95%: 2,34-151,19, p = 0,00052). Em relação aos grupos de risco para infecção pelo HIV, 44,87% dos pacientes com sorologia positiva para HBV informaram terem sido infectados por transmissão sexual. Quanto à faixa etária dos pacientes HIV+/HBV+, 16,66% tinham entre 18-30 anos, 62,82%, entre 31-50 anos e 16,66%, acima dos 50 anos de idade (p = ns). **Conclusão:** Esses achados corroboram a necessidade de se investigar sistematicamente a presença de marcadores para HBV em pacientes HIV+ das diferentes regiões do país.

**Unitermos:** coinfeção; HBV; HIV/Aids; Paraná; marcadores sorológicos.

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