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CONCISE ARTICLE

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High prevalence of hepatitis B virus infection among tuberculosis patients with and without HIV in Rio de Janeiro, Brazil

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Abstract To determine the prevalence and exposure factors associated with hepatitis B infection in tuberculosis patients with and without HIV type 1 coinfection, the presence of hepatitis B virus serological markers was investigated in a retrospective study. The seroprevalence of hepatitis B virus in patients with tuberculosis only was 14.6%, and in tuberculosis patients coinfected with HIV it increased to 35.8%. In patients with HIV and tuberculosis coinfection, homosexuality constituted the principal exposure factor, while in tuberculosis patients without HIV, a gradual increase in hepatitis B virus seroprevalence was noted along with increasing age. The results demonstrate that hepatitis B infection is highly prevalent in tuberculosis patients in Brazil and suggest that a vaccination program for the general population should be considered in order to prevent further hepatitis B infections.

Introduction

Hepatitis B virus (HBV) infection is one of the most common infectious diseases, with an estimated 2 billion people infected globally. Currently, over 350 million people are chronically infected, and 1–2 million deaths per year are directly or indirectly caused by the infection [1]. Immunocompromised individuals, such as those infected with HIV, have a greatly increased risk of developing chronic infection [2]. Worldwide, half of all individuals infected with HIV are also infected with TB. HIV and HBV coinfection is also common, since these diseases share similar potential routes of transmission [2].

Several serological tests can be used to evaluate HBV infections. HBV surface antigen (HBsAg) can be identified in a patient's serum 30–60 days after exposure to the virus, and it persists for variable periods of time. Anti-HBc develops in all HBV infections and persists indefinitely, but it does not develop following vaccination with hepatitis surface antigen (recombinant vaccine). Antibody to the surface antigen (anti-HBs) develops after a resolved infection or following vaccination and is responsible for long-term immunity. Previous studies have suggested that patients with chronic HBV infection are at increased risk for developing hepatotoxicity [3, 4], which is a common side effect of anti-TB drugs and highly active antiretroviral therapy (HAART) administered to TB- and HIV-1-infected patients, respectively [5, 6]. In our study, we examined the seroprevalence of HBV serological markers in TB patients with or without HIV coinfection who attended a Tuberculosis Reference Center in Rio de Janeiro.

Patients and methods

All patients who developed TB in the 4-year period from 1999 to 2002 and who were regularly followed up at the Tuberculosis Reference Center, FIOCRUZ, Rio de Janeiro, Brazil, constituted the eligible population. The diagnosis of TB was based on the result of an acid-fast bacillus smear and/or positive culture. Although all 357 TB patients studied had been serologically tested for HIV during their first visit, only 209 patients had been tested for HBV; these patients constituted the actual cross-sectional study group.

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Table 1 Characteristics of patients with hepatitis B/tuberculosis (TB) coinfection with or without HIV

Characteristic	No. (%) of patients	
	TB only (n=13)	TB/HIV coinfected (n=43)
Age category (year)		
17–39	2 (15.4)	28 (65.1)
40–75	11 (84.6)	15 (34.9)
P value	0.023	0.26
Sexual behavior		
Heterosexual	13 (100)	20 (46.5)
Homo/bisexual	0	17 (39.5)
P value	–	0.013*
Drug use		
Yes	0	5 (11.6)
No	12 (92.3)	30 (69.8)
P value	–	0.023**
Family income[a]		
0–2	9 (69.3)	31 (72.1)
>2	4 (30.7)	12 (27.9)
P value	0.36	0.003

[a]Numbers of minimum salaries (US$80 each) received per month

*Missing = 6 (13.9%)

**Missing = 8 (18.6%)

All clinical, serological and demographic data were extracted from the hospital's clinical protocols and retrospectively reviewed. Information regarding risk factors for HIV and HBV infection, such as sexual behavior, intravenous drug use (IVDU), gender, age, educational and economic status, and residency were also assessed.

Data were analyzed using the Statistical Package for the Social Sciences-Win 8.0 (SPSS, Chicago, IL, USA). Proportions (%) for categorical data, and means and standard deviations (SD) for continuous data were used to describe the HBV serological status, personal characteristics and social behavior of the study population. The chi-square test (proportions) and the Student *t*-test (means) were used to determine the two-tailed statistical significance of associations. Probability values less than 0.05 were considered significant. Prevalence ratios for exposure factors were calculated for the HBV group.

Results and discussion

The study population consisted of 209 TB patients who had been serologically tested for HBV infection. The overall prevalence of HBV was defined by the presence of anti-HBc in serum. Of the 209 patients studied, 120 (57%) were coinfected with HIV and 89 (43%) were not infected with HIV. The age of the patients ranged from 16 to 74 years, with a mean age of 39.7 years (SD = 11.6). Fifty-six (26.8%) patients had markers for HBV and six (2.8%) were identified as having active infection (HBsAg positive). Five (2.4%) patients were positive for isolated HBsAg antibodies indicating HBV recombinant vaccine response. Thirty-four (16.3%) patients had anti-HBc with anti-HBs, indicating a past resolved infection, and 16 (7.7%) had anti-HBc alone. The presence of anti-HBc alone is often interpreted as evidence of a remote resolved infection from which HBsAg antibodies have declined to undetectable levels, or of ongoing chronic infection with HBsAg that is escaping detection.

To the best of our knowledge, this study is the first to document the prevalence of HBV infection in TB patients in Brazil. The results show a high prevalence of HBV infection among TB patients without HIV coinfection (14.6%) as well as among those with HIV coinfection (35.8%) (P=0.001). The high prevalence of HBV infection among HIV-infected patients has also been observed in other studies [7, 8]. This may be related, in part, to the fact that the mode of transmission is similar for HBV and HIV, meaning the population at risk for HIV infection is also at risk for HBV infection. The prevalence of anti-HBc in the HIV-negative group was almost threefold higher (14.6%) than in the general population of Rio de Janeiro (5.5–5.8%) [9, 10].

Rio de Janeiro is located in the southeastern region of Brazil, which was recently classified as an area of low HBV endemicity [10]. In regions of low endemicity, where the lifetime risk of HBV infection is less than 20%, transmission is primarily horizontal and can occur via close person-to-person contact, sexual relations, needle-sharing among intravenous drug users, or occupational exposure to contaminated blood and blood products [1]. Exposure factors associated with hepatitis B infection in our TB patients are reported according to HIV status in Table 1.

Our results showed a significant association between HBV seroprevalence in the HIV-negative group and a gradual age increase (40–75 years), indicating horizontal transmission of HBV. Although the exact mechanism of transmission is unclear, horizontal transmission occurs by person-to-person contact; in large families living in small houses with many children sleeping together and sharing utensils and belongings, small wounds, wound exudates, and saliva of HBV-infected individuals may become sources for horizontal transmission [11–13]. In HIV-infected individuals, sexual behavior and intravenous

drug use were the risk factors most often associated with HBV infection, suggesting that HBV transmission occurred mainly by sexual contact or via the parenteral route. A strong association was found between HBV infection and individuals with a low socioeconomic status living in the poor and crowded regions bordering the city of Rio de Janeiro; these areas are characterized by a lack of proper sanitation and poor environmental conditions. Low socioeconomic status has also been frequently related to an increased risk of contracting TB, especially in overcrowded settings [14].

Our results showed that 148 (70.8%) patients had risk factors for HBV infection and only five (2.4%) of the HIV-coinfected patients were positive for vaccine antibodies. These findings suggest that HBV vaccination coverage remains low in most risk groups. This low coverage may be attributable to a lack of education regarding HBV prevention in the general population and the fact that HBV vaccination was first included in Brazil's national infant immunization calendar in 1998. Vaccination is currently offered to all newborn babies (with the first dose given at birth), to persons with an identified high-risk factor (e.g., immunocompromised individuals, healthcare workers, sex professionals), and to individuals living in highly endemic areas; it is also offered to adolescents aged 14–19 years. In Rio de Janeiro, the main target group for HBV vaccination is newborns, but there is also a large group of susceptible adolescents and adults not included in the routine vaccination program.

Several studies have indicated that HBV coinfection in patients with HIV and TB is a risk factor for the development of severe hepatotoxicity following the initiation of HAART and antituberculosis therapy, respectively, which may necessitate discontinuation of treatment [4, 15]. HBV vaccination is the only effective method for preventing primary hepatic cancer, cirrhosis related to chronic HBV infection and severe hepatotoxicity during antituberculosis and HAART therapy.

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