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Leprosy and hepatitis B coinfection in southern Brazil

Cleverson Leitão¹, Denis Ueda¹, Anna Carolina de Moraes Braga, Angelica B.W. Boldt, Iara J.T. Messias-Reason*

Laboratório de Imunopatologia Molecular, Department of Medical Pathology, Hospital de Clínicas, Federal University of Paraná, Curitiba, PR, Brazil

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ABSTRACT

To investigate the association of leprosy with hepatitis B virus (HBV) infection, as yet unknown for South Brazil, we assessed hepatitis B virus coinfection in 199 South Brazilian leprosy patients (119 lepromatous, 15 tuberculoid, 30 borderline, 12 undetermined and 23 unspecified) and in 681 matched blood donors by screening for the hepatitis B virus markers HBSAg and anti-HBc, using ELISA. Positive samples were retested and anti-HBc+ only samples were tested for the hepatitis B surface antibody (anti-HBs). There was a strong association between leprosy and hepatitis B virus infection (OR=9.8, 95% CI=6.4–14.7; $p=0.004 \cdot E^{-30}$), as well as an association between HBV infection and lepromatous leprosy, compared to other forms (OR=2.4, 95% CI=1.2–4.8; $p=0.017$). We also found that confinement due to leprosy was associated with hepatitis B virus infection (OR=3.9, 95% CI=2.1–7.4; $p=0.015 \cdot E^{-3}$). Leprosy patients are susceptible to develop hepatitis B virus infection, especially lepromatous. Institutionalized patients, who probably present a stronger Th2 response, have higher risk of being exposed to hepatitis B virus. This clearly emphasizes the need for special care to leprosy patients in preventing hepatitis B virus coinfection in South Brazil.

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Introduction

Leprosy is a long known infectious disease and still represents a major cause of morbidity and mortality in developing countries. According to data of the World Health Organization, more than 30,000 people are affected in the Americas.² In 2012 alone, there were 406 new admissions to Brazilian hospitals due to leprosy. In South Brazil, 36,628 patients were diagnosed with the disease in 2011 and 10.9% presented grade 2 disability

(11.4% in Paraná state), which is the highest rate in the country. South Brazil also has the 7th highest rate in Brazil of new case detection of leprosy with incapacity: 93.8%.¹

Many leprosy patients also have positive markers for other infections, such as HIV and HBV (hepatitis B virus).^{3–7} In central Brazil, leprosy along with hepatitis B has been the subject of former investigations,^{6,7} but nothing is known about this disease association in other Brazilian regions. In this work, we aimed to describe leprosy–HBV epidemiology in South Brazil.

* Corresponding author at: Laboratório de Imunopatologia Molecular, Department of Medical Pathology, Hospital de Clínicas, Federal University of Paraná, Rua General Carneiro, 181, 80060-150 Curitiba, PR, Brazil.

E-mail address: iarareason@hc.ufpr.br (I.J.T. Messias-Reason).

¹ Both authors contributed equally to this work.

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Materials and methods

Subjects and samples

Two hundred and three patients with leprosy from three different treatment centers were selected. Twenty-three of them were attended at Universidade Federal do Paraná's Clinical Hospital (HC-UFPR), 71 at Paraná's Hospital of Sanitary Dermatology (PHSD) and 109 at Regional Center of Specialities-Barão (CRS-Barão). The patients from now on referred as "institutionalized" are 60 patients hospitalized permanently in PHSD. The high prevalence of institutionalized patients is explained by their social conditions. Since they presented advanced forms of leprosy or were abandoned by their families, confinement was the best way to assist them. Four patients had to be excluded from the study. Two of them did not show up to have their blood samples taken, and access to the medical records was not possible for another two. Thus, 199 patients were designated as "cases" for all analysis purposes.

The patients were also divided in groups according to the clinical classification proposed by Ridley and Jopling.⁸ Diagnosis at presentation was lepromatous leprosy for 119 patients (59.8%), tuberculoid leprosy for 15 (7.5%), and borderline leprosy for 30 patients (15.1%); 12 patients (6%) had an undetermined form of leprosy, and 23 (11.6%) were unspecified. Those with unspecified form of the disease were excluded from the analysis of clinical forms (176 cases were considered).

Six hundred and eighty-one blood donors tested for anti-HBc from HC-UFPR Hemotherapy Service were selected as controls. Cases (average age of 52 ± 16 years) and controls (average age of 45 ± 12 years) were also matched for age-range groups. The first group comprised nine patients and 36 controls between 15 and 24 years of age. The second group had 75 patients and 200 controls between 25 and 49 years, and the third one, 115 cases and 345 controls above 50 years old. 77 (38.7%) patients and 269 (39.5%) controls were female, whereas 122 (61.3%) patients and 412 (60.5%) controls were male.

Patients and controls were selected in 2002 and 2003. The study was approved by the ethics committee of the Clinic Hospital and Health State Department, and all subjects were asked to give written an informed consent for their participation and to answer a standardized questionnaire to determine the history of the patients regarding possible blood transfusion and the existence of other infectious diseases.

HBV testing

Seven mL of blood were taken from each subject. The samples were centrifuged and serum aliquots stored at -20°C before HBV testing. An ELISA was used to detect the presence of anti-HBc (antibodies against HBV core antigen) (MONOLISA[®] a-HBc PLUS, BIO-RAD, Marnes La Coquette, France). To search for HBsAg, a sandwich ELISA was performed (MONOLISA[®] a-HBc PLUS, BIO-RAD, Marnes La Coquette, France). Patients positive for anti-HBc alone (HBsAg negative) were tested by microparticle enzyme immunoassay (MEIA) to detect antibodies against hepatitis B surface antigen (anti-HBs) (Murex anti-HBs, Murex Biotech Limited, Temple Hill, United Kingdom). All positive samples were retested using the same methods.

Statistics

Frequencies were compared using Fisher's exact test and odds ratios with the respective 95% confidence limits. Logistic regression models were used to adjust results for age, gender and assistance using the SPSS 13.0 software (IBM, USA).

Results

Of the leprosy patients, 39.7% were positive for HBV markers, in contrast to 6.3% of the control group (Table 1), suggesting a strong association between leprosy and HBV infection (79/199 vs. 43/681; OR=9.77, 95% CI=6.42-14.86; $p < 0.004 \cdot E^{-30}$). Of the leprosy patients, 26 (13.1%) received blood transfusion, of which twelve were positive for HbsAg and/or anti-HBc. Even after the exclusion of these possibly intravenously HBV-infected patients, leprosy and HBV infection remained associated (67/173 vs. 43/681; OR=9.38, 95% CI=6.08-14.48; $p = 0.006 \cdot E^{-24}$). There was no difference for HBV positivity according to gender and age ($p = 0.117$, Table 2). The following co-infections were also observed in HBV+ leprosy patients: seven were positive for syphilis, six for HCV, two for Chagas disease, one for HCV and syphilis and one for syphilis and Chagas disease.

There was also an association between HBV infection and lepromatous leprosy, compared with the other leprosy forms (unspecified patients were excluded) (55/119 or 46.2% vs. 15/57 or 26.3%; OR=2.4, 95% CI=1.2-4.8; $p = 0.017 \cdot E^{-30}$, see Table 3). This remained significant in the logistic regression after correction for age and gender and was independent of confinement ($p = 0.018$). We also found that confinement due to leprosy was associated with HBV infection (38/61 or 62.3%

Table 1 – Different HBV infection markers in leprosy patients and controls.

| | Patients (%) | Controls (%) | Institutionalized (%) |
|-----------------------|--------------|--------------|-----------------------|
| n | 199 | 681 | 60 |
| HBsAg only | 2 (1) | 0 (0) | 0 |
| HBsAg and anti-HBc | 3 (1.5) | 1 (0.15) | 1 (1.6) |
| Anti-HBc only | 24 (12.1) | 12 (1.76) | 14 (23.3) |
| Anti-HBc and anti-HBs | 50 (25.1) | 30 (4.41) | 21 (35) |
| Total | 79 | 43 | 36 |

n, number of individuals.

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