

ASSOCIATION BETWEEN LEPROSY AND HEPATITIS B INFECTION. A SURVEY IN GOIÂNIA, CENTRAL BRAZIL

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SUMMARY

This investigation presents the results of Hepatitis B virus screening among leprosy patients conducted in Central Brazil as a preliminary information for a HBV vaccination programme. The main objectives were to assess the seroprevalence of HBV serum markers among lepromatous patients and to analyse institutionalization as risk factor for HBV infection in this population. Two groups of lepromatous patients were studied, 83 outpatients and 171 institutionalized ones. Screening for HBV serum markers included the detection of HBsAg, anti-HBc by radioimmune assay (RIA). The prevalence of carrier state (HBsAg) was 4.8% and 8.8% among outpatients and institutionalized, respectively, ($p > 0.05$). Seroprevalence of exposure (all markers) was statistically significant different between outpatients (16.9%) and institutionalized ones (50.3%). Institutionalized patients had an almost four fold risk of HBV infection when compared to the outpatients, and the highest risks were among patients with more than 21 years of residence in the colony, after adjusting for age and sex.

KEY WORDS: Leprosy and Hepatitis B virus infection; Risk factors for Hepatitis B infection; Institutionalized leprosy patients.

INTRODUCTION

The association between Leprosy and Hepatitis B virus (HBV) infection has been a constant issue in the literature. However, there is a lack of agreement in the results of the studies conducted in areas of different endemicity of HBV infection^{1,2,4,5,6}. Despite of the controversy, an association between lepromatous type of leprosy patients and HBsAg seems to occur in areas where HBsAg rate exceeds 1 per cent in the general population and for the investigations which the sample population consists of institutionalized patients²⁶.

There are, however, some difficulties in interpreting the epidemiological data about leprosy and HBV infection relationship. In general, leprosy patients, particularly lepromatous type are subject to at least two different enhanced opportunities of HBV infection: segregation due to social forces (colonies), and/or hospitalization due to severity of

disease^{9,11,18}. Considering that many tropical diseases are unevenly distributed, the same individual may be at increased risk of both HBV infection and leprosy.

On the other hand, the association between carrier state and lepromatous leprosy could represent a true biological relationship. In this situation the depression of cellular immunity in lepromatous patients could render them more susceptible to infection with hepatitis B virus and/or could also interfere with the viral antigen (HBsAg) elimination. Furthermore the absence of a reliable marker for *Mycobacterium leprae* infection and the long incubation period of leprosy permit only to study the association of clinical leprosy and the different patterns of HBV serum markers.

Although leprosy remains a major health prob-

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lem in Brazil¹⁷, little attention has been focused on the association between leprosy and HBV infection^{19,23,24,27}.

This investigation presents the results of HBV serological screening among leprosy patients conducted in a region of Central Brazil as a preliminary information for a HBV vaccination programme. The main objectives were to assess the prevalence of HBV serum markers among lepromatous patients and to analyse institutionalization as risk factor for HBV infection in this population. The association of HBV serum markers and different types of leprosy are outside the scope of this study. An attempt was made to calculate a population index of immune response to HBV virus among lepromatous patients²⁶.

METHODS

Study Area - The data were collected as part of a project to evaluate immune response to HBV vaccination among leprosy patients in a survey conducted in Central Brazil.

The investigation was carried out between January and July 1990, in Goiânia (population 1,042,500 inhabitants) the capital of the State of Goiás, Central Brazil. The city is part of the Central-West region in the official programme for leprosy control. This region is considered to have the second highest endemic level of leprosy in the country. Prevalence and annual incidence rates (detection rates) are 3.2/1,000 and 49.6/100,000 inhabitants respectively¹⁶. The official Brazilian policy for the control of leprosy relies upon passive case detection. Regionally, the majority of leprosy patients are treated as outpatients by the public sector of the health system.

Goiânia is estimated to have low to intermediate endemicity for Hepatitis B infection with prevalences of 1.9% and 11.0% for HBsAg and anti-HBs (ELISA), respectively, according to previous study among first-time blood donors in 1989¹⁵. Vaccination against Hepatitis B is not part of the official immunization programme and no previous mass campaign has been conducted in the area.

Study Population and data collection - Two groups of subjects were studied, outpatients and institutionalized ones.

Outpatients were selected from the main outpa-

tient clinic for the leprosy control programme, Centro de Saúde Juarez Barbosa (CSJB) located in Central Goiânia. During the study period, all 83 newly diagnosed and untreated patients with lepromatous (LL), borderline lepromatous (BL) and mid-borderline (BB)²² were interviewed and had a blood sample collected during a self-presenting visit to the outpatient clinic. Lepromatous (LL), borderline lepromatous (BL) and mid-borderline (BB), considered to manifest similar impaired cell-immunities were pooled and referred as lepromatous^{10,25}.

174 lepromatous and borderline institutionalized patients were studied all of them from Colônia Santa Marta, a former leprosy colony, located near the city. This colony was built in the early fifties and leprosy patients in general of low socio-economic status and requiring special health care were institutionalized. Nowadays, it is structured as an open institution with one hospital and several wards (20-40 beds) and houses for patients with families. Approximately 80% of all lepromatous patients in the institutionalized group were included in the study. Considering that the patients in the colony have been institutionalized for a long time, no histopathological or bacteriological exams were performed due to their inconclusive results in chronically treated patients¹⁴. Only the patients with typical disabilities/sequelae of neuropathy, characteristics of the inactive lesions and long history of disease/long term treatment compatible with lepromatous type of leprosy were included as suggested by PONNIGHAUS et al., 1987²¹.

A standard questionnaire was applied to both populations, in the outpatient department of CSJB for the outpatients and mainly in the wards for the institutionalized ones. Age, sex, place of treatment, complete years of residence in the colony, previous hospitalization and history of blood transfusion were recorded.

Serologic diagnosis and classification of HBV marker status - 5 ml of blood was collected by vacutainer from each patient after the interview. All samples were centrifuged and stored at - 20° C until they were sent to the Laboratório da Escola Paulista de Medicina-São Paulo, Brazil. Commercially available radioimmunoassay kits (Abbot Laboratories, North Chicago, Illinois) were used for determination of HBsAg (Auzyme), antibody to hepatitis B surface antigen (anti-HBs) (AUSAB), antibody to hepatitis B core antigen (anti-HBc) (total) (CORZYME).

The following classification was used to categorize exposure to HBV:

1. HBsAg-positive status: "HBV carrier".
2. Any HBV marker -positive (HBsAg, anti-HBc and/or anti-HBs: "prior HBV infection or exposure to HBV virus".

A population index of an effective immune response to HBV was measured by the Probability of Persistent Infection (PPI), according to the formulae below²⁶:

$$PPI = \frac{HBsAg}{HBsAg + anti-HBs + anti-HBc}$$

The lower the PPI value for a group the better the antibody response as it implies clearance of the antigen.

Data Processing and Analysis

The data were processed and analyzed using the Statistical Package for Social Science (SPSS/PC, 1986) and "EGRET-Epidemiological Graphics, Estimation and Testing Package" (Serc, 1989) for multivariate analysis. Chi-squared test for trend was used to determine the significance in the frequency distributions. Estimates of relative risks for controlling for age and sex with 95% confidence intervals were calculated to assess the association between exposure of infection and place of residence. Three institutionalized patients were excluded from the analysis because of incomplete laboratory tests.

RESULTS

The mean ages were 34.6 (+/- 9.8 sd) for outpatients and 58.9 (+/- 14.5 sd) for the ones living in the colony (t test=13.8 p<0.001). Males accounted for 75.6% of the study population. The male/female ratio was 2.2 in the outpatients clinics and 3.7 in the institutionalized population. Prevalence of exposure among males and females in the two sub-groups were not statistically significant different.

There was a statistically significant difference between the overall seroprevalence of exposure for outpatients (22.9%) and the institutionalized ones (64.9%) (X²=39.5 p<0.001). The prevalence rate of

exposure increased with age for outpatients (X² for trend=4.3 df=1 P=0.04), but a similar pattern was not found for the patients in the institution (Table 1). The seroprevalence of anti-HBc + anti-HBs was 50.3% and 16.9% for institutionalized and outpatients, respectively (X²=26.2 p<0.01) (Table 2).

Using the data from Table 2 the Probability of Persistent Infection to HBV was 0.14 (15/111) for the institutionalized group and 0.21 (4/19) for outpatients (Fisher exact test p=0.48).

The prevalence of exposure increased with years of institutionalization, although half of the patients had already one marker of infection during their first 5 years in the colony (unadjusted analysis, Table 3). After adjusting for age and sex and taking the outpatients as the baseline category institutionalized patients had an almost four fold risk of HBV infection when compared to the outpa-

Table 1
Seroprevalence of HBV infection[@] among Lepromatous outpatients and institutionalized by age group.

Age group (years)	Outpatients Pos/Total(%)	Institutionalized Pos/Total(%)
10-29	2/26 (7.7)*	4/6 (66.7)**
30-49	15/51(29.4)	23/39 (59.0)
50-69	2/6 (33.3)	58/85 (68.2)
>=70	-/-	26/41 (63.4)
Total	19/83 (22.9)***	111/171 (64.9)***

@ Any marker

* x² for trend with age=4.3 df=1 P=0.04

** x² for trend with age=0.09 df=1 P>0.05

*** x²=39.5 P<0.001

Table 2
Seroprevalence of HBV infection among Lepromatous patients, outpatients and institutionalized in Goiânia-Central Brazil, 1990.

HBV markers	Institutionalized Pos/Total (%)	Outpatients Pos/Total (%)
HBsAg [@]	15/171 (8.8)*	4/83 (4.8)*
anti-HBc+anti-HBs	86/171 (50.3)**	14/83 (16.9)**
anti-HBc (only)	10/171 (5.8)	1/83 (1.2)
Any marker	111/171 (64.9)	19/83 (22.9)

@ HBsAg positive with or without antibodies

* x²=1.3 P=0.26

** x²=26.2 P<0.01

tients, and the highest risks were among patients with more than 21 years of residence in the colony (Table 4).

Table 3
Seroprevalence of HBV infection among Lepromatous patients according to years of residence in institution in Goiânia-Central Brazil, 1990.

Years Institutionalization	Pos/Total (%)
1-5	8/16 (50.0)*
6-10	27/53 (50.9)
11-15	18/29 (62.1)
16-20	15/22 (68.2)
>21	43/51 (82.4)
Total	111/171 (64.9)

* χ^2 for trend=13.9 df=1 P<0.01

Table 4
Relative risk and prevalence of HBV infection in Lepromatous leprosy patients in Goiânia-Central Brazil, 1990.

Years Institutionalization	Nº	Prevalence %	OR*	95% CL
Zero	83	22.9	1	-
1-5	16	50.0	3.9	1.1-12.7
6-10	53	50.9	2.6	1.1- 6.4
11-15	29	62.1	3.8	1.3-11.5
16-20	22	68.2	3.6	1.2-10.4
>=21	51	82.4	14.3	4.8-42.0
Total	254	51.2		

* Adjusted for age and sex.

DISCUSSION

This serological screening of HBV infection among lepromatous patients revealed a significant higher prevalence of antibodies (anti-HBs and anti-HBc) among institutionalized patients than outpatients, although similar pattern was not found for antigenemia (HBsAg).

Since the study was conducted in an area of low to intermediate endemicity of HBV infection, it is expected that the transmission of HBV infection occurs mainly in adult life and among high

risk groups¹³. In these circumstances, the increase in seroprevalence for HBV infection with age is usually attributed to the cumulative opportunity for infection^{3,12}.

In this study the prevalence of exposure to HBV among institutionalized lepromatous patients were higher than for outpatients for the same age groups. At least two hypotheses could be raised in order to explain this situation.

1. The patients admitted to the colony represent a different sample of leprosy patients with higher risks of HBV infection. In this circumstance the findings could be explained by a selection bias. It seems reasonable to assume that individuals with low socio-economic conditions are more likely to be sent to institutions, and low socio-economic conditions may determine the level of infection¹².

2. Institutionalization by itself could represent a risk factor for HBV infection. Infectious agents are known to spread more easily in semi-closed communities, and it has been well documented for HBV virus. Prisoners, army servicemen and mentally retarded individuals in institutions all for them have higher risk of infection with HBV than the general population^{7,8}.

In fact, both hypotheses seems to be supported by the available information. Prevalence rates tended to increase with years of institutionalization, but even short periods of time in the colony (1-5 years) was associated with high levels of exposure.

Differences in seroprevalence among types of leprosy could not be assessed considering that the sample was restricted to lepromatous type of leprosy. However, the capacity of mounting an antibody response, evaluated by the PPI does not suggest that the lepromatous patients in the sample have an impaired immune response since low PPI values were found, implying that this group of patients mount an adequate immune response. These findings confirm the results of a case-control study conducted in Greece²⁰. On the contrary in Papua New Guinea lepromatous patients were described as more likely to have an immune deficit in the response of HBV infection²⁶.

For the institutionalized patients 20% of the individuals could not be included due to the difficulties to locate the patients in the community. Un-

der these circumstances, it is possible that the more severe cases or more disabled ones were more likely to be in the wards during the investigation and would have been included. Therefore the population screened may not represent the whole institutionalized population. Information on age, sex, disabilities and clinical form of leprosy from the non-responders- "non-screened" were not collected making it impossible to estimate the degree of bias.

Nevertheless, our data strongly suggest that institutionalization is an important risk factor for HBV infection and that lepromatous patients are capable of mounting antibody responses to HBV infection. Although the association of HBV and leprosy has been assessed in many publications, the question whether HBV infection constitute a risk factor for leprosy or vice versa whether different types of leprosy constitute a risk factor for persistent of carrier state of hepatitis B virus can hardly be distinguished by descriptive studies. Case control studies would be a rational first line approach to assess the association between types of leprosy and HBsAg, particularly in areas of low endemicity of HBV infection.

RESUMO

Associação entre hanseníase e infecção pelo vírus da hepatite B. Estudo de prevalência realizado em Goiânia, Brasil Central.

Este estudo apresenta os resultados de investigação sorológica para o vírus da hepatite B (VHB) entre pacientes hansenianos como etapa inicial para um programa de vacinação contra Hepatite B na cidade de Goiânia - Brasil Central. Os principais objetivos foram determinar a soroprevalência dos marcadores sorológicos para hepatite B entre pacientes com hanseníase do polo lepromatoso da doença, e avaliar a institucionalização como fator de risco para a infecção pelo VHB. Foram estudados 83 pacientes ambulatoriais e 171 pacientes institucionalizados e os marcadores testados foram AgHBs, anti-HBs e anti-HBc, utilizando-se a técnica de radioimuno ensaio. A prevalência de portadores virais (HBsAg) foi de 4,8% e 8,8% para os pacientes ambulatoriais e institucionalizados, respectivamente ($P > 0,05$). A prevalência de exposição ao VHB (todos os marcadores) foi estatisticamente diferente entre os pacientes de ambulatório (16,9%) e os institucionalizados (50,5%). Os pacientes institucionalizados tiveram um risco 4 vezes

maior de infecção pelo HBV quando comparados aos pacientes ambulatoriais, mesmo após análise multivariada, controlada por sexo e idade.

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