Analysis of clinical data and T helper 1/T helper 2 responses in patients with different clinical forms of leprosy


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Abstract

Introduction: Currently, there are no laboratory tests or sensitive and specific molecular markers for the early diagnosis of leprosy. The aim of this study was to analyze the clinical characteristics of patients with leprosy and investigate their immunological profile, comparing this with the type of lesion and the presence or absence of a Bacillus Calmette-Guérin (BCG) vaccination scar.

Methods: Statistical analyses were performed by employing comparative tests (Pearson’s chi-square) to evaluate the variables in different clinical forms, considering significance at the 5% level.

Results: The study identified a predominance of lepromatous leprosy (26.9%) in patients aged between 34-53 years. Caucasians predominantly had borderline tuberculoid (BT) clinical forms (42%); a predominance of males with borderline lepromatous (19%) and lepromatous leprosy (26.9%) forms was observed; and the presence of BCG vaccination scars (27.5%) and lower limb nerves were more affected (38%) predominantly in the BT clinical form. Significant differences were identified, which included hypochromic lesions predominantly in the BT clinical form (24%); diffuse-type lesions predominantly in the tuberculoid (TT) clinical form (28%); ill-defined lesion border dominance in lepromatous leprosy (LL) clinical forms (30%); an irregular lesion limit predominantly in LL clinical forms (32%); and a predominant Th1 immune response in the BT clinical form (41.7%).

Conclusions: The evaluation of the immunological profile in leprosy patients may contribute to the more detailed diagnosis and possibly better characterization of the prognosis for these individuals.

Keywords: Mycobacterium leprae. Epidemiology. Th1/Th2 response. Tuberculoid. Lepromatous.

INTRODUCTION

Leprosy has a high rate of infectivity and low pathogenicity; however, majority of the population do not develop the disease. This fact indicates that there is an association of genetic and environmental factors on susceptibility and cause of resistance. The correct diagnosis of leprosy requires evolutionary clinical data of the disease, histopathological analysis and sputum smear microscopy, enabling determination of the form presented by the patient, such as: TT (tuberculoid), BT (borderline tuberculoid), BB (borderline borderline), BL (borderline lepromatous) and LL (lepromatous leprosy). This classification is necessary for the appropriate, specific therapeutic option to be delivered.

There are major differences in the endemicity of leprosy between different regions of Brazil. Mato Grosso is the State with the highest prevalence of leprosy; in 2014, the rate was 10.19 cases/10,000 inhabitants, which exceeds the national rate of 1.27 cases/10,000 inhabitants. There is a need to intensify leprosy surveillance, with more effective diagnosis and treatment of the disease, with an emphasis on the regions with the highest rates of disease in the country.

The immune response is of prime importance to disease susceptibility or resistance, fundamental to the defense of the organism against exposure to the bacillus, and is also associated with the development of the different clinical forms. These forms range from tuberculoid, with a predominantly cellular immune response, to lepromatous leprosy dominated by a humoral response. These responses are associated with specific mechanisms for the recognition of antigens, mediated by receptors present on the membranes of T and B lymphocytes. The immune response can be categorized into cellular or type 1 and humoral or type 2. The ability of lymphocytes with the cluster of differentiation 4 (CD4+), also known as helper T lymphocytes...
Lesions, whereas CD8+ T lymphocytes are more abundant in tuberculoid lesions, whereas CD8+ lymphocytes, which can represent a suppressor phenotype, predominate in lepromatous lesions. In patients with the LL type, there is no specific cellular immune response against M. leprae as bacterial proliferation occurs, with the presence of many lesions and extensive infiltration of the skin and nerves. CD4+ T lymphocytes are more abundant in tuberculoid lesions, whereas CD8+ lymphocytes, which can represent a suppressor phenotype, predominate in lepromatous lesions. In tuberculoid lesions, the distribution of lymphocytes is more ordered, with CD4+ T lymphocytes in the center of the lesions and CD8+ T lymphocytes with suppressive function.

The aim of this study was to analyze the clinical characteristics of patients with leprosy and investigating their immunological profile, comparing this with the type of lesion and the presence or absence of a scar related to Bacillus Calmette-Guérin (BCG) vaccination.

**METHODS**

**Patients**

This was a cross-sectional study of patients examined in the Diagnosis and Treatment Leprosy Service section, located at the Hospital Universitário Júlio Müller (HUJM), the Teaching Hospital of Universidade Federal de Mato Grosso (UFMT), Cuiabá, Mato Grosso State, Brazil, between November 2013 and September 2014. Seventy patients were categorized based on the clinical forms, according to the established criteria.

A standard questionnaire was used to collect information regarding the age, race, sex, lesion characteristics (color, type, border), region of the affected nerves, and presence or absence of a BCG vaccination scar. General physical and dermatological/neurological examinations were performed on all patients by the medical doctor responsible for the service. We assessed the overall condition of the patient's health and the lesion characteristics such as color (erythematous, hyperchromic, hypochromic), type (diffuse, plaque or nodular), border (well defined, ill defined), limit (irregular or regular) and an evaluation of the affected area of nerves (upper limbs and lower limbs) and protective sensation of hands and feet, through an esthesiometer with the use of Semmes-Weinstein (SW).

Patients with comorbidities, immunosuppressive diseases, renal failure and pregnant patients were excluded from our study.

**Ethical considerations**

This study meets the Resolutions No. 196/96 and No. 347 of 13 January 2005, of the National Health Council and was approved by the HUJM Ethics Committee, with protocol number 733/CEP-HUJM/09. All patients were asked to voluntarily participate in the research project. The informed consent form (ICF) was read to each participant, and the interview process was done only after the signing of the ICF.
Leprosy clinical form was not statistically associated with patient age, race or sex (p-value = 0.74, 0.07 and 0.10, respectively) (Table 1). With respect to patient age, 26 patients were aged between 34-53 years, with a predominance of the BT (n=7; 26.9%) and LL (n=7; 26.92%) clinical forms. Of the reported cases, 24 were aged between 14-3 years, with a predominance of the TT (n=6; 25.0%) and BB (n=6; 25.0%) clinical forms. Further, 19 patients were older than 54 years, with a predominance of the TT (n=4; 21.0%) and BL (n=6; 31.6%) clinical forms. Twenty-six patients were Caucasian with a predominance of the TT (n=6; 2%) and BT (n=11; 42.3%) clinical forms; 24 were Mulatto, with a predominance of the BL (n=6; 25.0%) and LL (n=6; 25.00%) forms; 20 were Black, with a predominance of the BB (n=5; 25.0%) and LL (n=6; 30.0%) forms. With respect to sex, 42 were males, predominantly with BL (n=11; 26.2%) and LL (n=11; 26.2%). The TT (n=6; 21.4%) and BT (n=10; 35.7%) clinical forms were predominantly found in the female patients.

We found significant associations to the varying clinical forms in relation to the color of the lesion (P = 0.001), type of injury (P = 0.027), lesion border characteristics (P = 0.001) and limits (irregular versus regular) of the lesions (P = 0.001) (Table 2). Thirty-three of the cases were hypochromic, with a predominance of TT (n=12; 36.4%) and BT (n=8; 24.2%) 23 were erythematous, with a predominance of BL (n=7; 30.4%) and LL (n=7; 30.4%); 14 were hyperchromic, with a predominance of the BT (n=5; 35.7%) and BB (n=3; 21.4%). As for the type of lesion, 50 cases were diffuse, with a predominance of the TT form (n=13; 26.0%) and BT (n=11; 22.0%); 12 were plaques with a predominance of the BT (n=4; 33.33%) and BB (n=4; 33.33%) forms; 8 were nodular with a predominance of the BV (n=3; 37.5%) and LL (n=5; 62.5%) forms. As for the lesion border characteristics, 43 of the cases were ill-defined, with a predominance of the BL (n=13; 30.2%) and LL (n=13; 30.2%) clinical forms; 27 were well-defined, with a predominance of the TT (n=12; 44.0%) and BT (n=7; 25.9%) forms. With regard to the limits of the lesion, 37 cases were irregular, predominantly BL (n=10; 27.0%) and LL (n=12; 32.4%); 33 of the cases were regular, with a predominance of the TT (n=12; 36.4) and BT (n=9; 27.3%) forms. In the analysis of the region of the affected nerves, no significant association was observed (P = 0.639).

Statistical associations were not found between the clinical form and the presence of a BCG vaccination scar (P = 0.359) (Table 3). Forty patients had a BCG scar, with a predominance of the BT (n=10; 26.7%) and BL (n=10; 26.7%) clinical forms; 30 cases had no scar, with a predominance of the TT (n=8; 26.7%) and LL (n=7; 23.3%) forms.

Immunoreactivity, in terms of Th1/Th2 responses, was observed by immunostaining with the cell markers CD4/CCR5 and CD4/CCR4 (Figure 1). The staining profile was associated with the differing clinical forms (P = 0.001); 36 cases were Th1, with a predominance of the TT (n=8; 26.7% and BL (n=10; 25.0%) clinical forms; 30 cases had no scar, with a predominance of the TT (n=8; 26.7%) and LL (n=7; 23.3%) forms.

There was a significant association (P = 0.001) between the clinical form of leprosy, the presence of a BCG vaccination scar, and Th1/Th2 immunoreactivity, associated with varying clinical forms of leprosy. Pearson’s chi-square test was performed to verify the association of each variable to the clinical form. Data were analyzed using Excel 2010 software and SPSS (version 20), considering a 5% level of significance.

### TABLE 1

Association of age, race, and sex of patients with the varying clinical forms of leprosy.

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>TT n (%)</th>
<th>BT n (%)</th>
<th>BB n (%)</th>
<th>BL n (%)</th>
<th>LL n (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>6 (25.0)</td>
<td>5 (20.8)</td>
<td>6 (25.0)</td>
<td>4 (16.7)</td>
<td>3 (12.5)</td>
<td>0.74</td>
</tr>
<tr>
<td>Race</td>
<td>6 (23.1)</td>
<td>11 (42.3)</td>
<td>3 (11.5)</td>
<td>3 (11.5)</td>
<td>3 (11.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td>6 (21.4)</td>
<td>10 (35.7)</td>
<td>5 (17.9)</td>
<td>4 (14.3)</td>
<td>3 (10.7)</td>
<td>0.10</td>
</tr>
</tbody>
</table>


Leprosy patients examined in Júlio Muller Teaching Hospital ambulatory in Cuiaba, Mato Grosso.
A, B and C: Tuberculoid leprosy patients with lymphocytes immunostained for DAPI (Panel A), CD4 (Panel B), and CCR5 (Panel C). Figure 1 D, E and F: Lepromatous leprosy patients with lymphocytes immunostained for DAPI (Panel D), CD4 (Panel E) and CCR4 (Panel F). Bar = 50µm. CCR: CC-Chemokine receptor; DAPI: 4',6-diamidino-2-phenylindole; CD4: cluster of differentiation 4.

**FIGURE 1** - Immunofluorescence analysis for CCR5 and CCR4. Figure 1 A, B and C: Tuberculoid leprosy patients with lymphocytes immunostained for DAPI (Panel A), CD4 (Panel B), and CCR5 (Panel C). Figure 1 D, E and F: Lepromatous leprosy patients with lymphocytes immunostained for DAPI (Panel D), CD4 (Panel E) and CCR4 (Panel F). Bar = 50µm. CCR: CC-Chemokine receptor; DAPI: 4',6-diamidino-2-phenylindole; CD4: cluster of differentiation 4.

**TABLE 2**

Association of color of the lesion, type of lesion, lesion border and limits, and region of nerves affected for patients with varying clinical forms of leprosy.

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>TT n (%)</th>
<th>BT n (%)</th>
<th>BB n (%)</th>
<th>BL n (%)</th>
<th>LL n (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color of Lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythematous</td>
<td>1 (4.4)</td>
<td>2 (8.7)</td>
<td>6 (26.1)</td>
<td>7 (30.4)</td>
<td>7 (30.4)</td>
<td></td>
</tr>
<tr>
<td>Hyperchromic</td>
<td>0 (0.0)</td>
<td>5 (35.7)</td>
<td>3 (21.4)</td>
<td>3 (21.4)</td>
<td>3 (21.4)</td>
<td></td>
</tr>
<tr>
<td>Hypochromic</td>
<td>12 (36.4)</td>
<td>8 (24.2)</td>
<td>4 (12.1)</td>
<td>5 (15.6)</td>
<td>4 (12.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Type of lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>13 (26.0)</td>
<td>11 (22.0)</td>
<td>9 (18.0)</td>
<td>10 (20.0)</td>
<td>7 (14.0)</td>
<td></td>
</tr>
<tr>
<td>Nodular</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td></td>
</tr>
<tr>
<td>Plaques</td>
<td>0 (0.0)</td>
<td>4 (33.3)</td>
<td>4 (33.3)</td>
<td>2 (16.7)</td>
<td>2 (16.7)</td>
<td>0.027</td>
</tr>
<tr>
<td>Border of the lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>well defined</td>
<td>12 (44.4)</td>
<td>7 (25.9)</td>
<td>5 (18.5)</td>
<td>2 (7.4)</td>
<td>1 (3.7)</td>
<td></td>
</tr>
<tr>
<td>ill defined</td>
<td>1 (2.3)</td>
<td>8 (18.6)</td>
<td>8 (18.6)</td>
<td>13 (30.2)</td>
<td>13 (30.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Limit of lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irregular</td>
<td>1 (2.7)</td>
<td>6 (16.2)</td>
<td>8 (21.6)</td>
<td>10 (27.0)</td>
<td>12 (32.4)</td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>12 (36.4)</td>
<td>9 (27.3)</td>
<td>5 (15.2)</td>
<td>5 (15.2)</td>
<td>2 (6.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Affected nerves</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower limbs</td>
<td>5 (16.7)</td>
<td>3 (9.0)</td>
<td>6 (20.0)</td>
<td>5 (16.7)</td>
<td>5 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Upper limbs</td>
<td>4 (20.0)</td>
<td>4 (20.0)</td>
<td>2 (10.0)</td>
<td>4 (20.0)</td>
<td>6 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Not affected</td>
<td>4 (20.0)</td>
<td>2 (10.0)</td>
<td>5 (25.0)</td>
<td>6 (30.0)</td>
<td>3 (15.0)</td>
<td>0.639</td>
</tr>
</tbody>
</table>

TT: Tuberculoid leprosy; BT: Borderline tuberculoid; BB: Borderline borderline; BL: Borderline lepromatous; LL: Lepromatous leprosy. *chi-square test. Leprosy patients examined in Júlio Muller Teaching Hospital ambulatory in Cuiaba, Mato Grosso.
individuals in the economically productive population, which causes high economic impacts due to their having to abstaining from work, caused by the development of permanent and physically disabling lesions\textsuperscript{31,32}. Importantly, as these patients are not able to work, they have the right to seek sickness benefits and even disability retirement\textsuperscript{33}. Associated with this, the most common clinical forms of leprosy in these patients are the BB, BL, and LL forms, which have higher transmission capability and cause greater incapacitation\textsuperscript{34}.

Regarding the ethnicity of patients, in our study, Caucasians were the predominant race, which differs from previous findings in the literature\textsuperscript{32,35,36} where Mulatos were the most prevalent affected population. It should be noted that many patients who are from different regions of the state and who are users of the HUJM in Cuiaba are predominantly Caucasians. The population of Mato Grosso is composed of 50.0\% mixed race, 38.9\% Caucasians and 9.8\% Blacks (IBGE, 2010)\textsuperscript{37}. Magalhães\textsuperscript{38} considers that the migration process in Mato Grosso territory contributed to the spread and evolution of leprosy in the 1970s and 1980s, with large flows of people of Caucasian origin into the state. Few studies have reported the influence of ethnic variation as a factor of exposure to the bacillus.

Men were more affected in this study, and were associated with the BL and LL clinical forms (26\% each). These data are consistent with the findings in the literature\textsuperscript{39,40}. According to Moreira et al.\textsuperscript{41} and Costa\textsuperscript{1}, men have greater risk for infection

**TABLE 3**

Association of the presence of a BCG vaccination scar with varying clinical forms of leprosy.

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>TT n (%)</th>
<th>BT n (%)</th>
<th>BB n (%)</th>
<th>BL n (%)</th>
<th>LL n (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG No</td>
<td>8 (26.7)</td>
<td>4 (13.3)</td>
<td>6 (20.0)</td>
<td>5 (16.7)</td>
<td>7 (23.3)</td>
<td></td>
</tr>
<tr>
<td>BCG Yes</td>
<td>5 (12.5)</td>
<td>11 (7.5)</td>
<td>7 (17.5)</td>
<td>10 (25.0)</td>
<td>7 (17.5)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

**BCG**: Bacillus Calmette-Guérin; **TT**: Tuberculoid leprosy; **BT**: Borderline tuberculoid; **BB**: Borderline borderline; **BL**: Borderline lepromatous; **LL**: Lepromatous leprosy. *chi-square test. Leprosy patients examined in Júlio Muller Hospital Teaching ambulatory in Cuiaba, Mato Grosso.

**TABLE 4**

Association of the immunoreactivity in patients with varying clinical forms of leprosy.

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>TT n (%)</th>
<th>TB n (%)</th>
<th>BB n (%)</th>
<th>BL n (%)</th>
<th>LL n (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Th1</td>
<td>11 (30.6)</td>
<td>15 (41.7)</td>
<td>6 (16.7)</td>
<td>3 (8.3)</td>
<td>1 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Th2</td>
<td>2 (5.9)</td>
<td>0 (0.0)</td>
<td>7 (20.6)</td>
<td>12 (35.3)</td>
<td>13 (38.2)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**TT**: Tuberculoid leprosy; **TB**: Borderline tuberculoid; **BB**: Borderline borderline; **BL**: Borderline lepromatous; **LL**: Lepromatous leprosy. *chi-square test. Leprosy patients examined at Júlio Muller Teaching Hospital ambulatory in Cuiaba, Mato Grosso.

**TABLE 5**

Association of BCG scar and immunoreactivity with varying clinical forms of leprosy.

<table>
<thead>
<tr>
<th>Clinical form</th>
<th>TT n (%)</th>
<th>BT n (%)</th>
<th>BB n (%)</th>
<th>BL n (%)</th>
<th>LL n (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG Th1 No</td>
<td>6 (35.3)</td>
<td>4 (23.5)</td>
<td>4 (23.5)</td>
<td>2 (11.8)</td>
<td>1 (5.9)</td>
<td></td>
</tr>
<tr>
<td>BCG Th1 Yes</td>
<td>5 (26.0)</td>
<td>11 (57.9)</td>
<td>2 (10.5)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>BCG Th2 No</td>
<td>2 (15.4)</td>
<td>0 (0.0)</td>
<td>2 (15.4)</td>
<td>3 (23.1)</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>BCG Th2 Yes</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5 (23.8)</td>
<td>9 (42.7)</td>
<td>7 (33.3)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**TT**: Tuberculoid leprosy; **BT**: Borderline tuberculoid; **BB**: Borderline borderline; **BL**: Borderline lepromatous; **LL**: Lepromatous leprosy. *chi-square test. Leprosy patients examined in Júlio Muller Teaching Hospital ambulatory in Cuiaba, Mato Grosso.
due to lifestyle factors. The higher incidence of physical disabilities in men may be related to less concern with self-image, particularly in relation to the body and aesthetics; thus, men are less likely to access health services and this may contribute to late diagnosis and subsequently predispose the patient to become a propagator of the disease.52,44,45.

The dermato-histopathological characteristics of skin lesions found in our study are consistent with findings in the literature.45,46,47,48 Assessment of the patients by dermatologic and histopathological data are fundamental to arrive at a more accurate diagnosis.49,50.

Regarding the region of the affected nerves, in this study BT and BB forms were more frequent in the lower limbs compared with other clinical forms. The involvement of the peripheral nerves is present in all clinical forms of leprosy, and in tuberculoid forms, the nerve damage is usually earlier, while in lepromatous leprosy it appears later.46,51 This variable is an important epidemiological indicator responsible for causing irreversible consequences, resulting in deformities and disabilities.45,52,53 Early diagnosis of neural integrity and the degree of disability is key to determining follow-up strategies, in order to guide appropriate treatment, prevent the advancement of neural disability and contribute to the physical rehabilitation.54,55,56.

Finally, the association of clinical forms with the immunoreactivity in terms of Th1 and Th2 responses associated with the type of leprosy patient was established. The literature shows that the CCR5 is a good cell marker for Th1 cells, as is CCR4 for Th2 cells.57 It is important to note that, in this study, we evaluated the skin lymphocytes, while in most studies, determination of phenotype of circulating leukocyte populations in the blood is assessed. In some studies that have compared the immunoreactivity of cells from the blood and the skin, the existence of dissimilar responses has been reported.58,59 This demonstrates that, at the inflammatory site where bacteria are concentrated, the immune response may vary according to what is classically reported in the literature.60

In this study, the majority of patients showed Th1 immunoreactivity, with the BT clinical form present at the highest prevalence (41%), while the remainder of the patients had Th2 characteristics, with a high prevalence of LL clinical forms (38%). These data corroborate findings from other studies that have shown similar results.58,59,60,61 However, other cell components may interfere with local immune responses and lymphocyte differentiation, such as the interaction with antigenic cells, like the Langerhans cells extracellular matrix components such as collagen fibers, fibronectin, and laminin, and other factors such as hormones.44 Thus, any changes in Th1 and Th2 response should be considered with caution. In addition, some studies have reported the tendency for variation in the immune response, especially in patients with borderline clinical profiles.62

The Th1/Th2 responses may have inconsistencies. Some patients may have different profile, including the presence of regulatory T cells or Th17 cells along with a classic Th1 or Th2 profile.46,58,65,66,67 This differential response could lead to vulnerability to infection with the bacteria, or a change in the clinical profile of patients from the tuberculoid pole to lepromatous.59 Future studies may indicate the presence of each cell type as a way to understand these changes in the immune profile of patients, and may thus enable further improvements in the prognosis of these patients.

Finally, the presence of a BCG vaccination scar in leprosy patients was assessed. Most of the patients had a vaccination scar, these being predominantly BT and BL clinical types. Several studies have shown that the BCG vaccine protects against leprosy, being one of the priority interventions established by the World Health Organization (WHO) to control the disease.60 Conversely, some studies have suggested varied protection by the BCG vaccine and this may be related to genetic factors.68,69 In this study most patients with leprosy who had a BCG vaccination scar and a Th1 immune response were tuberculoid while most patients without a BCG scar and with a Th2 response were lepromatous. Some studies demonstrate that BCG vaccination makes the individual most likely to develop a profile of M1 macrophages, inducing them to produce pro-inflammatory cytokines such as IL-1 and TNF-α, thereby developing a greater resistance to the bacteria.70

In conclusion, immunological evaluation of patients with leprosy can contribute to the more detailed diagnosis and possibly better characterization of prognosis in these individuals. Further, public health policies should encouraged BCG vaccination for individuals without vaccine scar, in order to provide greater protection against this disease.

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Conflict of Interest
The authors declare that there is no conflict of interest.

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