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Research Article

Association between clinical forms of leprosy and contacts with the vaccination state with BCG in five endemic municipalities in the Brazilian Amazon

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Abstract

Introduction: The World Health Organization (WHO) strategy for leprosy control from 2021 to 2030 focuses on interrupting transmission, reducing autochthonous cases to zero, and using a safe and effective vaccine and chemoprophylaxis. In 2020, 127,396 new cases were registered in the world, 19,195 new cases in the Americas, and, of these, 17,979 cases in Brazil, about 93.66% of the total in the Americas. Brazil is classified as a country with a high burden of the disease, occupying the 2nd place in the world, behind only India (WHO, 2020). Análise do período de 2010-2015 em publicação recente9, apresenta as seguintes cidades no estado do Pará nas quais se observou maiores taxas de incidência (detecção): Marituba, Belém, Marabá, Parauapebas e Altamira [9].

Material and method: This is an analytical retrospective study carried out in a database - Epi-Info resulting from records of Surveillance and Seroprevalence actions in five endemic municipalities for leprosy located in the Southeast and West of Pará. The following variables were analyzed: age, sex, Clinical Classification, vaccination status with BCG, and the result of the search for IgM antibodies against PGL-1 of Mycobacterium leprae by the “In house” ELISA technique.

Results: We evaluated 1551 records examined in the laboratory from 2014 to 2016, which were classified into 123 Multibacillary -MB patients (123/1551 = 7.93%); 71 Paucibacillary-PB patients (71/1551 = 4.57%); 451 Intradomicilliary Consanguineous Contacts - CCOSI (451/1551 = 29.07%) and 906 Non Consanguineous Contacts - CNCOS (906/1551 = 58.41%). 57 MB patients (13.47%), 13 PB patients (3.07%), 133 CCOSI (31.44%) and 220 CNCOS (52.00%) were positive for PGL-1. The correlation of the Classification with the vaccination status showed 57 MB patients without any BCG (57/125 = 45.6%) and only 3 patients with two doses of BCG (3/125 = 2.4%); 17 PB patients without any dose of BCG (17/69 = 24.63%); 80 CCOSI without any BCG (80/455 = 17.58%) and 171 CNCOS (171/906 = 18.87%). The odds ratio (OR) in the analysis between unvaccinated MB patients compared to CCOSI was statistically significant (OR = 14.25; $p < 0.0001$). The study shows the importance of using the BCG vaccine in healthy contacts of patients with leprosy, as it shows the probability of unvaccinated individuals being 14.25 times more likely to become ill with Multibacillary forms compared to CCOSI. In addition, the BCG vaccine has been in use for 80 years and is the only vaccine that we can use in leprosy control programs.

Conclusion: Although the leprosy epidemiological data analyzed recently (2010 - 2015) show a downward trend in the main indicators in Pará, such as the detection of new cases and prevalence, the endemic municipalities are still classified as hyperendemic for the population under 15 years of age and This proves that Surveillance is essential, as well as BCG vaccination according to the Ministry of Health Standards.

More Information

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Introduction

The new World Health Organization (WHO) leprosy strategy for the period 2021 to 2030 focuses on interrupting transmission and reducing new autochthonous cases to zero. This strategy is in line with the broader Global health trend, including the integration of services for multiple diseases, digitization and quantification, and targeted challenges for human resource capacity building, surveillance, and antimicrobial resistance [1].

The introduction of multidrug treatment in Brazil in the 1980s considerably reduced the number of leprosy cases in the world, in endemic countries, and in Brazil when we evaluated the endemic according to the Indicator "prevalence rate" there was an increase in the number of new cases from 2005 onwards and the possible explanation for the fact is that the bacteria is becoming resistant to the drugs used. Data from different countries indicate that 2% to 16% of leprosy cases do not respond to specific treatment [2].

The strategy promotes innovative experiments such as the use of active target case detection and the potential introduction of a safe and effective vaccine and calls on countries to develop "zero leprosies" roadmaps and provide chemoprophylaxis to all contacts of confirmed cases [1].

In this scenario, the availability of a safe and effective vaccine still seems far away, however, the Leprosy Control Program has made use of an efficient and safe vaccine to reduce the occurrence of severe and transmissible forms of the disease, the BCG vaccine. According to Bricks LF, 2004 [3], studies on the effectiveness of the BCG vaccine in immunizing individuals against leprosy demonstrate that the variations found concerning the protection conferred by it are due to several factors, such as host factors, environment, vaccine strains, dose, and administration method. The BCG vaccine used in Brazil contains live Calmette-Guérin bacilli of Mycobacterium Bovis, attenuated and lyophilized of the Moreau – Rio de Janeiro strain. Fundação Ataulpho de Paiva in Rio de Janeiro produces the BCG vaccine for intradermal use in 1 mg, 2 mg or 5 mg presentations (corresponding to 10, 20 or 50 doses [4].

The largest vaccine factory in the world, The Serum Institute in India was founded in 1966 in Pune (West India) and produces BCG vaccine using the Moscow strain, made up of attenuated strains of Mycobacterium Bovis, which has existed for over 80 years and it is the single most widely used vaccine of all current vaccines reaching millions of children worldwide [5].

To date, a safe and effective vaccine has not yet been developed to prevent leprosy. Thus, it is important that we can apply a vaccine known as BCG, which notably protects against the development of serious, transmissible forms of leprosy in the community [6,7]. Thus, this retrospective study aims to reiterate the efficacy/effectiveness of the BCG vaccine in protecting against severe forms of leprosy.

Material and methods

This is an analytical retrospective study carried out in the Epi-Info Database (Software version 7.2) in which records were made related to Surveillance and Seroprevalence actions for leprosy from 2014 to 2016 in five endemic municipalities in the state of Pará, located in the southeast and northeast of Pará: Goianésia, Curionópolis, Thailand, Xinguara and Canaã dos Carajás.

The variables considered predictive were: age, sex, operational classification, and vaccination status with BCG. The outcome variable was positivity for the PGL-1 antigen (phenolic glycolipid -1) represented by the disaccharide (ND-O-BSA) and Trisaccharide (NT-P-BSA) portion of the molecule. Two Epidemiological Indicators of analysis of the endemic were considered for comparison with the seroprevalence data by the studied municipality.

In the statistical analysis, bivariate assessments were used, such as positivity for PGL-1 by municipality studied and by sex, age, operational classification, vaccination status with BCG, and also secondary analyzes with vaccination status by sex, age, classification, and municipality with an α level of 0.05 (5%) considering statistical significance for p - value ≤ 5% and a confidence interval of 95%. Regarding descriptive statistics, the seroprevalence rates per municipality studied were compared with the detection rate and prevalence rate in the year of evaluation of the general data. The software used for this analysis was: Biostat 5.0 (Ayres, et al.) and Epi-Info, version 7.2.

Results

Seroprevalence was evaluated in five endemic municipalities in the state of Pará, Goianésia, Xinguara, Curionópolis, Thailand and Canaã dos Carajás, from 2014 to 2015, with 1551 records examined and the municipality of Goianésia had the highest rate of seropositivity to the antigen Mycobacterium leprae PGL-1 (229/429 = 53.37%) followed by the municipality of Curionópolis (80/429 = 18.67%), Thailand (53/429 = 12.35%), Canaã dos Carajás (37/429 = 8.62%) and Xinguara (30/429 = 6.99%), (Table 1).

Table 1: Seroprevalence index in five endemic municipalities in the Brazilian Amazon, 2014-2015.

County	Positive	%	Negative	Total	Detection /100 mil	prevalence /10 mil
1. Goianésia	229	53.37%	162*	391	28.44	6.72
2. Xinguara	30	6.99 %	62	92	10.50	8.10
3. Curionópolis	80	18.67%	198	278	28.44	7.96
4. Tailândia	53	12.35%	368	421	77.77	6.78
5. Canaã dos Carajás	37	8.62%	332	369	177.64	9.76
Total	429	100%	1122	1551		

*Foi um equívoco na hora de escrever o dado de Goianésia (olhar anexo).

Regarding positivity to anti-PGL-1 and gender, it was observed that women have a higher positivity index (275/429 = 64.10%) for the PGL-1 antigen than men (154/429 = 35 .90%), but there is no statistical significance in this difference (p = 0.95), (Table 2). The analysis of the variable Classification and the outcome of vaccination status with BCG showed that the probability of an individual without any BCG belonging to the Multibacillary-MB group is 14.25 times higher compared to the Consanguineous Intrahousehold Contacts-CCOSI group, (Table 3).

Positivity to anti-PGL-1 according to the classification of the sample showed a higher rate of positivity to anti-PGL-1 among the CNCOS group (220/423 = 52%), followed by the CCOSI group (123/423 = 31, 44%), followed by the MB group (57/423 = 13.47%) and finally, the BP group (13/423 = 3.07%). Statistical analysis showed differences between groups (Chi-Square = 30.62, p < 0.0001), (Table 3).

We evaluated 1551 records examined in the laboratory from 2014 to 2016, which were classified in 123 Multibacillary-MB patients (123/1551 = 7.93%); 71 Paucibacillary-PB patients (71/1551 = 4.57%); 451 Intradomiciliary Consanguineous Contacts – CCOSI (451/1551 = 29.07%) and 906 Non Consanguineous Contacts – CNCOS (906/1551 = 58.41%). 57 MB patients (13.47%), 13 PB patients (3.07%), 133 CCOSI (31.44%) and 220 CNCOS (52.00%) were positive for PGL-1. The correlation of the Classification with the vaccination status showed 57 MB patients without any BCG (57/125 = 45.6%) and only 3 patients with two doses of BCG (3/125 = 2.4%); 17 PB patients without any dose of BCG (17/69 = 24.63%); 80 CCOSI without any BCG (80/455 = 17.58%) and 171 CNCOS (171/906 = 18.87%). The odds ratio (OR) in the analysis between unvaccinated MB patients compared to CCOSI was statistically significant (OR = 14.25; p < 0.0001).

Table 2: Positivity to anti-PGL-1 according to sex in the sample studied in the period of 2014 and 2015.

positivity/sex	Positive	%	Negative	%	Total
Male	154	35.90%	403	35.92%	557
Feminine	275	64.10%	719	64.08%	994
Total	429	100	1122	100	1551

Table 3: PTositivity to anti-PGL-1 of *Mycobacterium leprae* according to the clinical classification and vaccination status with BCG in the sample studied in the period of 2014 and 2015.

Classificação/BCG	MB%	PB%	CCOSI%	CNCOS%	X^2	p - value
Sem BCG	57	17	80	171	47.65	0.0
1 dose	61	45	315	652		
2 doses	3	7	60	83		
Total	125	69	455	906 1551		

OBS: OR (MB x CCOSI) = 14.25, p < 0.0001, IC 95% 4.25 ≤ μ ≥ 47.70 – MB x CCOSI without any dose of BCG and with two doses.
OR (MB x PB) = 7.82, p = 0066, IC 95% 1.82 ≤ μ ≥ 33.58 - MB x PB without any dose of BCG and with two doses.
OR (MB x CNCOS) = 9.22, p < 0.0001, IC 95% 2.8 ≤ μ ≥ 30.32- MB x CNCOS without any dose of BCG and with two doses.

Discussion

Of 1551 records evaluated and examined in the laboratory from 2014 to 2016, 123 were classified as Multibacillary - MB patients (123/1551 = 7.93%); 71 paucibacillary patients – PB (71/1551 = 4.57%), 906 Non-Consanguinous Contacts - CNCOS (906/1551 = 58.41%) and 451 Intradomiciliary Consanguineous Contacts - CCOSI (451/1551 = 29.07%). 57 MB patients (57/423 = 13.47%) were positive for Mycobacterium leprae PGL-1 with Odds Ratio - OR = 2.064, p = 0.0006, 95% CI 1.37 ≤ μ ≥ 3.10 in the comparison between MB and CCOSI patients; 13 PB patients (13/423 = 3.07%) with Odds Ratio – OR = 3.85, p = 0.0002, 95% CI 1.91 ≤ μ ≥ 7.74 in the comparison between MB and PB patients, that is, the probability of positivity to the anti -PGL-1 is almost 4 times higher for MB patients compared to PB patients; 133 CCOSI (133/423 = 31.44%) and 220 CNCOS (220/423 = 52.00%), and the OR in the comparison between the CNCOS and CCOSI group was 0.76, p = 0.046, 95% CI 0.59 ≤ μ ≥ 0.98, that is, there is no statistically significant difference between the groups, however, when analyzing the Chi-square value (X^2 = 30.62, p < 0.0001) there was a difference between the groups (Table 3).

The analysis of the vaccination status and the Clinical Classification showed that the probability of an individual without any dose of BCG being in the MB group is 14.25 times higher compared to the CCOSI group (p < 0.0001, 95% CI 4.25 ≤ μ ≥ 47.70 (Table 3), a fact that reiterates the effectiveness of the BCG vaccine in protecting against severe forms of leprosy [6,7].

Considering the main epidemiological indicators for the analysis of endemic leprosy in the state of Pará, it is possible to infer that the seroprevalence index will not always reflect the actual detection in this study, as the seroprevalence will sometimes be higher than the detection in the general population or will be This is due to how the sample was selected and also to the fact that leprosy is a chronic disease and not an acute one, since those who became ill in a given year had already been infected for two or three years before and even were positive for the drug. -PGL-1, but without clinical signs [8]. In this study, for example, the municipality of Goianésia had a seroprevalence rate of 53.37% in 2015 and a detection coefficient of 28.44/100 thousand inhabitants in the same period, which is below the seroprevalence [9-11]. The municipality of Xinguara had a seroprevalence rate in 2015 of 6.99% and a detection rate in the same period of 10.50/100 thousand inhabitants [9,10] (Table 1).

The positivity by sex showed that women had a higher positivity rate (275/429 = 64.10%) than men (154/429 = 35.9%), however, no statistically significant difference was observed (p = 0.95); Most epidemiological studies on leprosy show that men are more likely to become ill from leprosy than women [9-12], although women are more likely to have a higher rate of positivity to the PGL-1 antigen, even though

they become ill. Minus 13, a fact that is attributed to hormonal issues. The fact that men get sick more is probably due to greater opportunities for social contacts or the nature of work or also because they are providers in the family (Table 2).

Regarding PGL-1 antigen positivity and the clinical classification of individuals in this study, it was observed that MB patients had a positivity rate of 57/423 = 13.47%, PB patients (13/423 = 3.07%); It is a fact that Multibacillary patients (Dimorphic and Virchovian forms), especially those with a bacteriological index - IB ≠ 0, have a predominantly humoral immune response pattern, and paucibacillary patients with IB = 0 have a predominantly cellular immune response pattern, which explains the positivity was much higher for MB patients compared to PB patients (OR = 3.85, p = 00002, 95% CI 1.91 ≤ μ ≥ 7.74); Many published scientific works are in agreement with this response dynamics in leprosy [13-15] (Table 3).

Thus, this retrospective study reiterates the importance of using the BCG vaccine in leprosy control programs, a fact shared by several authors [5-7].

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