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EPIDEMIOLOGICAL ANALYSIS OF NEW LEPROSY CASES IN AN OLD COLONY IN THE STATE OF MINAS GERAIS (2000-2016)

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ABSTRACT: The objective of this study was to describe and relate operational classification, BCG vaccination, and gender between new cases of leprosy in the Padre Damião Colony, municipality of Ubá, State of Minas Gerais, from 2000 to 2016. Data were collected from report forms and interviews, totalizing 43 new studied cases. The descriptive analysis indicated the predominance of the female gender, multibacillary form, and vaccinated individuals. Moreover, there was a decrease in the percentage of multibacillary cases in individuals with one or two BCG scars compared to those without scarring. In women with a scar, compared to those without a scar, there was a lower percentage of multibacillary cases. In men, paucibacillary cases were found only in individuals with two scars. Therefore, the BCG vaccine given in 1 dose is related to protection against the multibacillary form in women. In men, the second dose is required for protection against this clinical form.

KEY WORDS: Leprosy; BCG; *Mycobacterium leprae*.

ANÁLISE EPIDEMIOLÓGICA DE CASOS NOVOS DE HANSENÍASE EM UMA ANTIGA COLÔNIA DO ESTADO DE MINAS GERAIS (2000-2016)

RESUMO: O objetivo desta pesquisa foi descrever e relacionar classificação operacional, vacinação com BCG e gênero entre casos novos de hanseníase na Colônia Padre Damião, município de Ubá, Minas Gerais, de 2000 a 2016. Os dados foram coletados a partir de fichas de notificação e entrevistas, totalizando 43 casos novos pesquisados. Gênero feminino, forma multibacilar e vacinados predominaram na análise descritiva. Além disso, observou-se diminuição na porcentagem de casos multibacilares em indivíduos com uma ou duas cicatrizes de BCG em comparação com os sem cicatriz. Em mulheres com uma cicatriz, comparadas com as sem cicatriz, ocorreu menor porcentagem de casos multibacilares. Nos homens, casos paucibacilares foram encontrados somente em indivíduos com duas cicatrizes. Portanto, a vacina BCG administrada em 1 dose está relacionada com proteção contra a forma multibacilar em mulheres. Em homens, a segunda dose é necessária para se proteger contra essa forma clínica.

PALAVRAS-CHAVE: Hanseníase; BCG; *Mycobacterium leprae*.

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INTRODUCTION

Leprosy is a chronic disease caused by the bacillus *Mycobacterium leprae*, an intracellular parasite that mainly affects the

skin and peripheral nerves. Damage to peripheral nerves can result in sensory, motor, characteristic deformities and weaknesses[1].

For treatment purposes, the World Health Organization (WHO) established the operational classification system: patients with up to five skin lesions are classified as paucibacillary (BP), while those with more than five skin lesions are considered multibacillary (MB). However, when the smear test is available, patients with positive results are considered MB, regardless of the number of lesions[2].

The approval and use of multidrug therapy, starting in 1982, contributed to a marked reduction in the number of leprosy patients. This reduction drove members of the 44th session of the WHO Assembly (WHA) to pass resolution 44.9: Elimination of leprosy as a public health problem by the year 2000, that is, the reduction of prevalence of the disease to a level below one patient per 10,000 inhabitants[3]. Among the measures that accompanied this resolution, the following were included: the use of polychemotherapy and the Bacillus Calmette-Guérin (BCG) vaccine[4].

However, leprosy remains a significant health problem in several parts of the world, including Brazil. According to official reports from 121 countries, 213,899 new cases were reported worldwide in 2014. Of these, 125,785 (59%) occurred in India, 31,064 (15%) in Brazil and 17,025 (8%) in Indonesia. These three countries alone accounted for 81% of the total new cases notified worldwide[5].

The State of Minas Gerais has already achieved the goal of eliminating the disease as a public health problem. However, the municipality of Ubá, located in the area of Mata Mineira, presented rates of detection of new cases of leprosy characterized as hyper endemic and high, respectively, in the years 2004 and 2015, according to data from the Notifiable Diseases Information System (SINAN).

The Padre Damião Health House (CSPD), located in the municipality of Ubá, is a reference center for leprosy care that is part of the Hospital Foundation of Minas Gerais (FHEMIG). It was created in 1945 under the name of Leprosário Padre Damião, which received leprosy patients from various parts of the State of Minas Gerais. In the surroundings of the institution, the Boa Vista and São Domingos villages emerged, which currently comprise the Padre Damião colony.

Although the BCG vaccine was developed for use in tuberculosis[6], it is the only one administered to prevent leprosy. The presence of a scar has been recognized as a protective factor against the disease. Some studies demonstrate that BCG offers greater protection for MB forms compared to protection against PB forms of leprosy[7].

Regarding the additional dose of BCG, there are studies that indicate an increase in protection against leprosy compared to the single dose. This is a justification for revaccination of household contacts[8].

Although several studies confirm the non-specific protection provided by BCG in leprosy, there is still a need for studies that can evaluate the effectiveness of BCG in disease control programs, mainly on the requirements of revaccination and differential protection between MB and PB, and related to gender.

In this context, the present study aimed to describe and relate the operational classification, BCG scar and the gender of new cases of leprosy that occurred in the community around the Padre Damião Health House of the Hospital Foundation of Minas Gerais (CSPD- FHEMIG), municipality of Ubá, from 2000 to 2016.

METHODOLOGY

This was a retrospective, descriptive study with an interrelational approach to the variables: operational classification, BCG scar and gender. This study was conducted with the community around the CSPD, former Leprosário Padre Damião or Padre Damião Colony, with approximately 3,000 inhabitants and located in the rural area of the municipality of Ubá, State of Minas Gerais. The study population included the new cases reports to SINAN by the CSPD in the period from 2000 to 2016 and that were living in the community. Two new cases that were not found during home visits were excluded from the study.

Data on operational classification (PB or MB), BCG scar (none, one or two) and gender (female or male) were collected in three stages, from July 2016 to May 2017:

1- Analysis of the files of the CSPD reference service to survey the names, genders and medical records of patients diagnosed with leprosy in the period from 2000 to 2016;

2- Access to the medical records and the SINAN files. The analysis of the records was based on the verification of data such as: whether the patient was a new case, if the patient was a resident in the Padre Damião Colony, or if the patient was notified between 2000 and 2016. Finally, the operational classification was analyzed. Still from the data in the medical records, we sought the record of the presence of a BCG scar;

3- Visit to the houses with new cases that did not present information about BCG in their medical records. After agreeing with the terms of the research and signing the Free and Informed Consent Form (ICF), we analyzed for the presence of the BCG scar in the lower insertion of the deltoid muscle of the right arm.

This study was approved by the Research Ethics Committee of the Hospital Foundation of Minas Gerais (FHEMIG), according to Res. CNS 196/96 and complementary for research with human beings, under the number 135/2016.

Statistical analysis was run in Open Epi software (version 3.01) with Mid-P test applied between the variables. The results were presented in tables according to descriptive statistics through absolute and relative frequencies. Differences were considered statistically significant when the p-value obtained was <0.05.

RESULTS

The total number of new cases reported was 45, however, 2 were excluded because they were not found during the visit. Therefore, the study population was 43 new cases.

The descriptive analysis revealed the predominance of the female gender (60.47%) and the MB form (76.74%) among the evaluated cases. The presence of BCG scar (1 or 2) was considered as a way to assess the vaccination situation. The total number of individuals vaccinated with BCG corresponded to 60.47% among the 43 new cases of leprosy (Table 1). In addition, it was found that 74% of new cases were family contacts of patients being treated or already treated for leprosy.

When relating the operational classification to gender (Table 2), in both female and male gender, most new cases were classified as MB (80.77% and 70.59%, respectively). There was no statistically significant difference between these variables ($p = 0.467$).

As for the distribution of the operational classification according to BCG vaccination, 94.12% non-vaccinated patients (without scar) were classified as MB. The percentage of MB decreased to 68.42% in the presence of a scar and continued to decrease to 57.14% in the presence of two scars. In contrast, the percentage of PB increased with the presence of BCG scars. A statistically significant difference was detected only between the non-vaccinated and the vaccinated patients (1 or 2 scars) in relation to the operational classification, indicating that vaccination is preventing the MB form (Table 3).

In the female gender (Table 4), it was found that all women without any BCG scar were classified as MB. Women with a scar showed a significant drop in the percentage of this operational classification to 58.33%. However, those with two scars were all classified as MB.

When analyzing the male stratum, no difference was found in the percentage of MB cases between men without any scar and those with a scar. However, all men with two scars were classified as PB, showing statistically significant differences from men with none or one scar (Table 5).

There were no significant differences in the frequency distributions of none, one or two BCG scars when comparing men and women.

Table 1. Description of the variables of new cases of leprosy, Padre Damião Colony, Municipality of Ubá, State of Minas Gerais, Brazil, 2000-2016

Variables	N	%
Gender		
Female	26	60,47%
Male	17	39,53%
Operational Classification		
Multibacillary	33	76,74%
Paucibacillary	10	23,26%
BCG Scar		
None	17	39,53%
One	19	44,19%
Two	07	16,28%

Table 2. Distribution of the operational classification of new cases of leprosy according to gender, Padre Damião Colony, Municipality of Ubá, State of Minas Gerais, Brazil, 2000-2016

	Gender			
Operational Classification	**Female**		**Male**	
	N	**%**	**N**	**%**
Paucibacillary	05	19,23%	05	29,41%
Multibacillary	21	80,77%	12	70,59%
Total	**26**	**100%**	**17**	**100%**

Table 3. Distribution of the operational classification of new cases of leprosy according to BCF scarring, Padre Damião Colony, Municipality of Ubá, State of Minas Gerais, Brazil, 2000-2016

	Scar							
Operational Classification	**None**		**One**		**Two**		**One or Two**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Paucibacillary	1*	5,88%	6	31,58%	3	42,86%	9	34,62%
Multibacillary	16*	94,12%	13	68,42%	4	57,14%	17	65,38%
Total	**17**	**100%**	**19**	**100%**	**7**	**100%**	**26**	**100%**

* Significant difference between the group with no scar and the group with one or two scars ($p < 0.05$).

Table 4. Distribution of the operational classification of new cases of leprosy according to the BCG scar in females, Padre Damião Colony, Municipality of Ubá, State of Minas Gerais, Brazil, 2000-2016

Gender: Female						
	Scar					
Operational Classification	**None**		**One**		**Two**	
	N	**%**	**N**	**%**	**N**	**%**
Paucibacillary	0*	0%	5	41,67%	0	0%
Multibacillary	10*	100%	7	58,33%	4	100%
Total	**10**	**100%**	**12**	**100%**	**4**	**100%**

* Significant difference between the group with no scar and the group with one scar ($p < 0.05$).

Table 5. Distribution of the operational classification of new cases of leprosy according to the BCG scar in males, Padre Damião Colony, Municipality of Ubá, State of Minas Gerais, Brazil, 2000-2016

Gender: Male						
	Scar					
Operational Classification	**None**		**One**		**Two**	
	N	**%**	**N**	**%**	**N**	**%**
Paucibacillary	1*	14,29%	1*	14,29%	3	100%
Multibacillary	6*	85,71%	6*	85,71%	0	0%
Total	**7**	**100%**	**7**	**100%**	**3**	**100%**

* Significant difference between the group with no scar and the group with two scars ($p < 0.05$).

DISCUSSION

The new cases of leprosy revealed the predominance of the multibacillary form in the community, mainly in the absence of the BCG scar, as previously reported in previous studies. However, the differences observed in relation to genders are still poorly studied.

According to the WHO epidemiological bulletin 2016, Brazil is among the three countries that had the highest number of new cases (> 10,000), ranking second among all countries in the world[9]. Although the same bulletin shows, at national and international level, the predominance of males among new cases, the higher frequency of females observed in our results is in accordance with Brazilian studies[10-14]. Figueiredo and Silva[15] had already reported that the number of female cases was increasing, corroborating the finding.

The increase in the occurrence of leprosy among women can be explained, mainly, by the increasing participation in the labor market and, at the same time, approximation to the conditions of exposure to the bacillus to which men are usually subjected[11,13]. Additionally, the habit of women seeking health services more frequently compared to men can contribute to this increase[10,12].

The predominance of the MB form among new cases observed in the study is in agreement with the national data of the WHO Epidemiological Bulletin 2016 and with regional studies[16-18]. This may be the result of a late diagnosis[17], made after the evolution of the initial (undetermined) phase of the disease[19], which contributes to the maintenance of the chain of transmission of the disease in the community[20].

In view of the protective action of BCG vaccination on contacts of leprosy patients, whether neonatal BCG or revaccinated contacts[4], the Ministry of Health recommends the application of BCG on the examined contacts, without signs and symptoms of leprosy, according to the vaccination history and, or presence of the vaccine scar[21]. The fact that 74% of new cases are family contacts, combined with easy access to health services, may explain the majority of vaccinated people among new cases (60.47%), unlike the Brazilian study carried out in 2012[22], which found only 16.5% of the cases with vaccine scar and 44.7% of the cases with a family history of leprosy.

The distribution of the operational classification according to gender did not present significant differences. On the other hand, the higher absolute frequency of MB women compared to men with the same diagnosis is supported by the findings of Miranzi *et al.*[18], a retrospective study that used data from SINAN, which showed an association between the MB classification and females with a four times higher chance compared to men.

The presence of a BCG scar is recognized as a protective factor against leprosy, but with a degree of protection that varies between experimental studies (26-41%) and observational studies (61%)[23]. There are studies that demonstrate that this protection is provided in greater proportions for MB forms, as shown by Goulart *et al.*[24]. In this study, 1,396 family contacts were followed-up for five years in order to investigate risk factors for leprosy and found 98% protection against MB forms in the presence of BCG scarring. According to Muliyil et al.[25], BCG would cause changes in cellular immunity that would lead to an increase in the occurrence of milder forms (PB). This hypothesis was reinforced by the meta-analysis of Setia *et al.*[8]. In accordance with these studies, our results show that the distribution of the operational classification according to the vaccination showed 94.12% MB cases among the non-vaccinated (0 scar), and a significantly increased number of PB cases among the vaccinated (1 or 2 scars).

In the female gender, data from the present study also suggest that the presence of a scar may offer protection against the MB form due to the decrease in the percentage of this form among women with a BCG scar (58.33%) compared with those who had no scar (100%).

In males, the effect described above was not verified, probably due to the smaller number of new cases in this gender. According to the literature, it was expected that, in the presence of a BCG scar, there would be a decrease in the percentage of MB forms among men[8, 24, 25].

Also, according to the distribution of the operational classification according to vaccination, disregarding stratification by gender, the administration of two doses of BCG does not imply significant differences

in relation to the application of a single dose. However, when stratified by gender, differences were detected in men, which reflect possible additional protection from the second dose, which resulted in the directing of all cases to the PB form. Regarding the protective effect of the second dose, the longitudinal study carried out by Araújo *et al.*[26] in Brazil, which followed-up 2,992 individuals over 10 years, demonstrated a 95% reduction in the relative risk for the development of leprosy in individuals with two BCG scars compared to those with no scars. And according to Goulart *et al.*[24], an additional BCG vaccination can stimulate the shift of the Mitsuda test, used to assess specific cellular immunity against the bacillus, from negative to positive in leprosy contacts, reducing the risk of development of MB forms.

Given the MB classification of all women with two BCG scars and the greater number of MB women among new cases, the following factors associated with gender are possible explanations for the persistence of MB forms in women: genetic susceptibility due to polymorphisms in GAL3ST4 in women, which is associated with an increased risk of leprosy[27] and hormonal alterations during puberty or pregnancy that cause changes in host immunity[28].

The present study validated the hypothesis that the presence of the BCG scar offers greater protection against the MB form. Nevertheless, the existence of differential protection between the genders related to the number of doses of the vaccine cannot be confirmed due to the small sample size of the study population.

CONCLUSION

Therefore, the results indicate, in line with what is observed in the literature, the importance of BCG vaccination (1 or 2 doses) for protection against the MB form of leprosy, regardless of gender, in new cases reported by people living around the CSPD. In this same universe, the finding that 1 dose of BCG is sufficient for the reduction of MB cases in women, while in men 2 doses are necessary, suggests that gender-related differences influence the number of doses that must be applied to achieve protection.

Multicenter epidemiological studies with a larger universe of new cases are required to confirm or exclude the difference between genders with respect to the number of BCG doses sufficient to protect against the MB form.

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