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Original Article

Epidemiological and histopathological study of leprosy cases in the state of Sergipe, Brazil

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Leprosy is a disease with different ratings due to the diversity of clinical manifestations. The most used classification by Reference Centers is the histopathological, which has been considered to have better specificity and sensitivity. Thus, the aim of this study was to determine the histopathological types of profile of Leprosy patients from different parts of Sergipe, Brazil, from 1985 to 2005. For this purpose, it was used histopathological diagnosis reports filed at Prof. Dr. Nestor Piva Memorial from 1985 to 2005. There were 2,102 reports with Leprosy diagnosis, from which 1,165 (55.4%) cases were women, 1,224 (58.2%) cases were of mixed race and 1,835 (87.3%) were from the metropolitan area of Aracaju / SE. The mean age was 36.62 year. The smear microscopy classified 1,669 (79.4%) lesions as paucibacillary and there was a predominance of tuberculoid and indeterminate forms. Men were more likely to be multibacillary, as well as being the lepromatous pole. The determination of histopathological forms and the knowledge about the association and the epidemiological profile are important tools to contribute to public health policies.

Key words: Leprosy, Epidemiological and Histopathological.

Introduction

Leprosy (Hansen's disease) is a chronic and infectious granulomatous disease caused by *Mycobacterium leprae*, which affects the skin and peripheral nerves (Scollard et al 2006). In several countries, including Brazil, the disease is still considered a significant health problem (WHO 2011) due to its morbidity and socioeconomic impact, as a result of the complications (physical disabilities and deformities) produced during the clinical evolution of the disease (Moschioni et al 2010).

Worldwide, 228,474 new cases of Leprosy were reported in 2010. During this period, Brazil ranked

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second in number of cases (34,894) losing only to India, which had 126,800 cases. Within the Americas, Brazil was responsible for 92.92% of the cases (WHO 2011).

The disease prevalence has decreased in countries considered endemic after the adoption of control measures such as multidrug therapy and early cases diagnosis. In Brazil, the prevalence was 16.4 cases per 10,000 inhabitants in 1985, reducing to 2.1/10,000 in 2007 (Penna et al 2008). This decline was possibly influenced by operational factors such as early diagnosis and prompt treatment, integrated to the assistance at the primary health system. Nevertheless, these rates are not at the level recommended by WHO (1/10,000) (WHO 2005).

The cases distribution in the Brazilian territory is uneven among the five Regions. The North, Midwest and Northeast persist as endemic areas and concentrate the country's 10 main clusters (Brazil 2010). Although Sergipe is not part of any of the clusters it is a state in which leprosy is considered endemic and, in 2007, it presented a detection rate of 2.63 cases per 10,000 inhabitants (Brazil 2009).

Leprosy is characterized by a diversity of clinical, immunological and histopathological findings, which has allowed the emergence of different classifications. From the International Congress of Leprosy of the Madrid, in 1953, patients have been divided into groups according to the clinical form of the disease as indeterminate (I), tuberculoid (T), borderline (B) and lepromatous (L) (Gomes et al 2005). Ridley and Jopling (1966) introduced a classification system based on histopathological findings and cellular immunity level. From this system, leprosy patients were divided into five groups: tuberculoid (TT), borderline tuberculoid (BT), borderline-borderline (BB), borderline-lepromatous (BL) and lepromatous (LL). The indeterminate form (I) includes the cases that do not fit into any of the five groups (Lockwood et al 2007).

The World Health Organization (WHO), for treatment purposes, recommends a classification that categorizes patients into paucibacillary (PB), with 1-5 skin lesions and/or only one nerve trunk affected; and multibacillary (MB), with over five skin lesions and/or more than one nerve trunk affected. However, patients with positive smear microscopy are classified as MB, regardless of the number of skin lesions (WHO 1998).

However, many studies have shown discrepancies between the clinical and histological classifications (Vargas-Ocampo 2004). Moreover, the adoption of only the simplified WHO criteria can lead to errors in the classification and therefore in the treatment (Gomes et al 2005, Teixeira et al 2008). In Brazil, the clinical diagnosis must be accompanied by the smear microscopy and lesions histopathology for a better understanding of Leprosy, especially in endemic regions (Teixeira et al 2008; Santos et al 2013).

The aim of this study was to determine the profile of the Leprosy types based on the histopathological diagnosis in patients from different regions of Sergipe, Brazil, from 1985 to 2005. An analysis of the association between histopathological type and socio-demographic data was also performed.

Materials and Methods

This is a retrospective study with a quantitative approach based on the analysis of skin biopsies reports, presenting clinical and histopathological diagnosis of leprosy patients from January 1985 to December 2005. These reports were from Prof. Dr. Nestor Piva Memorial (PDNPM) that belongs to University Tiradentes (UNIT). This database had a collection of 250,000 histopathological reports of diverse biological material types from all regions of Sergipe.

From the 250,000 reports, 2,102 presented the histopathological diagnosis of leprosy, being then included in the present study. The information from these reports was organized into a questionnaire containing the year of diagnosis, age, sex, race (white), marital status, origin, smear microscopy and histopathological classification. A database was created from the information obtained, enabling exploratory analyses such as determination of simple and absolute frequencies and percentage for categorical variables and their representation through charts and graphs using descriptive analysis and association between variables. We used data from 1985 to 2005 as cumulative information.

The chi-square test (χ^2) was used to compare differences and distribution between proportions. Confirmation of the association between variables was performed using the Odds Ratio (OR) and confidence interval of 95% (IC95%). The level of significance for all analyzes was 5% ($p < 0.05$). Data were analyzed using SPSS 20.0 version.

The study was approved by the Ethics Committee in Human Research of Federal University of Sergipe.

Results

From the 2,102 patients' reports with histological diagnosis of Leprosy, 1,165 (55.4%) were women and 937 (44.6%) were men. Regarding the area, 1,835 (87.3%) were from the metropolitan area of Aracaju and 267 (12.7%) from the countryside. The disease was prevalent in brown individuals (1,224 cases - 58.2%), followed by white and black ones with 669 (31.8%) and 209 (9.9%) cases, respectively. Regarding marital status, 1,029 (48.9%) were married, 887 (42.2%) were single, 105 (5.2%) were widowed, 28 (1.3%) divorced and 53 (2.5%) did not report.

The patients' age ranged from 1 to 91 years, with an average of 36.62 years (±18.89). The age groups are presented in Figure 1. The age corresponding to the economically active population was the most affected. Children under 15 corresponded to 243 (11.6%) cases.

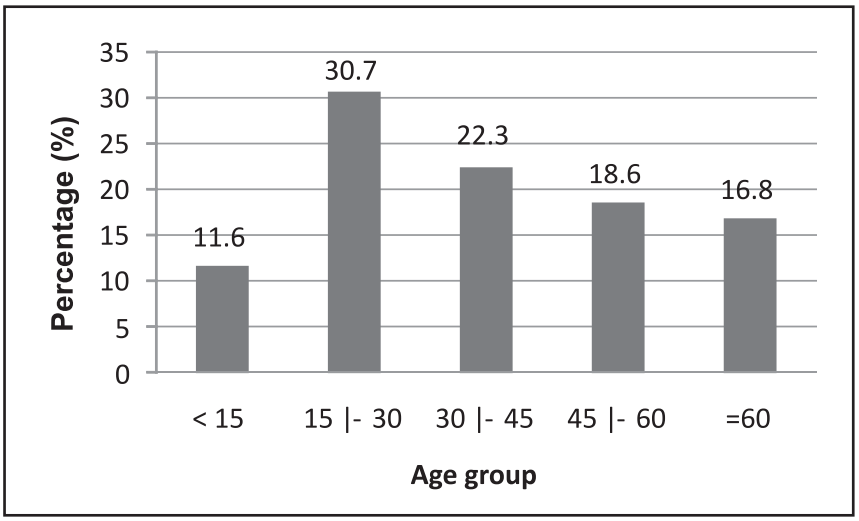

Fig 1 : Distribution of Leprosy cases according to age group PDNPM, Sergipe – Brazil. 1985-2005.

Smear microscopy data revealed that in 1,669 (79.4%) cases the smear was negative, being classified as PB, and 432 (20.6%) were smear positive and were considered MB. The gender association with the classification made after the lesion smear microscopy is shown in Table 1. From these data it was observed that men were more likely to be MB than women [OR = 3.490 (IC95% 2.785-4.374), p = 0.000].

The histopathological forms tuberculoid (TT) and indeterminate (I) were the most frequent among the individuals studied, with 917 (43.6%) and 707

Table 1 : Distribution of operational classification and histopathological type from the lesions smear microscopy, according to gender. PDNPM, Sergipe-Brazil, 1985-2005

Variables	Gender				OR (IC95%)	p[a]
	M		F			
	n	%	n	%		
OC						
Paucibacillary	641	38.4	1029	61.6		
Multibacillary	296	68.5	136	31.5	3.490 (2.785-4.374)	0.000
Histopathological Type						
Indeterminate	268	37.9	439	62.1	0.658 (0.547-0.791)	0.000
Tuberculoid	346	37.7	571	62.3	0.608 (0.501-0.724)	0.000
Borderline-tuberculoid	34	51.5	32	48.5	1.331 (0.815-2.175)	0.251
Borderline-borderline	9	64.2	5	35.8	1.244 (0.434-3.559)	0.683
Borderline-lepromatous	27	65.8	14	34.2	2.437 (1.270-4.674)	0.006
Lepromatous	256	71.7	101	28.3	3.956 (3.082-5.078)	0.000

OC= Operational classification based on smear microscopy; M = Male; F=Female; OR= Odds Ratio; IC95% = Interval of confidence 95%. [a] chi-square test (χ^2).

Table 2 : Distribution of histopathological types according to age group. PDNPM, Sergipe–Brazil, 1985-2005.

HT	Age group					Total	p[a]
	<15 n (%)	15|-30 n (%)	30|-45 n (%)	45|-60 n (%)	≥60 n (%)	n (%)	
I	85 (12.0)	263 (37.2)	184 (26.0)	110 (15.6)	65 (9.2)	707 (100)	0.000
TT	115 (12.5)	242 (26.4)	174 (19.0)	194 (21.2)	192 (20.9)	917 (100)	0.000
BT	3 (4.5)	10 (15.2)	19 (28.8)	20 (30.3)	14 (21.2)	66 (100)	0.001
BB	1 (7.1)	3 (21.4)	0 (0.0)	6 (42.9)	4 (28.6)	14 (100)	0.079
BL	6 (14.6)	19 (46.4)	12 (29.3)	1 (2.4)	3 (7.3)	41 (100)	0.039
LL	33 (9.2)	108 (30.3)	80 (22.4)	61 (17.1)	75 (21.0)	357 (100)	0.000

HT=Histopathologic type; I=Indeterminate; TT=Tuberculoid; BT=Borderline-tuberculoid; BB=Borderline borderline; BL= Borderline-lepromatous; LL = lepromatous.
[a] chi-square test (χ^2).

(33.6%) cases, respectively. The lepromatous (LL) corresponded to 357 (17.0%), whereas all borderline forms (BT, BB and BV) had a frequency of 121 (5.8%). The analysis of the association between the histopathological type and gender showed that men were more likely to belong to the histopathological types borderline-lepromatous (OR = 2.437, 95% CI 1.270 to 4.674) and lepromatous (OR = 3.956, 95% CI 3.082 to 5.078) than women (Table 1).

Table 2 presents the distribution of histopathological type according to age. Indeterminate and tuberculoid forms were the most frequent in all age groups (p=0.000). Lepromatous form (p=0.000) was more frequent in individuals ranging from 15 to 30 years of age.

Discussion

Biological and socio-cultural factors have been identified as the main reasons for the high leprosy incidence among men (Moreira et al 2008, Magalhães and Rojas 2007). In endemic regions WHO data indicate that males have been more affected than females reaching double the number of cases (Arora et al 2008, WHO 2011). In Brazil, the number of men annually detected has prevailed (Brazil 2010). However, in the present study, females were the most prevalent (55.4%), corroborating with other studies (Campos et al 2005, Amaral and Lana 2008, Melão et al 2011, Raposo and Nemes 2012). One possible explanation for this is that, traditionally, women have higher tendency to look for healthcare services (Silva et al 2012, Raposo and Nemes 2012). Thus, the female population has more opportunities for diagnosis due its frequent contact with health professionals.

Leprosy diagnosis was more common in mixed ethnicity individuals. This occurrence might be associated with the region's ethnic composition, where miscegenation has been very present for centuries. This assertion corroborates with other studies conducted in other states of northeast Brazil (Raposo and Nemes 2012, Kerr-Pontes et al 2006, Corrêa et al 2012).

The findings on this study revealed that leprosy has reached the age group under 15 years old in a lower proportion. These data are consistent with those reported by other studies (Arora et al 2008, Melão et al 2011, Raposo and Nemes 2012). The detection in this age group has been considered an endemicity indicator, implying that the bacillus *M. leprae* transmission in the community has not shown the decline rates expected (Gomes et al 2005, Norman and Joseph 2004, Imbira et al 2009). This has occurred even with the use of control measures proposed by WHO and implemented by the Unified Health System (SUS), specifically by the introduction of Family Health Strategy. However, in endemic areas for leprosy it is important to make an active search in the population, especially among the youngest in order to detect cases as early as possible and thus avoid the problems the disease can cause in the course of its evolution (Ferreira et al 2008).

In the present study there was a predominance of cases in the population considered economically active. This may harm the economy since this population segment may develop disabilities, injuries, reactional states, moving away from the productive activity and generating a high social cost (Campos et al 2005, Amaral and Lana 2008).

The smear microscopy can be a diagnosis support and consists of an important tool for the correct classification of individuals with leprosy, assisting in a proper treatment and avoiding relapses, complications and disease transmission (Teixeira et al 2008, Pardillo et al 2007, Santos et al 2013). In the present study, the smear microscopy was negative in 79.4% of patients classified as PB. Other studies also found PB higher rates (Raposo and Nemes 2012, Pereira et al 2008) but in countries with the highest incidence worldwide

there is a predominance of the MB form (WHO 2009, WHO 2011). When a high percentage of PB diagnosed cases is observed we may be led to believe that either the diagnosis is occurring as early as possible, decreasing the chances of occurrence of the severe forms of the disease and its complications, or that the disease still persists, since immunologically competent individuals are becoming ill (Mendonça et al 2008, Simon et al 2011).

However, when evaluating the association between gender and the operational classification based on the lesion smear microscopy, it was observed that there was men predominance in the MB form so the chance of impairment for this form of leprosy was 3.49. Since the transmission occurs through MB individuals (Bakker et al 2004), we can infer that men, in the studied population, were probably more related to the transmission.

Regarding histopathological type, there was a predominance of tuberculoid and indeterminate forms in all age groups in the studied population. These forms are found in regions of the world where the disease is endemic or hyperendemic. It is known that these disease forms are present in immunologically competent individuals that would not have gotten sick if the contact with the *M. leprae* had not been constant. The predominance of these forms in a region is an important epidemiological indicator of the disease (Hinrichsen et al 2002).

The lepromatous form of leprosy, on the other hand, corresponds to the pole of low resistance within the disease spectrum and it is characterized by the chronicity of its evolution (Pardillo et al 2007) and is intimately present in immunologically depressed individuals (Simon et al 2011) or in those who delay looking for health services for treatment (Silva et al 2012). In the present study, it was observed a significant association between the lepromatous form and the male gender with a chance about four times higher than females [OR = 3.956 (95% CI 3.082 to 5.078), p = 0.000]. However, this study has its limitations and it cannot be extended to the community since data was used from a health center.

Conclusion

The histopathological profile analysis of leprosy can contribute to a better understanding about the disease and its different clinical forms. In addition, the knowledge of the most frequent histopathological forms and the association with the patients' epidemiological profile indicates the endemicity degree. This may help public health agencies to plan educational activities in order to diagnose the disease early and reduce its transmission.

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