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Short Communication

Leprosy in Southern Brazil: a twenty-year epidemiological profile

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Abstract

Introduction: This study evaluated leprosy rates in Rio Grande do Sul, an area with a historically low prevalence. However, recent studies are lacking. **Methods:** Data extracted from a National Database were analyzed for clinical features and compared to 1980s data. Tendency was assessed via stationarity analysis. **Results:** Between 1990 and 2011, 4,770 cases were reported (0.21/10,000 inhabitants; 95% CI = 0.19-0.24). Detection was slightly higher among males, 1.9% cases were among children and most multibacillary (74.7%) at diagnosis. **Conclusions:** Leprosy is controlled in RS, but most cases are multibacillary. Early identification is important to avoid disabilities due to late diagnosis.

Keywords: Leprosy. Epidemiological survey. Rio Grande do Sul.

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that primarily affects Schwann cells and the skin. The upper airways are the main entry point and route of elimination of the bacillus[1]. Disease characteristics are dependent on host immune response, generating a wide clinical and histopathologic spectrum from a pole of resistance (tuberculoid pole) to a pole of susceptibility (lepromatous pole). Besides these opposing poles, there are two additional clinical forms: indeterminate and borderline, whose features may vary from one pole to another in the disease evolution[1,2]. The World Health Organization (WHO) also classifies leprosy operationally, for chemotherapeutic purposes as either paucibacillary (PB) (cases with up to five skin lesions and/or one impaired nerve) and multibacillary (MB) (cases with more than five skin lesions and/or one or more affected nerves). The PB and MB classifications correspond approximately to the tuberculoid and lepromatous poles, respectively[1].

When not diagnosed and treated early, leprosy and its associated sequelae can cause disabilities and physical deformities, leading to occupational and psychosocial problems[3]. Leprosy is curable if diagnosed early which can prevent the development of long-term sequelae and reduce rates of transmission through disruption of the transmission chain[1].

Leprosy is a major public health problem in Brazil[1] and in several countries globally. At the end of 2000, leprosy rates were still endemic in 15 countries (prevalence above 1.0/10,000 inhabitants). According to WHO, in 2009, Brazil remained one of six countries in the world with the highest prevalence of leprosy[4,5]. In 1991, the WHO elimination target was defined as a prevalence less than 1 case per 10,000 inhabitants. The same year, multidrug therapy (MDT) with rifampicin, clofazimine, and dapsone was implemented as the main strategy to combat and eliminate leprosy, in addition to early detection[6].

Around 80% of new cases are diagnosed in countries located in the intertropical area[7]. In Brazil, more than 30,000 new cases of leprosy are diagnosed annually. In 2014, the prevalence of leprosy in Brazil was 1.27/10,000 inhabitants. However, the Rio Grande do Sul (RS),Brazil's most Southern state (at the border with Uruguay and Argentina), is considered an area where the disease is eliminated, having the country's lowest prevalence at 0.16/10,000 inhabitants[8]. Thus, few recent studies have examined the epidemiology of leprosy in RS, making it difficult to evaluate disease trends for the last twenty years. Therefore, this study aimed to compare leprosy data from RS in the 1980s to that observed in the period from 1990 to 2011 and to assess the current situation of leprosy in RS.

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This was an ecological study, in which leprosy data in RS were analyzed for the period 1990-2011 by evaluating data included in the Notifiable Diseases Information System [*Sistema de Informação de Agravos de Notificação* (SINAN) database[5]. The SINAN is the national registration system for notifications and investigations of leprosy cases. Data were collected for cases with notification and residence in RS across the following variables: new cases by sex and age, WHO operational classification and clinical form.

Detection rates overall and for children younger than 15 years of age were extracted from population data collected by the 2000 Census and population estimates of the Brazilian Institute of Geography and Statistics [*Instituto Brasileiro de Geografia e Estatística* (IBGE)][9], available on the website of the Department of Informatics of the Unified Health System [*Departamento de Informática do Sistema Único de Saúde* (DATASUS)][8]. Descriptive data analysis was performed through calculation of simple absolute and percentage frequencies for categorical variables. Results were compared with data published by Cestari et al[10], referring to 1980s data and were presented as rates per 10,000 inhabitants using 95% confidence intervals (95% CI). To test the stationarity of graphically presented data, the Dickey-Fuller test was used through the *R Project Package - t series.*

TABLE 1

New cases of leprosy by sex and age group for the periods 1982-1988 and 1990-2011.

Year of diagnosis	Unknown	0-14 yo	Percentage	≥15 yo	Percentage	Total	Male	Female	Ratio
1982-1986	0	23	2.2	999	97,8	1,022	508	524	0.97
1987-1988	0	18	5.4	314	94.6	332	185	151	1.23
Total 1982-1988	**0**	**41**	**3.0**	**1,313**	**96.9**	**1,354**	**693**	**675**	**1.03**
1990	0	6	3.5	167	96.5	173	105	68	1.54
1991	1	5	2.8	171	97.2	176	92	84	1.10
1992	4	7	3.2	211	96.8	218	109	109	1.00
1993	4	3	1.7	174	98.3	177	96	81	1.19
1994	2	6	3.1	185	96.9	191	116	75	1.55
1995	5	2	1.1	189	98.9	191	97	94	1.03
1996	6	3	1.4	217	98.6	220	120	100	1.20
1997	5	6	2.7	212	97.2	218	109	109	1.00
1998	2	4	1.9	198	98.0	202	119	83	1.43
1999	0	0	0	216	100	216	121	95	1.27
2000	0	5	2.2	225	97.8	230	112	118	0.95
2001	0	5	2.2	219	97.8	224	121	103	1.17
2002	0	6	2.1	280	97.9	286	143	143	1.00
2003	0	5	1.8	265	98.1	270	130	140	0.93
2004	0	10	3.8	255	96.2	265	120	145	0.83
2005	0	2	0.7	263	99.2	265	134	131	1.02
2006	1	0	0	251	99.6	252	126	126	1.00
2007	0	4	1.8	222	98.2	226	111	115	0.97
2008	0	2	0.9	215	99.1	217	122	95	1.28
2009	0	2	1.0	191	98.9	193	94	99	0.95
2010	0	5	2.9	165	97.1	170	93	77	1.21
2011	0	2	1.0	188	98.9	190	103	87	1.18
Total 1990 - 2011	**30**	**90**	**1.9**	**4,679**	**98.1**	**4,770**	**2,493**	**2,277**	**1.09**

TABLE 2

New cases of leprosy by clinical form for the periods 1982-1988 and 1990-2011, and according to the WHO classification for the period 1990-2011.

Year of diagnosis	T	%	L+B	%	Unknown	%	PB	%	MB	%	Total
1982-1986	236	25.6	687	74.4	-	-	-	-	-	-	-
1987-1988	35	12.4	247	87.6	-	-	-	-	-	-	-
Total 1982-1988	**271**	**22.5**	**934**	**77.5**	-	-	-	-	-	-	-
1990	27	17.9	124	82.1	0	0.0	49	28.3	124	71.7	173
1991	31	19.5	128	80.5	0	0.0	48	27.3	128	72.7	176
1992	35	17.3	167	82.7	0	0.0	51	23.4	167	76.6	218
1993	38	24.2	119	75.8	0	0.0	59	33.3	118	66.7	177
1994	41	23.3	135	76.7	0	0.0	56	29.3	135	70.7	191
1995	40	22.5	138	77.5	0	0.0	53	27.7	138	72.2	191
1996	44	21.1	164	78.8	0	0.0	56	25.4	164	74.5	220
1997	33	16.4	168	83.6	0	0.0	50	22.9	168	77.1	218
1998	39	20.2	154	79.8	0	0.0	48	23.8	154	76.2	202
1999	48	24.0	152	76.0	0	0.0	62	28.7	154	71.3	216
2000	36	17.9	165	82.1	2	0.9	61	26.5	167	72.6	230
2001	38	21.6	138	78.4	3	1.3	78	34.8	143	63.8	224
2002	33	15.4	181	84.6	7	2.4	65	22.7	214	74.8	286
2003	41	20.2	162	79.8	5	1.8	62	22.9	203	75.2	270
2004	39	17.6	182	82.3	3	1.1	61	23.0	201	75.8	265
2005	37	16.5	187	83.5	1	0.4	50	18.9	214	80.7	265
2006	42	80.1	167	79.9	2	0.8	55	21.8	195	77.4	252
2007	17	11.8	127	88.2	1	0.4	44	19.5	181	80.1	226
2008	36	22.1	127	77.9	1	0.5	53	24.4	163	75.1	217
2009	32	20.2	126	79.7	0	0.0	44	22.8	149	77.2	193
2010	32	23.9	102	76.1	0	0.0	40	23.5	130	76.5	170
2011	27	19.7	110	80.3	1	0.5	34	17.9	155	81.6	190
Total 1990-2011	**786**	**19.6**	**3,223**	**80.4**	**26**	**0.5**	**1,179**	**24.7**	**3,565**	**74.7**	**4,770**

T: tuberculoid form; **L+B**: lepromatous + borderline forms; **PB:** paucibacillary; **MB:** multibacillary; **%:** percentage.

The results of this study showed that, during the period of 1990-2011, 4,770 cases of leprosy were registered in RS. The new-case detection rate identified was considered low by patterns normally observed in Brazil [(0.21 cases/year per 10,000 inhabitants (95%CI = 0.19-0.24)]. This was similar to the 1980s rate of, 0.25 cases/year per 10,000 inhabitants (95% CI = 0.20-0.27).

This study identified a decrease in detection of new cases with the stationarity analysis showing no significant result (p = 0.701). However, parameters were softened to reduce variability among the evaluated years. Therefore, the data obtained shows a declining trend in the detection of new cases over the 30 years observed (**Figure 1A**).

The rate of new cases from the 1990s was slightly higher among males with a mean male/female (M/F) ratio of 1.09, reaching 1.5 in some years within the period. This pattern was not observed between 1975 and 1988 within which a M/F mean ratio of 1.00 was observed (**Table 1**). The new-case detection rate in children younger than 15 years of age decreased during the 1990-2011 period compared to the 1980s (1.9% vs 3.0%) (**Table 1**).

Throughout both periods, there was a higher average detection of lepromatous and borderline leprosy forms, from 77.5%/year in the 1980s to 80.4%/year during the period 1990-2011 (**Table 2**). Moreover, when grouped according to the WHO operational classification (**Table 2**), there was a 74.7% rate of MB detection during the period 1990-2011. This rate coincides with the classification according to clinical form if the MB classification is considered as the lepromatous and borderline leprosy forms. It was also observed - by stationarity analysis of the incidence percentage of MB cases within the last 22 years - that an upward trend in the proportion of these cases was identified in this study, because there was no significant stationarity (p = 0.342) (**Figure 1B**). No pattern was identified regarding percentage of diagnoses according to the disability grade 2. (**Figure 1C**).

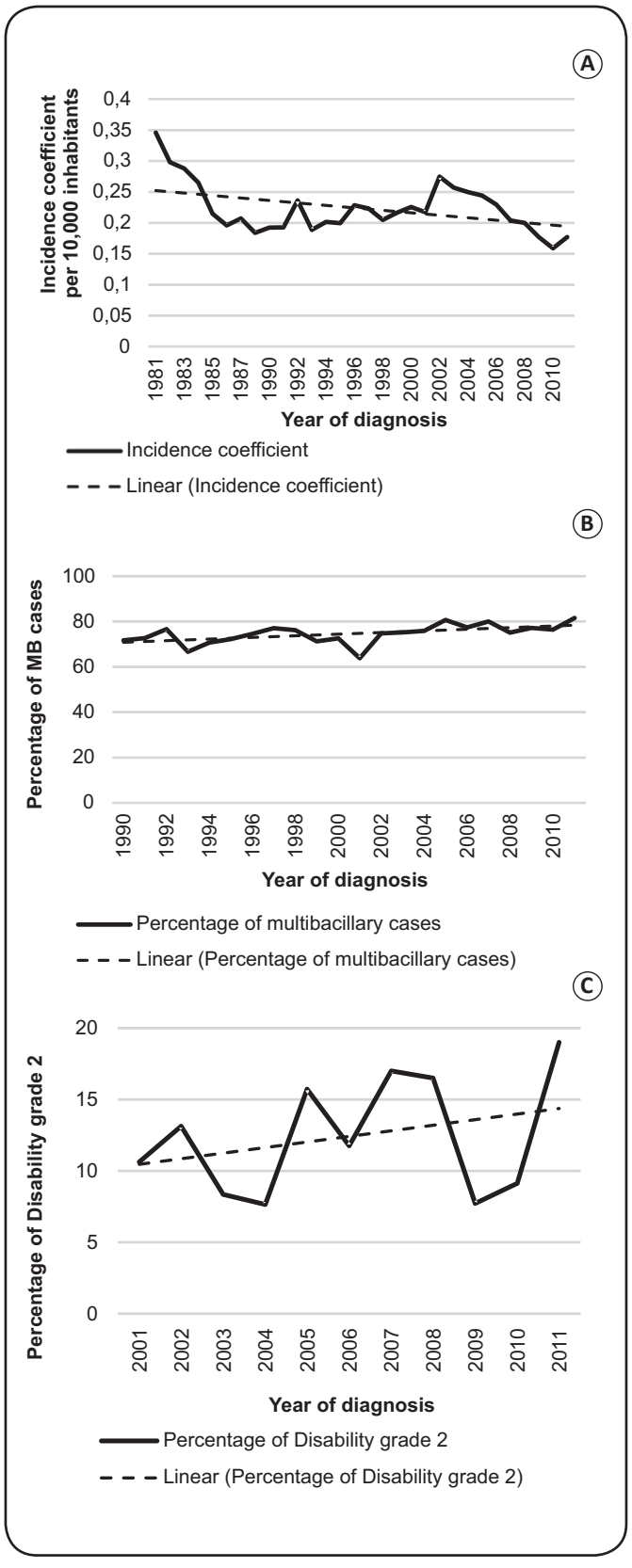

FIGURE 1 – (A) Annual detection rate of new cases of leprosy in RS 1981-2011, with linear trend line. (B) Annual detection percentage of MB cases in RS 1990-2011, with linear trend line. (C) Annual percentage of diagnosis according to the disability grade 2 (2001-2011), with linear trend line. MB: multibacillary.

According to Ministry of Health parameters, a geographical region can be classified as: (A) hyperendemic - 4.00 cases or more/10,000 inhabitants; (B) very high - from 2.00 to 3.99 cases/10,000 inhabitants; (C) high - from 1.00 to 1.99 cases/10,000 inhabitants; (D) intermediate - 0.20 to 0.99 cases/10,000 inhabitants; or (E) low - less than 0.2 cases/10,000 inhabitants[11]. As shown in **Figure 1**, RS has remained classified as low/intermediate endemicity during the past 30 years. The recent slight decrease in the incidence of leprosy in RS compared to the 1980s is likely due to the introduction of multidrug therapy (rifampicin + dapsone + clofazimine) in 1991, which reduced disease transmission through interruption of the transmission chain upon initiation of treatment. Detection rates serve as indicators of leprosy transmissibility in Brazil and, according to WHO, leprosy detection has showed no decline in recent years[1]. Despite this, regional indicators of RS have always remained below the national average.

Leprosy is a chronic, low mortality, and late mortality disease that often goes undiagnosed, especially in low endemicity areas. Additionally, stigma still surrounds a diagnosis of leprosy causing patients to avoid seeking health services for confirmed diagnosis and treatment. Owing to this, estimating the actual magnitude of leprosy is very difficult, given that a low number of new cases and low rate of registration could either mean that the disease is not significant in the area, or that there are operational problems (such as a high number of unreported cases)[12,13]. Therefore, to indirectly assess the real magnitude of the disease, WHO recommends the use of the proportion of MB patients and the proportion of new cases in children younger than 15 years of age as valid epidemiological indicators[12]. New cases of leprosy in children younger than 15 years of age are related to the bacillus transmission chain within the community and the existence of an active transmission focus[14]. Currently, detection rate among the 0-14-year age group is considered, by the Brazilian Ministry of Health, the primary disease control indicator[3]. However, this indicator is most useful for high prevalence areas with high rates of diagnosis in children and adolescents. In low prevalence areas, such as RS, the rate of newly affected children younger than 15 years of age is very low. The same limitation can be applied to the operational classification: high prevalence regions have mainly PB, while in low prevalence areas, the MB forms are more frequently identified[15].

The later diagnosis and greater proportion of MB cases in areas with lower prevalence can also be explained by immunological factors. Approximately 80% of the population is potentially resistant to leprosy and able to develop cell-mediated immunity against the bacillus[12]. However, such capacity is not present at birth but is developed over the years when the infection occurs early. It is therefore common, in endemic areas, to acquire cellular immunity, which occurs at the expense of PB infection. The younger the individual has contact with the disease, the greater the likelihood of developing the PB form, which explains the higher proportion of PB-affected young people in endemic areas[12,14]. As the number of potentially contagious patients in hyperendemic areas is greater, the probability of an individual receiving a sufficiently

high bacterial load able to cause an infection before adulthood is greater in those regions. Consequently, PB forms will often be more commonly diagnosed in these areas. However, in low endemicity areas, individuals are less often exposed to the bacillus, so infection occurs later and thus the proportion of MB cases is higher[12,14]. This phenomenon is even more relevant in the current context where populations are aging and, therefore, may demonstrate impaired immunological responses. Studies have shown that among aged populations, there is also a greater risk of developing leprosy reactions[15], which constitutes the primary cause of physical disabilities in patients with leprosy. Therefore, even in sites with low endemicity, the occurrence of leprosy would have potential socio-economic consequences not only to the individual, but also to families and communities. Issues such as leprosy reaction episodes and physical disabilities may be temporary or become permanent, including restriction of productive activities, which can even occur after completion of treatment. Nevertheless, the manner in which leprosy behaves in response to changes in immunity among older patients must be better evaluated because, in areas such as RS, patterns of leprosy are characterized by aged MB patients[10,12]. Observing these specific profiles among populations from other regions might generate insights to promote specific strategies of prevention and improvement in heath among these populations.

In conclusion, it can be confirmed that RS remains a low endemicity area for leprosy with the disease virtually eliminated. This is exhibited by low detection rates among patients younger than 15 years of age (lower than were recorded in the 1980s) and preponderance of MB cases (according to WHO operational classification) with an upwards trend. However, it is impossible to determine the true prevalence of leprosy using only these indicators because many cases are still underreported or diagnosed late. Considering this, WHO also recommends that the degree of disability at diagnosis is used as an epidemiological indicator to estimate the delay in diagnosis[12]. Thus, there is a growing trend in the diagnosis of cases with a degree of disability equal to 2 (**Figure 1C**), which allows inference that the case has been diagnosed late.

Despite the extremely high detection rates and high prevalence of leprosy in most of Brazil, RS has achieved the goal of eliminating the disease (<1.00/10,000 inhabitants) by reaching a prevalence of 0.16/10,000 in 2009[8]. However, care must be taken in the interpretation of this data because the diagnosis may be occurring late, which increases the potential for transmission. Furthermore, it should be noted that the more prevalent MB form predisposes to increased reactional cases, especially erythema nodosum leprosum (one of the main causes of disability and the most observed reaction in this form of the disease)[13].

Finally, although leprosy is now considered to be eliminated from RS, the data presented highlight the need for intensified control activities, such as searching for active disease with available rapid tests for contacts to improve early diagnosis to avoid reaction outbreaks and subsequent disabilities.

Conflict of interest

The authors declare that there is no conflict of interest.

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