

ORIGINAL ARTICLE

LEPROSY IN BORDER COUNTRIES IN SOUTH AMERICA: AN ECOLOGICAL STUDY

Keurilene Sutil de Oliveira¹, Marcos Augusto Moraes Arcoverde², Enrique Jorge Deschutter³, Alex Junior da Silva⁴, Adriana Zilly⁵, Reinaldo Antonio da Silva Sobrinho⁶

ABSTRACT

Objective: to characterize the epidemiological clinical profile and spatial distribution of the incidence of leprosy in border territories of South America.

Method: this is an ecological study. The study included the Province of Misiones in Argentina and the Southern Region of Brazil. The population consisted of 10,319 new leprosy cases diagnosed between 2010 and 2016.

Results: the state of Paraná was the most endemic, representing 70.2% (n=7.247) of the cases. There was a predominance of multibacillary operational classification (79.8%, n=8,233) and Grade 0 of physical disability (50.6%, n=5,223). In Misiones, 18.9% used a substitution treatment regimen. In the period, a hyperendemic situation was observed in 780 (65.5%) of the studied cities/departments.

Conclusion: the study revealed that the regions studied have high endemicity, active transmission and late diagnosis of leprosy. These intertwined trends in the strength of morbidity and recent and persistent transmission of the disease increase the relevance of leprosy as a public health problem in the region.

DESCRIPTORS: Leprosy; Incidence; Spatial analysis; Border health; Transmissible diseases.

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¹Nurse. Master's degree in Public Health in the Border Region. Nurse in the City Hall of Foz do Iguaçu. Foz do Iguaçu, PR, Brazil. 

²Nurse. Doctor's degree in Public Health. Professor at the Western Paraná State University. Foz do Iguaçu, PR, Brazil. 

³Biochemist. Doctor's degree in Public Health. Director and professor of the subject Public Health and Transmissible Diseases. National University of Misiones. Posadas, Misiones, Argentina. 

⁴Mathematician. Specialist in Methodology of Mathematics and Physics Teaching. Western Paraná State University. Foz do Iguaçu, PR, Brazil. 

⁵Biologist. Doctor's degree in Biological Sciences. Professor at the Western Paraná State University. Foz do Iguaçu, PR, Brazil. 

⁶Nurse. PhD in Public Health. Coordinator and professor of the post-graduation program (Stricto Sensu) in Public Health in the Border Region of the Western Paraná State University. Foz do Iguaçu, PR, Brazil. 

HANSENÍASE EM PAÍSES FRONTEIRIÇOS NA AMÉRICA DO SUL: UM ESTUDO ECOLÓGICO

RESUMO

Objetivo: caracterizar o perfil clínico epidemiológico e a distribuição espacial da incidência da hanseníase em territórios fronteiriços da América do Sul.

Método: trata-se de um estudo ecológico. O estudo compreendeu a Província de Misiones na Argentina e a Região Sul do Brasil. A população foi composta por 10.319 casos novos de hanseníase, diagnosticados entre 2010 e 2016.

Resultados: o estado do Paraná foi o mais endêmico, representando 70,2% (n=7,247) dos casos. Houve predomínio da classificação operacional multibacilar (79,8%, n=8.233) e Grau 0 de incapacidade física (50,6%, n=5.223). Em Misiones 18,9% utilizaram esquema de tratamento substitutivo. No período, notou-se uma situação hiperendêmica em 780 (65,5%) dos municípios/departamentos estudados.

Conclusão: o estudo mostrou que as regiões estudadas apresentam alta endemicidade, transmissão ativa e diagnóstico tardio da hanseníase. Essas tendências entrelaçadas à força de morbidade e de transmissão recente e persistente da doença, ampliam a relevância da hanseníase como problema de saúde pública na região.

DESCRITORES: Hanseníase; Incidência; Análise espacial; Saúde na fronteira; Doenças transmissíveis.

LEPRA EN LOS TERRITORIOS FRONTERIZOS DE SUDAMÉRICA: ESTUDIO ECOLÓGICO

RESUMEN:

Objetivo: caracterizar el perfil clínico epidemiológico y la distribución espacial de la incidencia de la lepra en los territorios fronterizos de Sudamérica.

Metodología: se trata de un estudio ecológico. El estudio incluyó la Provincia de Misiones en Argentina y la Región Sur de Brasil. La población estaba compuesta por 10.319 nuevos casos de lepra diagnosticados entre 2010 y 2016.

Resultados: el estado de Paraná fue el más endémico, representando el 70,2% (n=7.247) de los casos. Predominaron la clasificación operacional multibacilar (79,8%, n=8.233) y el Grado 0 de discapacidad física (50,6%, n=5.223). En Misiones, el 18,9% utilizó un régimen de tratamiento de sustitución. En el periodo se observó una situación hiperendémica en 780 (65,5%) de las ciudades/departamentos estudiados.

Conclusión: El estudio mostró que las regiones estudiadas tienen alta endemicidad, transmisión activa y diagnóstico tardío de la lepra. Estas tendencias entrelazadas en cuanto a la fuerza de la morbilidad y la transmisión reciente y persistente de la enfermedad aumentan la importancia de la lepra como un problema de salud pública en la región.

DESCRIPTORES: Lepra; Incidencia; Análisis Espacial; Salud Fronteriza; Enfermedades Transmisibles.

INTRODUCTION

Mycobacterium leprae is the bacillus that causes chronic infectious disease, called leprosy, which infects macrophages and Schwann cells⁽¹⁾. There are several clinical manifestations, the most prevalent being skin lesions with decreased sensitivity and thickened subcutaneous nerves⁽²⁾.

The entry portal of the bacillus is the upper airway and occurs by direct transmission⁽³⁾, and due to severe permanent physical disabilities, which lead to serious limitations in the performance of daily activities, leprosy is considered a worldwide public health problem⁽⁴⁾.

Leprosy cases in Brazil declined by 26% between 2001 and 2011⁽⁵⁾. In 2014, the prevalence was 1.2/10,000 inhabitants, corresponding to 25,738 cases under treatment. In the same year, Brazil presented a general detection coefficient of new cases of 15.3/100,000 inhabitants, which corresponds to 31,064 new cases of the disease, presenting a classification of high endemicity, according to official parameters⁽⁶⁾. In 2017, the total number of new leprosy cases in Brazil was 22,940, of which 1,718 were in children under 15 years of age, indicating active transmission of the disease⁽⁴⁾.

In Argentina, the number of new leprosy cases in 2010 was 354, rising to 586 cases in 2015. Leprosy is endemic in the provinces of the northwest, northeast and center of the country: Chaco, Formosa, Corrientes, Misiones, Santa Fé, Entre Ríos, Córdoba, Santiago del Estero, Tucumán, Salta, Jujuy, Buenos Aires and Capital Federal⁽⁷⁾.

The distribution of the disease is not uniform in Argentina, in the southern part of the country the reduced notification of new cases seems related to the migration of temporary workers. However, projections indicate a sustained upward trend in the proportions of multibacillary cases (MB) with grade two physical disability. Most cases are concentrated in the north of the country, precisely in territorial spaces near the border with Paraguay and Brazil where the level of endemicity is high. Such aspects demonstrate that there is active bacillary circulation and risk of new cases appearing⁽⁸⁾.

Every year more than 200,000 new leprosy cases are reported worldwide, as a result, the World Health Organization (WHO) has set a goal to stop the transmission of leprosy worldwide by 2020, highlighting the need to measure the disease burden more broadly⁽⁹⁾, including promoting intersectoral partnerships at the international and national levels. Even countries with few patients, such as Argentina, should maintain surveillance and referral services, especially due to migration from countries where leprosy is still endemic⁽¹⁰⁾.

The risk of leprosy transmission and the influence of the epidemiological situation in neighboring regions⁽¹¹⁾ show the importance of spatial analytical studies to identify geographical areas in which specific interventions can be performed for disease control⁽¹²⁾. Specially the border regions, where there is a lack of studies and fragility in monitoring the migration of populations between different countries⁽¹¹⁾.

Based on the above, this study aims to characterize the epidemiological clinical profile and the spatial distribution of leprosy incidence in border territories of South America.

METHOD

This is an epidemiological study of the ecological type. The study included the Province of Misiones in Argentina and Southern Brazil, shown in Figure 1.



Figure 1 - Geographical location of Southern Brazil and the Province of Misiones Argentina. Province of Misiones (AR), Paraná (BR), Santa Catarina (BR), Rio Grande do Sul (BR), 2010 to 2016

Argentina is composed of 23 provinces and the capital city of Buenos Aires is called the autonomous city of Buenos Aires. Each entity has its own constitution, but they coexist in a federal system. The provinces are divided into departments, except the province of Buenos Aires, which is divided into parties⁽¹³⁾.

The Province of Misiones is located in the Northeast Region of the country and is therefore part of one of the leprosy endemic regions. Almost all its territorial limits are comprised of rivers and more than 80% are international borders to the north and east with Brazil, to the west with Paraguay and to the south with the province of Corrientes (Argentina). It is politically organized in 17 departments, divided into 75 municipalities. The total area is approximately 29,801 km², and in 2014 the population was 1,175 million⁽¹⁴⁾.

In this study we used the departments of Misiones as a unit of analysis, because the population of the municipalities was small for comparison with the Brazilian municipalities, and in Argentina, the municipal unit is politically and administratively different from Brazil, which reinforces the use of departments as a unit of analysis in the neighboring country.

The health sector in Argentina is structured based on three main sub-sectors: the public sub-sector with financing and public provision, the mandatory social insurance sub-sector and, finally, the private sub-sector⁽¹⁵⁾.

The Southern Region of Brazil consists of three states: Paraná, Santa Catarina and Rio Grande do Sul. In 2016, Paraná had an estimated population of 11,242,720 million inhabitants living in the 399 municipalities, and its area is approximately 199,307.939 km². Santa Catarina has 295 municipalities and territory of 112,872 km², and its estimated population in 2014 was 6,727 million. The state of Rio Grande do Sul is divided into 497 municipalities, its total area is 281,730.223 km² and the population in 2014 was 11,207 million inhabitants⁽¹⁶⁾.

The study population consisted of 10,319 new leprosy cases (International Statistical Classification of Diseases and Health Related Problems - ICD 10 from A30.0 to A30.9) that were diagnosed in the period from 2010 to 2016 in the three states of southern Brazil and the province of Misiones in Argentina. The period analyzed was chosen because it was the period in which complete data were found for all variables elected for analysis in both countries.

The data search was conducted in the first half of 2018. For the South Region of Brazil, the data were requested by the Electronic System of the Citizen Information Service (e-SIC) provided by the Ministry of Health - Brazil. Regarding the Province of Misiones, the data were obtained through the Ministry of Health of Misiones-Argentina.

For descriptive analysis, the variables gender, operational classification, degree of physical disability and treatment regimen were used. To construct the standardized incidence rate of leprosy per 100,000 inhabitants, we used the variable new cases reported and the resident population by territory. The incidence rate was directly standardized considering age and gender.

In the descriptive analysis, the data were presented in absolute and relative frequency. For the spatial autocorrelation, the Moran Global and Local Index (Local Index of Spatial Association - LISA) was used as a statistical tool. The pattern of distribution of leprosy incidence was examined on a smaller scale by means of the local Moran, producing a specific value for each municipality/department, allowing the visualization of clusters with significant spatial associations. This analysis was performed only in the Brazilian territory due to incompatibility in the union of geographic projection files. For this statistical analysis, the significance value of 5% was considered.

The research followed the ethical precepts of the National Health Council and Helsinki Declaration of the World Medical Association, and all determinations of Resolution 466/2012 by the National Health Council. The study was approved by the health institution and the Ethics Committee for Research involving Human Beings, and the approval number was 2,588,573.

RESULTS

There were 10,319 new cases of leprosy in the Southern Region of Brazil and in the Province of Misiones, Argentina. The state of Paraná was the most endemic, with 7,247 (70.2%) cases registered. Of the total, 6,082 (59%) male cases were identified. There was a predominance of the multibacillary operational classification 8,233 (79.8%) and Grade 0 of physical disability 5,223 (50.6%). However, 468 (4.5%) patients were not evaluated for the degree of physical disability (Table 1).

Table 1 - Distribution of new leprosy cases diagnosed according to gender, operational classification and degree of physical disability. Province of Misiones (AR), Paraná (BR), Santa Catarina (BR), Rio Grande do Sul (BR), 2010 to 2016

		MISIONES		PARANÁ		SANTA CATARINA		RIO GRANDE DO SUL		TOTAL	
		N	%	n	%	n	%	n	%	n	%
GENDER	Female	118	43,7	2916	40,2	640	40,6	563	46	4237	41
	Male	152	56,3	4331	59,8	937	59,4	662	54	6082	59
OPERATIONAL CLASSIFICATION	Paucibacillary	40	14,8	1462	20,2	370	23,5	214	17,5	2086	20,2
	Multibacillary	230	85,2	5785	79,8	1207	76,5	1011	82,5	8233	79,8
DEGREE OF PHYSICAL DISABILITY	Grade 0	155	57,4	3754	51,8	799	50,7	515	42	5223	50,6
	Grade I	103	38,2	2461	34	472	29,9	390	31,8	3426	33,2
	Grade II	12	4,4	810	11,2	193	12,2	187	15,3	1202	11,7
	Not evaluated	-	-	222	3	113	7,2	133	10,9	468	4,5

Regarding the type of treatment, 7,539 (73%) used multidrug therapy (MDT) MB and 2,099 (20.4%) paucibacillary MDT (PB). In the province of Misiones 51 (18.9%) cases used a substitution treatment regimen (Table 2).

Table 2 - Distribution of leprosy cases, according to the treatment regimen. Province of Misiones (AR), Paraná (BR), Santa Catarina (BR), Rio Grande do Sul (BR), 2010 to 2016

		MISSIONES		PARANÁ		SANTA CATARINA		RIO GRANDE DO SUL		TOTAL	
		n	%	n	%	n	%	n	%	n	%
TYPE OF TREATMENT	MDT/PB	27	10	1503	20,8	363	23	206	16,8	2099	20,4
	MDT/MB	192	71,1	5329	73,5	1148	72,8	870	71	7539	73
	ROM	46	17	-	-	-	-	-	-	46	0,4
	DAP	5	1,9	-	-	-	-	-	-	5	0,05
	OSR	-	-	415	5,7	66	4,2	149	12,2	630	6,1

Table Caption: MDT- Multidrug therapy. PB- Paucibacillary. MB- Multibacillary. ROM- Rifampicin/Ofloxacin/Minocycline. DAP - Dapsone. OSR - Other substitutive regimens.

In the period, a hyperendemic situation was observed in 780 (65.5%) of the studied municipalities/departments. Highlighting the state of Paraná, which presented 284 (71.2%) of the municipalities with hyperendemic rates, with the municipalities of Anahy, Rancho Alegre and Ramilândia registering the highest incidence rates of 1395.68, 855.37 and 588.17 cases per 100 thousand inhabitants, respectively. Data from Rio Grande do Sul presented 47 (9.46%) hyperendemic municipalities, the most affected being Sede Nova (192 cases/100 thousand inhabitants), Três Passos (187.72 cases/100 thousand inhabitants) and Rolador (178.45 cases/100 thousand inhabitants) (Figure 2).

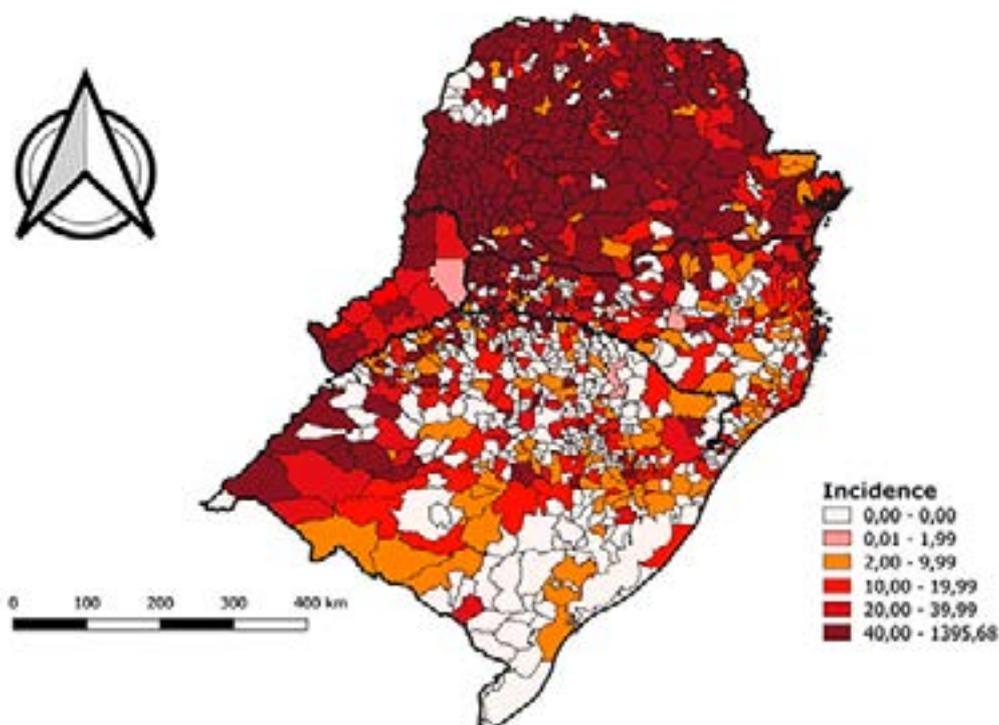


Figure 2- Incidence rate of leprosy per 100,000 inhabitants. Province of Misiones (AR), Paraná (BR), Santa Catarina (BR), Rio Grande do Sul (BR), 2010 to 2016

Note: Classification of incidence rates - low (less than 2.00), medium (2.00 to 9.99), high (10.00 to 19.99), very high (20.00 to 39.99) and hyperendemic situation (greater than or equal to 40.00).

The state of Santa Catarina has evidenced 61 (20.68%) hyperendemic municipalities, the highest rates being in Anchieta (274.88 cases/100 thousand inhabitants), Mondaí (234.26 cases/100 thousand inhabitants), and Dionísio Cerqueira (214.16 cases/100 thousand inhabitants).

The province of Misiones presented seven (41.18%) hyperendemic departments, especially the departments of Eldorado (457.88 cases/100,000 inhabitants), Puerto Iguazú (150.78 cases/100,000 inhabitants), and Posadas (88.75 cases/100,000 inhabitants), which had the highest rates of incidence.

Still regarding Figure 2, we highlight the municipalities where the incidence in the period remained 0 (zero), but which are surrounded or near to municipalities with high rates of incidence, as in RS and SC, or even by hyperendemic municipalities, with this situation being more visible in PR. Brazilian municipalities without leprosy records surrounded by hyperendemic municipalities occur in the three Brazilian states.

As for the spatial analysis, the incidence rate in the southern region of Brazil presented a significant spatial association with the Moran global index $I = 0.3405$ ($p=0.001$). The local detailing of the spatial analysis is verified by LISA, represented in Figure 3.

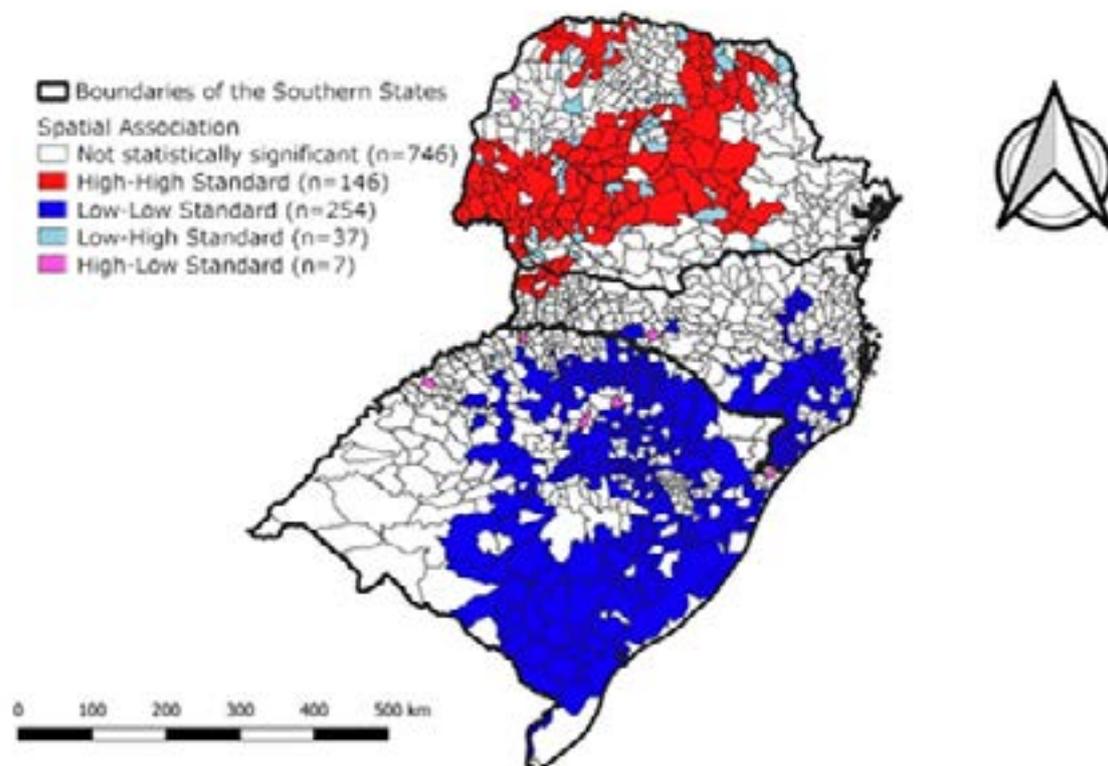


Figure 3 - Local Spatial Association Index (LISA). Province of Misiones (AR), Paraná (BR), Santa Catarina (BR), Rio Grande do Sul (BR), 2010 to 2016.

In Figure 3, the state of Paraná presents high rates of local High-High and Low-High correlation, different from those observed in the other states. The regions highlighted in

red (Upper-Upper) have a high incidence and their neighbors with high values, and the light blue regions (Lower-Upper), present regions with low incidence, but surrounded by regions with high rates.

The state of Santa Catarina has municipalities with a high-high standard near the border region. And a very extensive cluster, with a Low-Low pattern, is verified between municipalities of Santa Catarina and Rio Grande do Sul, that is, municipalities with low incidence located near municipalities with low incidence. However, it is important to highlight some municipalities with a high-low pattern (pink), which means municipalities with high fenced incidence or close to municipalities with low incidence (Figure 3). Even though this is not the pattern pursued by other studies, this association deserves attention when it comes to an epidemiological event with the importance and characteristics of leprosy.

DISCUSSION

As reported in other researches⁽¹⁷⁾, this study also revealed a higher number of cases of leprosy in men, but with little difference between the two genders, as observed by other researchers⁽¹⁸⁻²⁰⁾. Some authors state that greater exposure to risk environments, especially in the workplace, contributes to increasing the number of cases in men and the concern with body aesthetics would justify a large number of female cases⁽²⁰⁻²¹⁾.

In the studied population there was a predominance of multibacillary patients, remembering that it is essential to perform the operational classification of leprosy cases, only then is the treatment form directed by MDT. The classification is based on the number of skin lesions, with PB patients presenting up to five skin lesions with negative intradermal smear microscopy, and MB patients presenting more than five lesions or positive intradermal smear microscopy. Knowing that MB patients constitute the group with the greatest responsibility for transmission, due to the high bacillary load⁽²²⁾, this study shows the severity of the situation in all regions, due to a large number of MB patients.

Among the communicable diseases, leprosy is one of the major causes of peripheral neuropathy and disability in the world⁽²³⁾. It is one of the main causes of avoidable disabilities, responsible for about 3 million disabled people worldwide⁽²⁴⁾.

Physical disabilities in leprosy are related to sequelae and deformities and indicate a late diagnosis. A large part of the population studied presented grade I already at the time of diagnosis, indicating a situation that affects the lives of thousands of people, because it compromises defense mechanisms, such as the ability to feel pain and touch, making them more vulnerable to the risks of accidents, burns, wounds, among others⁽²⁵⁾.

As far as treatment is concerned, since 1940, dapsone has been used alone in the treatment of leprosy and has been for about three decades. However, the prolonged, discontinued and inadequate use of monotherapy with this drug leads to the development of dapsone-resistant cases. The introduction of the use of clofazimine and rifampicin enabled the combined use of the drugs and a better response to the elimination of *Mycobacterium leprae*. Other drugs, such as ofloxacin and minocycline, are also used as alternative drugs if any MDT drug is contraindicated⁽⁹⁾.

This study showed a large percentage of patients who used a substitution treatment regimen, indicating drug intolerance to MDT/WHO drugs, which results in a worrying picture. Patient classification and new therapeutic approaches, including variation in the duration and composition of regimens, have been discussed. Surveillance of this endemic disease is being carried out within an integrated context using clinically relevant indicators, with follow-up of patients after discharge being indispensable for the evaluation of therapeutic results⁽²⁶⁾.

As presented in this article, it is possible to observe many municipalities with low

incidence, surrounded by hyperendemic municipalities, and, despite the trend to eliminate leprosy, these regional disparities ultimately help to maintain the endemic disease. And although, theoretically, leprosy control actions are implemented throughout the network of public health services, one of the difficulties evidenced is the passive detection of cases. There is evidence that, when there is an active search for cases, unexpectedly higher rates of incidence were found, even in well-developed regions⁽⁴⁾.

The socioeconomic inequalities between regions are noted as the main reasons for the high rates of the disease, however, we report a Human Development Index (HDI) of 0.756 in the Southern Region of Brazil and 0.829 in the Province of Misiones. The state of Paraná, listed in the study as the most endemic, is located in the socioeconomic extreme, which is said to be favorable in Brazil, showing the complexity of interaction among the determinants of health⁽²⁷⁾.

It is worth noting that some of the territories examined include a border area, which leads us to an idea of connecting territories and, in order to understand, we must consider the entire territorial whole of both countries. Therefore, it is another territoriality, surpassing the views of subjects, in this case Brazilians and Argentinians, with different identities⁽²⁸⁾ and also the risks related to this constant coexistence between countries, because, besides the risk of migration of sick Brazilians, there may still be contamination of Argentinians in Brazil, and reciprocally, due to exposure to the bacillus. Both the incidence analysis and the spatial association analysis demonstrate risk areas in the border region of Brazil with Argentina.

It is important to highlight that cross-border interactions exceed the economic issue, involving a whole set of material and non-material interactions, from economic-commercial practices to those caused by the lack of public or private services, such as health, which generate constant transits between one side and another of the border⁽²⁸⁾.

Among the limitations of the study, it is important to consider the particular bias of ecological studies, namely: the evidence of the investigation cannot be inferred casuistically for the individual level, being only representative for the populations under study. In addition, the acquisition of information through secondary databases can bring failures concerning the process of investigation/notification or data entry, which are fed directly by municipal health units.

CONCLUSION

The study evidenced that the Southern Region of Brazil and the Province of Misiones in Argentina present high endemicity, active transmission and late diagnosis of leprosy. These trends, intertwined with the force of morbidity and recent and persistent transmission of the disease, including late diagnosis and likely hidden endemic due to the high percentage of multibacillary cases and cases with visible disabilities, increase the relevance of leprosy as a public health problem in the Southern Region of Brazil and the Province of Misiones Argentina.

Given the adverse scenario of borders, we suggest the development of studies in spatial clusters, which include, in addition to the control and surveillance actions established by the Ministries of Health of the countries involved, new active search strategies, campaigns and educational actions aimed at early diagnosis and treatment.

To this end, a debate and differentiated public policy initiatives for border areas are needed to establish an agenda aimed at strengthening active leprosy surveillance. This agenda needs to involve the precepts of ethical, human and supportive care in order to achieve truly desirable results for leprosy control in the world.

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Corresponding author:

Keurilene Sutil de Oliveira

Universidade Estadual do Oeste do Paraná

R. Pompeu de Toledo, 333 - 85858-490 - Foz do Iguaçu, PR, Brasil

E-mail: keurisutil@gmail.com

Role of Authors:

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - KSO, MAMA, AJS

Drafting the work or revising it critically for important intellectual content - KSO, MAMA, JHD, AZ, RAAS

Final approval of the version to be published - KSO, MAMA, JHD, AJS, AZ, RAAS

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - KSO
