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BRIEF COMMUNICATIONS

Leprosy bacilloscopy notifications in the Brazilian Unified Health System and COVID-19 pandemic: an ecological investigation

Notificações de baciloscopia para hanseníase no Sistema Único de Saúde brasileiro e a pandemia de COVID-19: uma investigação ecológica

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Abstract

Objective: to evaluate leprosy bacilloscopy exam notifications in the Brazilian Unified Health System (SUS) from April 2018 to March 2022. **Methods:** an ecological study was carried out using open-access data from the SUS. **Results:** the temporal tendency of leprosy bacilloscopy was considered significantly decrease over time ($p < 0.05$), as well as there was a significant decrease in the first and second pandemic years when compared to the control interval in all Brazilian regions ($p < 0.05$). **Conclusion**: leprosy bacilloscopy exams remain negatively affected by the COVID-19 pandemic in the SUS.

Keywords: Unified Health System; *mycobacterium leprae*; leprosy; COVID-19.

Resumo

Objetivo: avaliar o número de notificações de baciloscopia para hanseníase no Sistema Único de Saúde brasileiro (SUS) de abril de 2018 até março de 2022. **Método**: foi realizado um estudo ecológico com dados de acesso aberto do SUS. **Resultados:** a tendência temporal da baciloscopia da hanseníase foi considerada significativamente decrescente ao longo do tempo ($p < 0.05$), bem como houve uma redução significativa no primeiro e segundo ano de pandemia quando comparado ao intervalo-controle em todas as regiões brasileiras ($p < 0.05$). **Conclusão**: os exames de baciloscopia da hanseníase permanecem afetados negativamente pela pandemia de COVID-19 no SUS.

Palavras-Chave: Sistema Único de Saúde; mycobacterium leprae; hanseníase; COVID-19.

INTRODUCTION

Leprosy can be understood as an infectious and contagious disease triggered by *Mycobacterium leprae* (Hansen's bacillus)[1]. In Public Health, leprosy is considered a Neglected Tropical Disease (NTD), often associated with vulnerability contexts, such as unsatisfactory sanitary conditions and difficulties to access health services[2]. The diagnosis of this disease takes into account clinical signs and symptoms, such as the presence of skin lesions with sensory disturbance (e.g. loss of thermal and painful sensitivity), supported by laboratory complementary exams. For this purpose, leprosy bacilloscopy is a simple and inexpensive microscopic analysis to detect the presence of Hansen's bacilli. This exam is carried out using a skin smear of possibly infected tissues, using the Ziehl-Neelsen technique to identify acid-fast bacillus resistance (AFB). It is important to recognize that bacilloscopy has been a valuable tool for leprosy diagnosis, especially in classifying patients and in the absence of other approaches[1,2].

The leprosy diagnosis and management in Public Health is even more relevant for underdeveloped countries due to the existence of health inequities associated with social, economic, and demographic disparities in accessing health services, such as Brazil. Temporal and spatial analyses have been developed to understand the dynamics of leprosy in this country, identifying priority areas for health actions, aiming at early diagnosis and timely treatment. Despite the efforts, there are hyperendemic areas of leprosy in Brazil, demonstrating the persistence of this disease as a truly public health problem[3,4].

This epidemiological scenario gained a new perspective in 2020: the COVID-19 pandemic. Considering the decrease in health actions to restrict the spread of SARS-CoV-2, especially non-urgent care, the diagnosis and treatment of several health conditions were negatively impacted in health systems, such as leprosy. Regarding this disease, there was a concern about the diagnosis of new cases during the outbreak, as well as access and adherence to treatment. In the opposite direction, there was a recommendation to stop actions related to NTDs by World Health Organization (WHO), such as the active search for new leprosy cases. Hence, in 2020, the decrease in leprosy diagnoses in Brazil was estimated at 41.4%[5,6].

Considering the aforementioned evidence, a question arose: was there a decrease in the number of leprosy bacilloscopy notifications in the Brazilian Unified Health System (SUS) after the COVID-19 pandemic onset? Then, the objective of this study

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was to evaluate the number of leprosy bacilloscopy notifications in the Brazilian Unified Health System, considering the last 48 months. The alternative hypotheses tested were: (H_1) that there was a significant decrease of leprosy bacilloscopy notifications in 2020 (first pandemic year), (H_2) but not in 2021 (second pandemic year) when compared to the pre-pandemic control interval (two years before COVID-19 pandemic onset).

An analytical ecological study was carried out using open-access data available from the Outpatient Information System (SIA) - Department of Informatics of the Brazilian Unified Health System (DATASUS; https://datasus.saude.gov.br/). Considering the type of study, there was no ethical approval requirement under the resolution 510/2016 of the National Health Council - Brazil[7]. Then, there is no reference to participants, and the data refer to a population.

The number of monthly leprosy bacilloscopy notifications (SIA/SUS code #0202080056) from the last 48 months was retrieved, considering the interval between April 2018 and March 2022 (two years before the emergence of the COVID-19 pandemic and two subsequent pandemic years). Regional (North, Northeast, Southeast, South, and Midwest) and national (Brazil) numbers were considered, based on the notifications presented by local health departments, both normalized per 100.000 residents (taking into account the population projections from the Brazilian Institute of Geography and Statistics (IBGE) for each region and Brazil between 2018 and 2022) also retrieved in DATASUS.

PAST software (version 4.3, Oslo, Norway) was used for statistical analysis, adjusting the significance level (p) at 5% ($\alpha = 0.05$) in all comparisons. The median of the number of leprosy bacilloscopy notifications was presented as a central tendency measure, followed by the 95% confidence interval ($CI_{95\%}$) by the bootstrap approach. Assumptions for statistical design were verified by the Durbin-Watson (autocorrelation hypothesis) and Shapiro-Wilk (normality) tests. Then, the temporal tendency was evaluated by the Prais-Winsten regression method to adjust β1 coefficient values and to standardize the approach regarding residual normality, considering the logarithmic transformation (log10) of the dependent variable (monthly notifications of leprosy bacilloscopy per 100.000 residents). The monthly percent change (MPC; %) was estimated using the expression: $[(-1+10^{\beta 1})*100]$, as well as $[(-1+10^{\beta 1(lower)})*100]$ and $[(-1+10^{\beta 1(upper)})*100]$ for MPC $CI_{95\%}$. The β1 lower and upper values were obtained by the expression: [(β1) ± (t-critical value*β1-standard error)][8].

In each period (pre-pandemic as a control interval, first and second year after the COVID-19 pandemic onset) the value of the dependent variable for each region was compared to the national estimate using the Mann-Whitney (U) pairwise test. The comparison of the dependent variable between the control interval and the pandemic years (as a before-and-after COVID-19 assessment) was performed using the Wilcoxon (W) rank-test for all regions (considering the annual seasonality observed in the North, Northeast, and Southeast regions; $p < 0.05$), standardizing the approach. Here, the control interval values were obtained by the classic mean between the period from April 2018 to March 2019, with the interval between April 2019 to March 2020 (monthly ranking of the control datasets with the pandemic years). In addition to the comparison, the median of the difference between the intervals (control interval versus first or second pandemic year) was expressed with $CI_{95\%}$, also by the bootstrap approach.

Figure 1 and Table 1 present the median of monthly leprosy bacilloscopy notifications in the Brazilian Unified Health System per 100.000 residents in each region and Brazil, considering the control interval, first and second pandemic years. In the control interval (pre-pandemic), the North, Northeast, and Midwest regions reported the highest numbers of leprosy bacilloscopy (significantly higher than the national estimate; all $p < 0.05$), as well as Southeast and South, reported the lowest numbers (significantly lower than the national estimate; all $p < 0.05$). This pattern was not affected by the COVID-19 pandemic and was also observed in the first and second pandemic years, maintaining statistical significance in relation to the national estimate.

Figure 1. Median of monthly leprosy bacilloscopy notifications in the Brazilian Unified Health System per 100.000 residents.

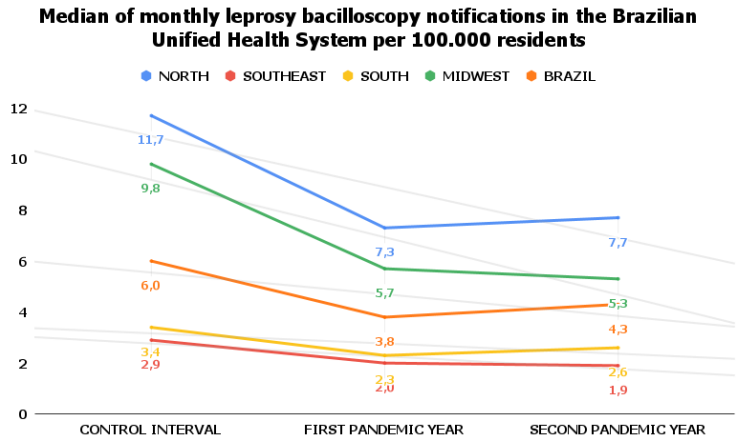

Table 1. Leprosy bacilloscopy notifications in the Brazilian Unified Health System per 100.000 residents.

Variable	Region					
	North	Northeast	Southeast	South	Midwest	Brazil
April 2018 - March 2020 (control interval)						
Median (monthly)	11.7‡	8.85‡	2.90‡	3.40‡	9.75‡	6.00
$CI_{95\%}$	[10.7, 12.7]	[8.50, 9.60]	[2.70, 3.10]	[3.20, 3.55]	[9.40, 11.3]	[5.80, 6.30]
April 2020 - March 2021 (first pandemic year)						
Median (monthly)	7.30‡	5.90‡	1.95‡	2.30‡	5.70‡	3.80
$CI_{95\%}$	[6.75, 8.45]	[5.55, 6.75]	[1.85, 2.25]	[2.20, 2.70]	[3.10, 6.85]	[3.45, 4.45]
Difference (median)	-4.55	-3.00	-1.05	-1.30	-3.80	-2.40
$CI_{95\%}$	[-3.05, -5.60]	[-1.75, -3.65]	[-0.80, -1.65]	[-1.15, -1.45]	[-0.50, -5.30]	[-0.50, -3.00]
Difference (%) (median)	-39.3	-34.3	-37.8	-36.0	-45.5	-38.0
$CI_{95\%}$	[-31.3, -46.2]	[-24.5, -41.6]	[-33.7, -59.3]	[-27.9, -39.5]	[-24.5, -65.1]	[-14.5, -44.2]
p	<.001*	0.001*	0.001*	0.001*	0.002*	<.001*
April 2021 - March 2022 (second pandemic year)						
Median (monthly)	7.65‡	6.95‡	1.85‡	2.55‡	5.25‡	4.30
$CI_{95\%}$	[6.25, 8.70]	[5.95, 7.75]	[1.60, 2.00]	[2.35, 2.85]	[4.75, 6.10]	[4.05, 4.70]
Difference (median)	-3.95	-2.20	-1.10	-1.00	-4.10	-2.00
$CI_{95\%}$	[-2.85, -5.35]	[-1.70, -3.35]	[-1.00, -1.65]	[-0.55, -1.55]	[-2.70, -4.70]	[-0.45, -3.00]
Difference (%) (median)	-37.6	-25.5	-37.2	-32.8	-47.6	-34.4
$C_{l95\%}$	[-34.1, -53.6]	[-20.5, -38.0]	[-32.2, -49.5]	[-27.7, -51.8]	[-43.8, -53.0]	[-17.9, -49.8]
p	<.001*	0.042*	<.001*	0.001*	<.001*	<.001*
Temporal tendency						
MPC (%)	-1.39	-0.96	-1.30	-2.32	-2.50	-2.25
$CI_{95\%}$	[-0.08, -2.69]	[-0.02, -1.89]	[-0.13, -2.46]	[-0.01, -4.58]	[-0.05, -4.89]	[-0.04, -4.42]
p	<.001*	0.036*	<.001*	0.010*	0.002*	0.016*
Tendency	Decreasing	Decreasing	Decreasing	Decresing	Decreasing	Decreasing
R^2	0.553	0.223	0.476	0.123	0.175	0.229

*: significant P-value (<0.05); ‡: significant statistical difference when compared to the national estimate (Brazil; P-value <0.05); MPC: monthly percent change (%); R2: coefficient of determination.

Moreover, as expected, there was a significant decrease in leprosy bacilloscopy notifications in all Brazilian regions per 100.000 residents in the first pandemic year (all p <0.05), accepting H1. However, unexpectedly, there was no recovery of these numbers in the second pandemic year as hypothesized. Then, the decreases observed remained significantly lower when compared to the control interval (all p <0.05), rejecting H_2 in all Brazilian regions.

Table 1 also presents the temporal tendency of leprosy bacilloscopy notifications in the Brazilian Unified Health System per 100.000 residents in the last 48 months, evaluated in each region and in Brazil. Corroborating the results already mentioned, there was a significant and decreasing temporal tendency for this variable in all Brazilian regions, as well as in Brazil (all p <0.05).

The results presented corroborate previous evidence about the leprosy epidemiological scenario in Brazil. The COVID-19 pandemic has significantly affected the diagnosis of leprosy in Brazil. The North, Northeast, and Midwest regions (with the highest numbers of leprosy bacilloscopy in the control

interval, above the national estimate) have significantly higher standardized mortality rates than the South and Southeast regions, considering data from 2008 to 2018 from DATASUS. These outcomes highlight the need to improve leprosy control in these Brazilian regions[9].

Although the dynamics of leprosy are complex, other evidence has already discussed possible components that contribute to the causality of these outcomes in the North, Northeast, and Midwest regions: unfavorable socio-environmental (increased urbanization, worse sanitation condition, and agglomeration of domiciles) and socioeconomic (poor education, food insecurity and low-income) conditions. Moreover, there is evidence that men, blacks, older and who perform manual work may be more affected by the disease[3,10]. It is reasonable to hypothesize that the epidemiological scenario and the characteristics of these regions contribute to the outcome observed here concerning leprosy bacilloscopy as a direct effect.

This evidence raises concerns and hypotheses about how these unfavorable conditions, in addition to impacting mortality-related outcomes, can impact access to health care for leprosy, such as bacilloscopy exams in the Brazilian Unified Health System. Also, what will be the contribution of leprosy bacilloscopy exams decrease (demonstrated here) in future outcomes in leprosy in Brazil? These questions may be further investigated to clarify the state of the art in the future.

Furthermore, the outcomes of this investigation are directly linked to the Brazilian literature on leprosy since the opportunistic and adequate diagnosis of this disease should be a concern in this country. It is important to consider that the stigma and fear associated with leprosy, as well as the lack of knowledge about the signs and symptoms of patients, can result in delayed medical appointments, triggering the late diagnosis of leprosy[11]. Moreover, in addition to late diagnosis, mis- or undiagnosed cases perpetuate the leprosy transmission chain, leading to more severe and disabling cases. Therefore, as recommended by the WHO, it is important to test for the presence of AFB, especially in patients with more than five skin lesions (multibacillary, in whom leprosy bacilloscopy is a valuable tool whenever available), to provide an accurate diagnosis[12,13].

According to a previous investigation, the Northeast and Midwest regions had the highest proportion of misdiagnosis (per 1.000 new cases) between 2003 and 2017[12]. Evaluating data from 2007 to 2015, another previous investigation demonstrated how the number of underreported leprosy cases is an important outcome for understanding late diagnosis in all Brazilian regions, discussing the role of access to health services for the correct and timely diagnosis of this disease. There, the probability of underreporting was higher in regions that perform fewer leprosy diagnoses, such as the South and Southeast (which also performed fewer leprosy bacilloscopy exams in the last 48 months, as demonstrated here)[13].

Nevertheless, after the COVID-19 pandemic onset, there was an increase in the proportion of multibacillary cases in 2020, established at 8.1% for Brazil[6]. However, considering the entire epidemiological scenario, it is possible that this outcome was observed due to the decline in paucibacillary diagnosis, as well as the perspective that multibacillary patients may seek health services more frequently due to the worst health conditions experienced from the disease (more severe and disabling cases), leading to the diagnosis of this patients. In any case, both possibilities reflect weaknesses in leprosy control, reinforcing the need for adequate diagnostic actions5,6 and establishing a link with the outcomes demonstrated here.

In addition, the leprosy bacilloscopy test is not available in all health services for people with leprosy suspicion, which results in the absence of this exam in investigations and reports of this disease in Brazil (which would allow more robust analyses). Moreover, leprosy bacilloscopy can be considered invasive, especially for younger age groups. Recent evidence has sought to clarify which laboratory methods can contribute more assertively to the diagnosis of leprosy, considering the method to collect biological material and the technique of analysis, seeking to overcome these limitations[14,15].

Ultimately, it is possible to conclude that there was a significant decrease in monthly notifications of leprosy bacilloscopy in the Brazilian Unified Health System after the COVID-19 pandemic onset, both in the first and second pandemic years, considering the last 48 months in all Brazilian regions. Future investigations may consider this decrease to assess leprosy-related outcomes in Brazilian Unified Health System, especially related to multibacillary patients. The main limitation of this conclusion, in addition to the ecological approach (in which there is no adjustment of the dependent variable for the characteristics of the individuals), is the possibility of under- or misreporting by the local health departments.

REFERENCES

1. Santos MASD, Mercadante LM, Pegas ES, Kadunc BV. Relationship between bacilloscopy and operational classification of Hansen's disease in patients with reactions. An Bras Dermatol. 2018 May-Jun; 93(3): 454-456. doi: https://doi.org/10.1590/abd1806-4841.20186725.

2. Belotti NCU, Nardi SMT, Paschoal VDA, Montanha JOM, Pedro HDSP, Gazetta CE. Laboratory diagnosis of leprosy: two staining methods from bacilloscopy and rapid ml flow test. Int J Mycobacteriol. 2021 Oct-Dec; 10(4): 393-397. doi: https://doi.org/10.4103/ijmy.ijmy_206_21.

3. Silva CLM, Fonseca SC, Kawa H, Palmer DOQ. Spatial distribution of leprosy in Brazil: a literature review. Rev Soc Bras Med Trop. 2017 Jul-Aug; 50(4): 439-449. doi: https://doi.org/10.1590/0037-8682-0170-2016.

4. Barbosa CC, Bonfim CVD, Brito CMG, Souza WV, Melo MFO, Medeiros ZM. Spatial analysis of epidemiological and quality indicators of health services for leprosy in hyperendemic areas in Northeastern Brazil. Rev Inst Med Trop S Paulo. 2020; 62: e93. doi: https://doi.org/10.1590/s1678-9946202062093.

5. Matos TS, do Nascimento VA, do Carmo RF, Fernandes TRMO, de Souza CDF, da Silva TFA. Impact of the COVID-19 pandemic on the diagnosis of new leprosy cases in Northeastern Brazil, 2020. Int J Dermatol. 2021 Aug; 60(8): 1003-1006.

doi: https://doi.org/10.1111/ijd.15705.

6. Paz WS, Souza MDR, Tavares DDS, Jesus AR, Santos AD, Carmo RF, et al. Impact of the COVID-19 pandemic on the diagnosis of leprosy in Brazil: an ecological and population-based study. Lancet Reg Health Am. 2022 May; 9: 100181. doi: https://doi.org/10.1016%2Fj.lana.2021.100181.

7. Brazil. Resolution n. 510 - April 7 2016 [Internet]. Dispõe sobre as normas aplicáveis a pesquisas em ciências humanas e sociais. Diário Oficial da União, Brasília (2016 may. 24); Sec. 1:44.

8. Antunes JLF, Cardoso MRA. Using time series analysis in epidemiological studies. Epidemiol Serv Saude. 2015 Jul-Sep; 24(3): 565-576. doi: https://doi.org/10.5123/S1679-49742015000300024.

9. Miguel CB, da Mota PB, Afonso BO, Agostinho F, Cazzaniga RA, de Abreu MCM, et al. Leprosy morbidity and mortality in Brazil: 2008-2018. Braz J Infect Dis. 2021 Nov-Dec; 25(6):101638. doi: https://doi.org/10.1016/j.bjid.2021.101638.

10. Pescarini JM, Strina A, Nery JS, Skalinski LM, Andrade KVF, Penna MLF, et al. Socioeconomic risk markers of leprosy in high-burden countries: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2018 Jul; 12(7): e0006622. doi: https://doi.org/10.1371/journal.pntd.0006622.

11. Henry M, GalAn N, Teasdale K, Prado R, Amar H, Rays MS, et al. Factors contributing to the delay in diagnosis and continued transmission of leprosy in Brazil – an explorative, quantitative, questionnaire based study. PLoS Negl Trop Dis. 2016 Mar; 10(3): e0004542. doi: https://doi.org/10.1371%2Fjournal.pntd.0004542.

12. Neves KVRN, Nobre ML, Machado LMG, Steinmann P, Ignotti E. Misdiagnosis of leprosy in Brazil in the period 2003-2017: spatial pattern and associated factors. Acta Trop. 2021 Mar; 215:105791. doi: https://doi.org/10.1016/j.actatropica.2020.105791.

13. Oliveira GL, Oliveira JF, Pescarini JM, Andrade RFS, Nery JS, Ichihara MY, et al. Estimating underreporting of leprosy in Brazil using a Bayesian approach. PLoS Negl Trop Dis. 2021 Aug;15(8): e0009700. https://doi.org/10.1371%2Fjournal.pntd.0009700.

14. Moraes PC, Eidt LM, Koehler A, Pagani DM, Scroferneker ML. Epidemiological characteristics and trends of leprosy in children and adolescents under 15 years old in a low-endemic State in Southern Brazil. Rev Inst Med Trop Sao Paulo. 2021 Dec; 63: e80. doi: https://doi.org/10.1590%2FS1678-9946202163080.

15. Torres RT, Fachi MM, Böger B, Marson BM, Ferreira VL, Pontarolo R, et al. Sensitivity and specificity of multibacillary and paucibacillary leprosy laboratory tests: a systematic review and meta-analysis. Diagn Microbiol Infect Dis. 2021 Jun; 100(2): 115337. doi: https://doi.org/10.1016/j.diagmicrobio.2021.115337.

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