



Epidemiological profile of leptospirosis in Brazil from 2018 to 2023

Perfil epidemiológico da leptospirose no Brasil de 2018 a 2023
Perfil epidemiológico de la leptospirosis en Brasil de 2018 a 2023

Site doi: <https://doi.org/10.17058/reci.v15i3.20097>

Submitted: 12/12/2024

Accepted: 07/24/2025

Available online: 11/02/2025

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ABSTRACT

Background and Objectives: Leptospirosis is caused by the bacterium *Leptospira*, which is transmitted in rainy weather. The disease has different manifestations depending on how it develops, and can lead to death. Early detection can prevent serious developments, but there is limited information and standardization of the most affected profile. The objective of this study was to identify the epidemiological profile of leptospirosis from 2018 to 2023 in Brazil. **Methods:** a quantitative study, ecological, with secondary data collection from the Notifiable Diseases Information System (SINAN) and the SUS Hospital Admissions System, using Tabnet/DATASUS, using the following variables: gender, age group, race, schooling, disease progression, years and region of notification. **Results:** there were 16,866 notifications and 1,586 deaths from leptospirosis in Brazil in the period analyzed, with 56.03% of cases progressing to hospitalization and 9.40% to death. The profile most affected was male, aged between 20 and 59, brown, with completed high school. Incidence and mortality rates prevailed in the South, but the fatality rate was higher in the Northeast. **Conclusion:** Although more than half of leptospirosis cases progress to hospitalization, patients have more than an 80% chance of cure. Therefore, this study helped in the more current recognition of leptospirosis cases, in order to contribute to policies to prevent and control the disease.

Keywords: Health Profile. Epidemiology. Leptospirosis. Deaths. Brazil.

RESUMO

Justificativa e Objetivos: A leptospirose é causada pela bactéria *Leptospira*, que possui transmissão associada e intensificada por climas chuvosos. A doença apresenta diferentes manifestações a depender da evolução, podendo levar ao óbito do portador. A detecção precoce pode prevenir evoluções graves, porém há limitações de informações e padronização do perfil mais acometido. O objetivo deste estudo foi identificar o perfil epidemiológico da leptospirose de 2018 a 2023 no Brasil. **Métodos:** estudo quantitativo, ecológico, com coleta de dados secundários no Sistema de Informação de Agravos de Notificação (SINAN) e no Sistema de Internações Hospitalares do SUS (SIH/SUS), por meio do Tabnet/DATASUS, utilizando-se as variáveis: sexo, faixa etária, raça, escolaridade, evolução, anos e região de notificação. **Resultados:** ocorreram 16.866 notificações e 1.586 mortes por leptospirose no Brasil no período analisado, com evolução para internação em 56,03% dos casos e óbitos em 9,40%. O perfil mais afetado foi pacientes do sexo masculino, de 20 a 59 anos, pardos, com ensino médio completo. As taxas de incidência e mortalidade prevaleceram no Sul, porém a taxa de letalidade foi maior no Nordeste. **Conclusão:** Apesar de mais da metade dos casos de leptospirose evoluírem para internação, os pacientes apresentam mais de 80% de probabilidade de cura. Portanto, este estudo auxiliou no reconhecimento mais atual dos casos de leptospirose, a fim de contribuir com políticas de prevenção e controle da doença.

Descritores: Perfil de Saúde. Epidemiologia. Leptospirose. Morte. Brasil.

RESUMEN

Justificación y Objetivos: La leptospirosis es causada por la bacteria *Leptospira*, que tiene asociada una transmisión que se intensifica en climas lluviosos. La enfermedad tiene distintas manifestaciones según su evolución y puede conducir a la muerte. La detección precoz puede evitar una evolución grave, pero la información y la normalización del perfil más afectado son limitadas. El objetivo de este estudio fue identificar el perfil epidemiológico de la leptospirosis de 2018 a 2023 en Brasil. **Métodos:** estudio cuantitativo, ecológico, con recolección de datos secundarios del Sistema de Información de Enfermedades de Declaración Obligatoria (SINAN) y del Sistema de Internación Hospitalaria del SUS, utilizando Tabnet/DATASUS, con las siguientes variables: sexo, grupo de edad, raza, escolaridad, evolución, años y región de notificación. **Resultados:** Hubo 16.866 notificaciones y 1.586 muertes por leptospirosis en Brasil durante el período analizado, con 56,03% de los casos evolucionando a hospitalización y 9,40% a muerte. El perfil más afectado fue hombres, de entre 20 y 59 años, morenos, con estudios secundarios completos. Las tasas de incidencia y mortalidad prevalecieron en el Sur, pero la tasa de mortalidad fue mayor en el Noreste. **Conclusión:** Aunque más de la mitad de los casos de leptospirosis requieren hospitalización, los pacientes tienen más del 80% de posibilidades de curarse. Por lo tanto, este estudio ayudó a reconocer los casos de leptospirosis de forma más actualizada, con el fin de contribuir a las políticas de prevención y control de la enfermedad.

Palabras Clave: Perfil de Salud. Epidemiología. Leptospirosis. Muertes. Brasil.

INTRODUCTION

Leptospirosis is a zoonosis with a global distribution and is endemic throughout Brazil.¹ Caused by the bacterium *Leptospira*, the disease is typically transmitted through direct contact with the mucous membranes or broken skin of humans, who are accidental hosts, or indirectly through water or food contaminated with the urine of rodents infected with the microorganism.² Studies indicate that the incidence of infection is strongly associated with tropical and subtropical climates, due to frequent rainy periods that favor the transmission cycle. Brazil is particularly prone to the development of the disease, especially in regions with high rainfall and densely populated urban centers characterized by poor social, environmental, and sanitary conditions.^{3,4}

Recent studies estimate the occurrence of approximately 1.03 million new cases and 58,900 deaths from leptospirosis each year worldwide. Despite these alarming figures, leptospirosis remains a neglected disease of major global importance.⁵ In Brazil, between 2016 and 2019, an average of 3,926 cases were reported annually, with a fatality rate of 8.9%. The high incidence results in significant public health expenditures, including hospital costs and productivity losses due to workers' absences, thereby affecting individual and household incomes.⁶

The clinical presentation of the disease is variable, ranging from asymptomatic or subclinical forms to severe cases that may result in death. The Brazilian Ministry of Health reported that the overall case fatality rate for leptospirosis is approximately 9%, rising to over 50% in cases that progress to pulmonary hemorrhage.⁷

Furthermore, several complications may occur, including electrolyte imbalances, pancreatitis, anemia, aseptic meningitis, myocarditis, acute respiratory failure, neurological disorders, vascular lesions, and acute renal failure, which, in advanced stages, can lead to acute tubular necrosis.^{5,7}

Leptospira comprises hundreds of infectious serovars, each with distinct pathogenicity. Consequently, symptom severity may vary depending on the infecting serovar, with some strains causing more aggressive disease manifestations.⁸ Recent studies have shown that the serovars Icterohaemorrhagiae, Copenhageni, Canicola, and Pomona are the most prevalent in Brazil, with the first two being most commonly associated with severe clinical outcomes.⁹

The progression of the disease is commonly associated with late diagnosis and inadequate treatment, causing the condition to worsen rapidly.¹⁰ Therefore, early and accurate detection can prevent deaths from leptospirosis.¹¹ Management is not always correct due to limited information or lack of standardization of clinical investigation.¹²

Leptospirosis is known to be an occupational disease, very common among workers in cattle, rice, sugarcane, sewage, and other at-risk groups, all of whom perform activities in highly humid environments that favor the transmission of the pathogen.¹³ However, there is currently no predictive or scoring model that indicates which patients are most likely to develop the severe form.⁵ To assist in identifying the most susceptible individuals during clinical diagnosis and identify the regions with the greatest need for more effective prevention and control measures, new, updated studies addressing this topic at the national level are necessary, as these are fundamental for public health management in Brazil. Targeted searches of the PubMed and SciELO databases were conducted in May 2025, using the descriptors "leptospirosis," "epidemiology," "Brazil," and "profile," filtered for the period 2018–2023. The search yielded 14 studies, none of which addressed the national context, demonstrating the need for further study on this topic.

Given the lack of recent research on the most affected regions and population groups, this study aims to identify the epidemiological profile of leptospirosis from 2018 to 2023 in Brazil.

METHODS

This is a quantitative, ecological study, collecting secondary data on the epidemiological profile of leptospirosis in Brazil from 2018 to 2023. Data were collected from the Notifiable Diseases Information System (SINAN) and the SUS Hospital Admissions System (SIH/SUS), managed by the Health Surveillance Secretariat in conjunction with state and municipal health departments. These data are available on the website of the Unified Health System Information Technology Department (DATASUS), accessed on August 6, 2024.

The study population comprises all reported cases and hospitalizations for leptospirosis during the period and throughout the country analyzed.

Data collection used the variables sex, age group, race, education level, progression, years, and region of notification, which were extracted from SINAN, and the variables region and year of care, which were extracted from SIH/SUS. Reported cases were used in the SINAN database, and hospitalizations for icterohemorrhagic leptospirosis, other forms of leptospirosis, and unspecified leptospirosis were used in the SIH/SUS database. The inclusion criteria were all reported cases of leptospirosis in the SINAN database and all hospitalizations for icterohemorrhagic leptospirosis, other forms of leptospirosis, and unspecified leptospirosis in the SIH/SUS database. There were no exclusion criteria.

Subsequently, a descriptive statistical analysis of the variables was performed using Microsoft Excel® (version 2504), presented as proportions and absolute numbers in the results. The indicators calculated and presented were incidence, incidence rate, mortality rate, and case-fatality rate. Furthermore, the denominator used to calculate the rates was the population from the 2022 census, conducted by the Brazilian Institute of Geography and Statistics (IBGE). No association or significance tests were used, as this is a descriptive study.

Because the study was conducted using secondary, public domain data sources, with the individuals' identities protected, submission to the Research Ethics Committee was not required, in accordance with Resolution No. 510/2016 of the National Health Council.

RESULTS

A total of 16,866 cases of leptospirosis were recorded in Brazil during the analyzed period. The South and Southeast regions had the highest number of cases in total, with 5,516 and 5,387 cases, respectively, followed, in decreasing order, by the Northeast (3,348), North (2,263) and Central-West, with 352 (Figure 1).

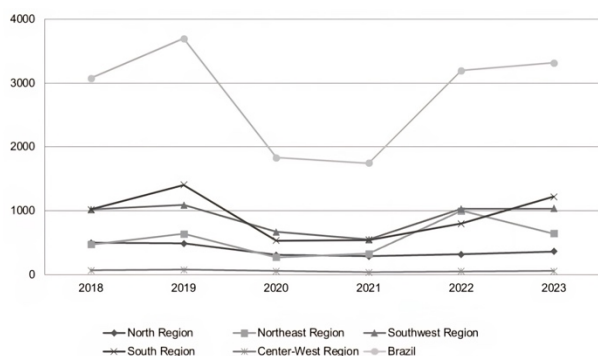


Figure 1. Leptospirosis cases by region and year of notification, Brazil, 2018-2023.

The regions that presented the highest incidence rates of leptospirosis per 100,000 inhabitants, in the period analyzed, were the South (18.42) and North (13.03), with the Central-West being the region that presented the lowest rate (2.16) (Table 1).

Table 1. Incidence rate of leptospirosis per 100,000 inhabitants from 2018 to 2023.

Incidence per 100,000 inhabitants	
Country	
Brazil	8.30
Regions	
North	13.03
Northeast	6.12
Southeast	6.34
South	18.42
Central-west	2.16

The highest number of cases occurred in 2019, with 3,698 cases, and in 2023, with 3,318. The lowest number occurred in 2021, with 1,744 cases. Despite the reduction in cases at the beginning of the years studied, there was an increase in cases in 2022 and 2023 (Figure 2).

There were 11,466 hospitalizations due to leptospirosis in Brazil during the period analyzed, suggesting that 67.98% of cases likely progressed to hospitalization, although the percentage is uncertain due to data being taken from different databases and possibly inconsistent in some records. The South and Southeast regions had the highest total hospitalizations, with 3,981 and 3,318, respectively, followed, in descending order, by the Northeast (2,731), North (1,263), and Central-West (173). The highest number of hospitalizations occurred in 2019, with 2,666, and the lowest in 2021, with 1,159 (Figure 2).

Regarding disease progression, 80.03% of cases were cured and 9.40% resulted in death from the reported condition (Table 4). The Southeast and Northeast regions had the highest number of deaths from the disease in total, with 665 and 438 deaths, respectively, followed, in decreasing order, by the South (304), North (150) and Central-West, with 29. The highest number of deaths from the reported disease occurred in 2019, with 325 deaths and 2022, with 320. The lowest number occurred in 2021, with 181 deaths (Figure 2).

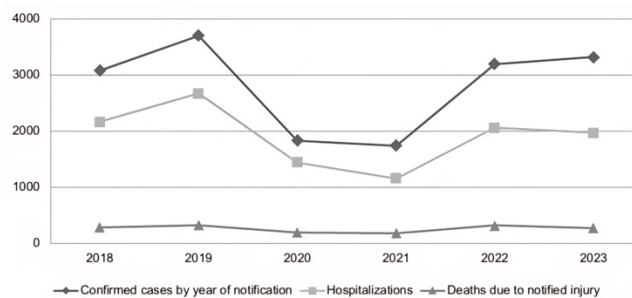


Figure 2. Leptospirosis cases, hospitalizations, and deaths by year of notification, Brazil, 2018-2023.

The regions that presented the highest mortality rates due to leptospirosis per 1,000,000 inhabitants, in the period analyzed, were the South (10.15) and North (8.64), with the Central-West region presenting the lowest rate (1.78) (Table 2).

Table 2. Leptospirosis mortality rate per 1,000,000 inhabitants from 2018 to 2023.

Deaths per 1,000,000 inhabitants	
Country	
Brazil	7.80
Regions	
North	8.64
Northeast	8.01
Southeast	7.83
South	10.15
Central-west	1.78

The regions with the highest fatality rates for leptospirosis in Brazil were the Northeast and Southeast, with 13.08% and 12.34%, respectively, while the South region had the lowest rate, with 5.51% (Table 3). The highest fatality rate occurred in 2020 (10.58%) and the lowest in 2023 (8.31%).

Table 3. Leptospirosis fatality rate from 2018 to 2023.

	Fatality rate
Country	
Brazil	9.40%
Regions	
North	6.62%
Northeast	13.08%
Southeast	12.34%
South	5.51%
Central-west	8.23%

Cases were more frequent in males, with 13,846 cases (82.09%), in the age group of 20 to 39 years, with 6,391 notifications (37.89%) and in individuals of mixed race, with 7,160 cases (42.45%). Although most notifications of leptospirosis ignored or left blank the field of education of the patients, it was noted that, when this variable was informed, patients with complete secondary education were the most affected, with 2,363 cases (14.01%) (Table 1).

Table 4. Demographic profile of confirmed cases of leptospirosis in Brazil, 2018-2023 (n=16.866).

	N (%)
Gender	
Ignored	1 (0.01)
Female	3.019 (17.90)
Male	13.846 (82.09)
Age range	
Blank/Ignored	2 (0.01)
<1 year	101 (0.60)
1-4 years	67 (0.40)
5-9 years	279 (1.65)
10-14 years	613 (3.63)
15-19 years	1.234 (7.32)
20-39 years	6.391 (37.89)
40-59 years	6.061 (35.94)
60-64 years	949 (5.63)
65-69 years	560 (3.32)
70-79 years	505 (2.99)
>80 years	104 (0.62)
Race	
Indigenous	69 (0.41)
Yellow	101 (0.60)
Black	1.074 (6.37)
Ignored/White	1.489 (8.83)
White	6.973 (41.34)
Brown	7.160 (42.45)
Education	
Unknown/Blank	7.226 (42.84)
Illiterate	180 (1.07)
Incomplete 1 st to 4 th grade of elementary school	1.130 (6.70)
Complete 4 th grade of elementary school	688 (4.08)
5 th to 8 th grade of elementary school	1.988 (11.79)
Complete elementary school	1.168 (6.93)
Incomplete high school	1.148 (6.81)
Complete high school	2.363 (14.01)

	N (%)
Incomplete higher education	215 (1.27)
Complete higher education	491 (2.91)
Not applicable	269 (1.59)
Outcome	
Unknown/Blank	1.581 (9.37)
Cure	13.498 (80.03)
Death due to the notified cause	1.586 (9.40)
Death due to another cause	201 (1.20)

DISCUSSION

Leptospirosis is considered the most widespread zoonotic disease worldwide.¹⁵ According to studies analyzing leptospirosis prevalence data, Brazil ranks third among countries in the Americas.¹⁶ However, this study examined incident cases of the disease reported in the Notifiable Diseases Information System (SINAN), which revealed the presence of leptospirosis in all Brazilian regions, although in varying proportions.

It is important to note that data on leptospirosis-related deaths were obtained from SINAN, not from the Mortality Information System (SIM), as the focus of this study was specifically on the outcome variable, not solely on deaths. In other words, we analyzed the number of incident cases, the number of recovered cases, deaths from the notified disease, and deaths from other causes.

Leptospirosis was initially described in rural environments; however, with globalization, it has become increasingly common in urban areas—particularly in less developed nations with low socioeconomic conditions and inadequate sanitation.¹⁶ In this context, understanding the spatial distribution of leptospirosis is crucial for the effective planning of preventive measures.

The incidence of infection is strongly associated with tropical and subtropical climates, as well as regions with high rainfall.¹⁶ The tropical climate predominates in the Southeast and Central-West regions, while the subtropical climate occurs mainly in the South of Brazil.¹⁷ When considering incidence rates per 100,000 inhabitants, this study observed that the South region presented the highest rate in the country, followed by the North and Southeast regions—consistent with the association between the infection and areas of high rainfall. However, a divergence was identified in the Central-West region, which had the lowest incidence rate among all regions. This contrasts with expectations for a predominantly tropical region, given its climatic association with the disease. This lower-than-expected reporting pattern may indicate an actual reduction in cases due to lower population density, reporting delays, underreporting, or clinical similarities with other diseases that lead to underdiagnosis.¹⁸

A study analyzing the prevalence of leptospirosis in the Americas found a higher concentration of cases in

countries with tropical and subtropical climates, such as Colombia and Brazil, with prevalence rates of 29% and 21%, respectively.¹³ Although these data cannot be directly compared to the findings of the present study—which focuses on the incidence of reported cases—they align in showing a greater occurrence of leptospirosis in hot and humid regions. Nevertheless, it is important to emphasize that each country exhibits distinct epidemiological characteristics related to the disease's behavior. For instance, a study revealed differences in seasonal patterns between São Paulo, where hospitalizations due to leptospirosis were seasonal and peaked during the rainy season, and Colombia, which showed no seasonality despite having a bimodal precipitation regime across most of its territory.¹⁹

Similarly, a study analyzing the spatial and temporal incidence of leptospirosis in northeastern Argentina found that warmer, more humid climates were most frequently associated with the disease. In Argentina, leptospirosis is seasonal, with the highest number of cases and outbreaks recorded during warmer seasons with moderate temperatures, and flooding events emerging as the main risk factor.¹² Therefore, understanding both the similarities and differences in leptospirosis patterns across regions is essential to correctly identify risk factors and the epidemiological profile for each location, enabling more targeted and effective preventive measures.

Regarding the temporal evolution of leptospirosis cases, one study found that climate change—driven by rising global surface temperatures—poses a major challenge to public health, contributing to the emergence and reemergence of many communicable diseases, including waterborne diseases such as leptospirosis. In this context, the present study showed a considerable increase in leptospirosis cases in Brazil between 2018 and 2023, except in 2020 and 2021, when the numbers declined compared to previous years. Thus, the increasing incidence of leptospirosis in Brazil from 2018 to 2023 is a reality. However, establishing a causal relationship with climate change would require the analysis of specific environmental data, which was beyond the scope of this study.²⁰

This study also demonstrated that approximately 68% of reported leptospirosis cases with monitored outcomes progressed to hospitalization, highlighting the high hospital morbidity associated with the disease in Brazil.

A comparison with a study that analyzed leptospirosis in Brazil and Alagoas between 2009 and 2019 revealed cure and mortality rates similar to those found in the present study (2018–2023): approximately 83.1% of patients recovered, while 8.6% died from the disease.²¹ These findings suggest a possible pattern of stability in cure and mortality rates over time. Another study from 2005 reported an average case fatality rate of 12% in Brazil, a value close to that observed in the regions with

the highest fatality rates in the current study.²² Together, these observations indicate a relative stability in the cure and mortality rates of leptospirosis over the years, suggesting that despite regional variations, there is a temporal trend toward homogeneity between the most affected regions and the country as a whole.

Comparing the epidemiological profile of leptospirosis cases in Brazil with a previous study covering the years 2007 to 2015, sex and age criteria were evaluated. Regarding sex, in the 2007 to 2015 study, men were more affected by human leptospirosis than women, with the most affected age group being 20 to 59 years old. This data remained unchanged for the period evaluated in this study (2018–2023).²³

The age group affected is directly related to individuals of working age, with this disease having a strong association with occupational activities, especially in the agricultural sector and waste collection and separation, which can lead to economic losses for the country.²⁴ The greater incidence among males is due to their greater propensity and vulnerability to acquiring diseases due to their greater exposure to risk factors, whether environmental, behavioral, or cultural. Associated with this, they often do not seek health services until the disease worsens.²⁵

Other variables that can be compared between the two studies are the categories of race/ethnicity and education. In a study that addressed leptospirosis as a doubly neglected disease in Brazil, Martins identified that between 2007 and 2015, the most prevalent color/race in leptospirosis cases were, in decreasing order of number of cases: white, brown, black, yellow and indigenous, while the classification of education of the most affected individuals, in decreasing order, by leptospirosis, were cases in which education was ignored, incomplete 5th to 8th grade, and complete high school. The two educational levels with the lowest number of leptospirosis cases were complete higher education and incomplete higher education.²³

Compared to the present study, the only change observed in the color/race item was the inversion of white for brown, so that the latter became the predominant color among leptospirosis cases.²³ The variation in the disease incidence among brown individuals is also due to the increase in the number of cases, especially in the Central-West region, where this race predominates.²⁶ Regarding educational level, when comparing the profile from 2007 to 2015, it was found that the three previously mentioned categories remain the most prevalent in the population profile of leptospirosis. However, only an inversion was observed among individuals who had incomplete 5th to 8th grades and completed high school.²³ This can be interpreted as an improvement in the evolution of educational development in Brazil, reflecting the data indicated in

The country's education levels.²⁷ The education levels with the lowest number of cases remained the same.

Based on these analyses, it can be seen that there were no significant changes in the epidemiological profile of leptospirosis between 2007 and 2015 and 2018 and 2023. Therefore, according to the results of this study, the people most affected by this disease are men, aged between 20 and 59, of mixed race, and with less education.²³ The limited variation in this profile allows for the continuation of prevention efforts without the need for major changes in planning in the most affected areas. Furthermore, it facilitates the development of control measures in regions that have seen an increase in cases compared to previous years.

However, it is important to emphasize that this study has certain limitations. The first is that it is an ecological study, therefore not suitable for identifying cause-and-effect relationships. Other limitations include possible underreporting, as data were collected only from DATASUS. Therefore, not considering information about supplementary services, including health plans, insurance, and private services, may reduce the true number of leptospirosis cases. It is worth noting that potential errors were avoided through careful analysis of the information generated in tables by DATASUS, allowing more than one participating member to make observations and checks to avoid potential biases. Furthermore, the SIH only records SUS hospitalizations, meaning the number of hospitalizations may be even higher than reported in the system. Finally, we used the 2022 demographic census conducted by IBGE as the denominator for calculating leptospirosis incidence and mortality rates. However, the analysis covered the period from 2018 to 2023, so the population in other years is not necessarily the same as in the 2022 census.²⁷

According to the results obtained in the study, it is concluded that the epidemiological profile of leptospirosis cases in Brazil, during the analyzed period, was male patients, aged between 20 and 59 years old, of mixed race, and with a high school diploma. The incidence and mortality rates prevailed in the South and North, but the fatality rate was higher in the Northeast and Southeast. Although leptospirosis has an incidence of 8.30 per 100,000 inhabitants, its fatality rate is only 7.30 per 1,000,000 inhabitants, demonstrating a high cure rate among those affected. Because leptospirosis is more prevalent in certain climatic and socioeconomic conditions, the studies presented demonstrate that it follows a specific pattern of affected patients and regional distribution over time in Brazil. This suggests that it will likely continue this trend in the coming years. Therefore, further studies analyzing the distribution of leptospirosis and its relationship with climate factors are necessary to continually update information about this disease in the country and thus

enable the development of effective measures to contain it.

Therefore, despite its limitations, it is believed that this study helped identify individuals most susceptible to the disease and identify the regions with the highest cases and morbidity and mortality outcomes, contributing to more multidisciplinary public policies for disease prevention and control, as well as health education strategies for the national population.

Although the data were collected in DATASUS, a platform that gathers information on a wide range of diseases and procedures performed in the country, the literature indicates deficiencies in the quantity, accuracy, and integration of the data. A study evaluated and compiled the limitations of using DATASUS as a data source in research and found that there are absences of clinical and individual information that are not collected from patients or entered into the platform, a reliance on filling out forms in hospitals, and underreporting due to the lack of data from private resources or regional coverage limitations due to differences in population densities and access to the health system, in addition to the period of the Covid-19 pandemic, which may have reduced the number of reported cases in 2020 and 2021.

However, DATASUS is an important tool for data collection in ecological quantitative research, as it integrates data at the national level, gathers information from various databases, and is widely used for calculating indicators, population trends, disease distribution, and planning for the country's public health policies.

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AUTHORS' CONTRIBUTIONS

Lucas Charuri de Andrade Castello Branco contributed to the abstract, methodology, interpretation and description of results, conclusions, review, and statistics. **Barbara Zorzi Sanfins** contributed to the abstract, methodology, interpretation and description of results, conclusions, review, and statistics. **Fernanda Emanoeli Souza** contributed to the bibliographic research, abstract writing, introduction, discussion, table preparation, figures, and review. **Amanda Caixeta Campos** contributed to the bibliographic research, introduction, discussion, and review. **Viethor Luiz Senna de Moraes** contributed to the bibliographic research, discussion, and review. **Guilherme de Andrade Ruela** contributed to the supervision, writing, and review of the article.

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

Please cite this article as: Branco LCAC, Sanfins BZ, Souza FE, Campos AC, de Moraes VLS, Ruela GA. Epidemiological profile of leptospirosis in Brazil from 2018 to 2023. Rev Epidemiol Control Infect [Internet]. 2025 Oct. 16;15(3). Available from: <https://seer.unisc.br/index.php/epidemiologia/article/view/20097>