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Epidemiological Profile of Human Rabies in the Northern Region of the State of Pará during the period from 2000 to 2019

Perfil epidemiológico de la rabia humana en la región norte del estado de Pará durante el período 2000 a 2019

Perfil Epidemiológico da Raiva Humana na Região Norte do Estado do Pará durante o período de 2000 a 2019

ABSTRACT

The objective was to carry out an analysis of the number of notified cases of the human rabies virus in the northern region of Brazil in the period from 2000 to 2019. This is an observational study, based on epidemiology, based on data from SINAN in the period from 2000 to 2019. 2019. Maps and graphs were prepared for spatial analysis of the number of cases. In the period from 2000 to 2006, 61 cases were observed. Since, in 2004 and 2005 there were some outbreaks. In the period from 2006 to 2015 there were no notifications. In the years 2016 to 2019, 16 cases were reported. From 2000 to 2019, 316 cases were registered in the country. The Northeast region had the highest number of cases in Brazil during the study period (N = 204; 65%), followed by the North region (N = 77; 24%). Thus, the optimization of disease control, through the adoption of regulatory resources, stands out as the best measure for the control of rabies.

DESCRIPTORS: Human Anger, Epidemiology, Collective Health, Public Health.

RESUMEN

El objetivo fue realizar un análisis del número de casos notificados del virus de la rabia humana en la región norte de Brasil en el período 2000 a 2019. Se trata de un estudio observacional, basado en la epidemiología, con base en datos del SINAN en el período de 2000 a 2019. 2019. Se elaboraron mapas y gráficos para el análisis espacial del número de casos. En el período de 2000 a 2006, se observaron 61 casos. En 2004, se produjeron algunos brotes. En el período de 2006 a 2015 no hubo notificaciones. En los años 2016 a 2019 se notificaron 16 casos. De 2000 a 2019, se registraron 316 casos en el país. La región Nordeste tuvo el mayor número de casos en Brasil en el período estudiado (N = 204; 65%), seguida de la región Norte (N = 77; 24%). Así, la optimización del control de enfermedades, mediante la adopción de recursos regulatorios, se destaca como la mejor medida para el control de la rabia.

DESCRIPTORES: Rabia Humana, Epidemiología, Región Norte, Salud Pública.

RESUMO

Objetivou-se realizar uma análise do número de casos notificados do vírus da raiva humana na região Norte do Brasil no período de 2000 a 2019. Trata-se de estudo observacional, de base epidemiológica, com base em dados do SINAN no período de 2000 a 2019. Foram elaborados mapas e gráficos para análise espacial do número de casos. Observou-se, no período de 2000 a 2006, 61 casos. Sendo que, nos anos de 2004 e 2005 ocorreram alguns surtos. No período de 2006 a 2015 não houveram notificações. Já nos anos de 2016 a 2019 foram notificados 16 casos. De 2000 a 2019 foram registrados 316 casos no país. A região Nordeste obteve maior número de casos no Brasil no período estudado (N=204; 65%), em seguida a região Norte (N=77; 24%). Assim, a otimização do controle da doença, pela adoção de recursos regulatórios, destaca-se como a melhor medida para o controle da raiva.

DESCRITORES: Raiva Humana; Epidemiologia; Saúde Coletiva; Saúde Pública.

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INTRODUCTION

Human Rabies is an acute viral encephalitis caused by a virus of the genus *Lyssavirus*, of the Family *Rhabdoviridae*. The infected patient may present with an acute neurological condition (encephalitis), which presents forms of hyperactivity, followed by a paralytic syndrome with progression to coma, with no possibility of laboratory diagnosis, but with a history of exposure to the likely source of infection.¹

The genus *Lyssavirus* has 8 genotypes, and genotype 1 - Rabies virus (RABV), the only one present in Latin America and Brazil, can be expressed, according to the profile, in 12 antigenic variants, according to their respective natural hosts (land or air). In Brazil, 7 antigenic variants were found: variants 1 and 2, isolated from dogs; variant 3, vampire bat *Desmodus rotundus*; and variants 4 and 6 of insectivorous bats *Tadarida brasiliensis* and *Lasiurus cinereus* *Tadarida brasiliensis* e *Lasiurus cinereus*.¹

Wild mammals serve as a large and uncontrollable reservoir for wild rabies, which is an increasing threat to humans

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and domestic animals around the world. A hierarchy of susceptibility for the different species of wild mammals is described, with the most affected species being: foxes, coyotes, jackals and wolves, in that order. Wild rabies is characterized by the involvement of one or more major species (small carnivores and mustelids), especially in regions where this model remains stable for many years.^{2,3}

In Brazil, a country where rabies is enzootic, all epidemiological cycles occur, with the rural rabies cycle prevailing. The vampire bat of the species *Desmodus rotundus*, commonly known as the “common vampire bat,” is the main reservoir of rural rabies, hence also called “desmodina rabies”, in Latin America.⁴ There was an increase in canine rabies control activities (1973), when the National Human Rabies Prophylaxis Program (PNPR - Programa Nacional de Profilaxia da Raiva Humana) was instituted in the country, which sought to reduce the disease in domestic animals. The actions of the PNPR were gradually expanded until its implementation was completed, throughout the country, in 1977. These actions were strengthened when, in 1983,

the Pan American Health Organization (PAHO) developed the 'Action Plan for the Elimination of Urban Rabies in Major Cities in Latin America', resulting in the international commitment to eliminate human rabies transmitted by dogs in the Americas by 2012.^{5, 6, 7 and 8}

Due to the high degree of lethality, human rabies becomes a serious public health problem, with endemic areas in the North and Northeast regions of the country. In the years 2004 and 2005, with the occurrence of human rabies outbreaks in the states of Pará and Maranhão, the bat became the main responsible for cases of human rabies, with 86,5% of cases in these two years, surpassing the rates of canine transmission.⁹

The Northern Region of Brazil encompasses the states of Acre, Amapá, Amazonas, Pará, Rondônia, Roraima and Tocantins. It is marked by its peculiarities, which include the accentuated socioeconomic inequality and also the geographic isolation in relation to the more developed regions of the country. Its social indicators are among the worst in Brazil, in contrast to its expressive economic and population growth, well above the national average. The means of transport commonly used is the river, and the travel time from one municipality to another can exceed 15 days, leaving many cities geographically isolated, and in which there are high levels of poverty.¹⁰ This study aims to analyze the number of reported cases of the human rabies virus in Northern Brazil in the period 2000 to 2019.

METHOD

This is an observational, cross-sectional, retrospective, epidemiological-based study, carried out through the investigation of studies that portray approaches with an emphasis on the spatial distribution of human rabies in the Northern region of Brazil, compared to the correlation of available registration data of public access on SINAN made available at the Department of Informatics of the

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Unified Health System (DATASUS) in the period 2000 to 2019, whose distribution of development stages is distinguished into two aspects:

The first, having its design related to the search for studies of methodology applicable to the proposed theme, in which the identification of the approach was promoted, under which, it was possible to outline which perspective would be performed in order to establish the initial study proposal; formulation of the guiding question; elaboration of inclusion and exclusion criteria for articles; construction of instruments to collect relevant data from the articles found; query and search and selection of search descriptors in databases and access platforms; evaluation and analysis of selected articles in the research; choice of the theoretical product for the presentation of the study; interpretation and discussion of the results obtained.

The second was based on the search, identification and registration of reported cases of human rabies in the period described, submitting the search to the determinants of subdivisions based on regions. The maps with epidemiological data for each region were made using the QGIS program. The Excel program was used for data tabulation and graph construction. In addition, a basic percentage and arithmetic mean were performed.

The survey of studies obtained in the literature was carried out from September to December 2020. The selected databases were: Nature, Medical Literature Analysis and Retrieval System Online (Medline) and Scientific Electronic Library Online (SciELO). We chose to stick to studies published in English and Portuguese. The selected descriptors were: Human Rabies, Epidemiology, Public Health and Public Health. The most recent articles, published in the last 10 years, texts made available in full and research classified as original were privileged. As for the data collection, the filters of the SINAN platform were used for the search, based on the previously established period (2000-2019). To record

the object of study, the Microsoft Excel program was used and the data were prepared for global processing. Then, the maps were built and delimited based on the study proposal using the QGIS program.

RESULTS

In the North region, there were 77

confirmed cases in the study period, and of these, 61 cases were registered between 2000 and 2005. There was an outbreak of human rabies cases in 2004 and 2005 caused by vampire bats (figure 1), surpassing the number of canine transmissions that until now was the main responsible for the notifications. The outbreaks occurred in the state of Pará, affecting rural and riverside areas. There were 39 cases

and 26 deaths laboratory confirmed.

In the years 2006 to 2015 there were no notifications in the North region (figure 1). Amazonas and Rondônia, both have 5 confirmed cases in the years of study, and in Amazonas in 2002 there were 2 confirmed cases and in 2017, 3 cases resulting from an outbreak in the same family, 2 died. In Rondônia in 2000, 4 cases; 2001, 4 cases; and 2004, 1 reported case. In 2018, a new outbreak occurred in the state of Pará, in the municipality of Melgaço, affecting a total of 10 people (figure 1).

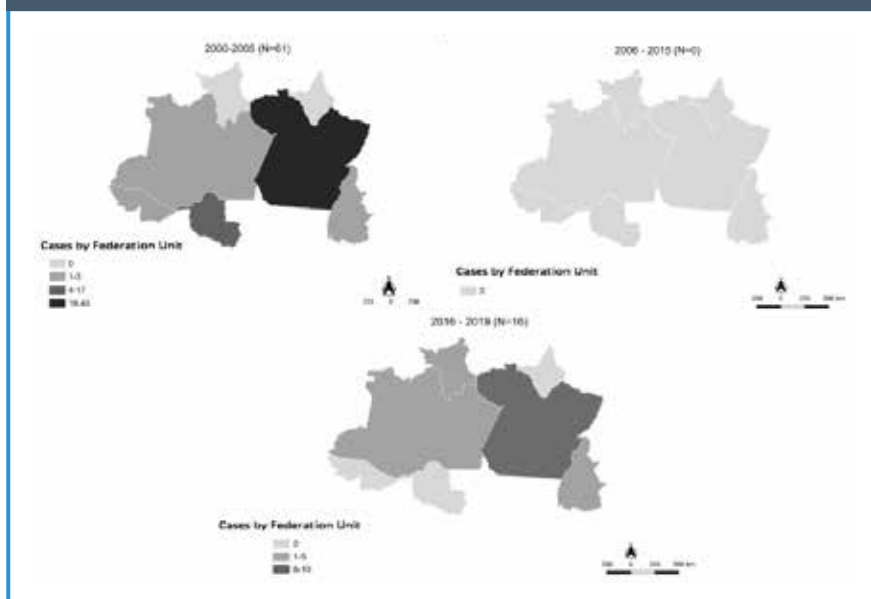
In Acre and Tocantins, there were 3 notifications in both in the total period from 2000 to 2019. In Roraima there were only 2 cases in total, this occurred in 2016. In Amapá there was no record of human rabies cases in the period studied.

From 2000 to 2019, 316 cases were registered in the country, an average of 16 cases per year of human rabies in Brazil, with a predominance of males and rural residents. The highest frequency of exposure was due to animal bites, in the case of dogs and bats. Regarding the number of notifications per region, figure 2 prevailed as the largest number of cases in the study period, the Northeast region (N=204; 65%), followed by the North region (N=77; 24%), Southeast (N=24; 8%), Midwest (N=18; 6%) and the South region (N=2; 1%). It was observed that the majority of cases occurred between 2000 and 2008, despite the linear decrease in human rabies cases in Brazil (figure 2), the North and Northeast region showed greater fragility to case outbreaks.

DISCUSSION

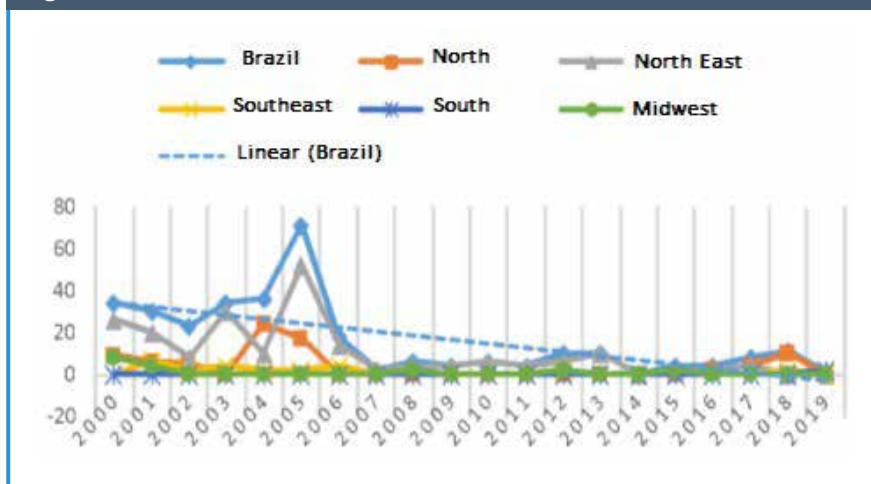
The control of human rabies is possible, especially in these isolated and high poverty regions, given the access to vaccination, which has been one of the main means of controlling the disease in Brazil in recent years. There is a certain difficulty in promoting the actions of the PNPR, and, therefore, the low vaccination coverage in the face of

Figure 1 - Spatial distribution of reported human rabies cases (N=77), Northern Brazil, 2000-2019



Source: The authors

Figure 2: Distribution of human rabies notifications in Brazil and in Brazilian regions, 2000 to 2019.



Source: The authors

a large contingent of susceptible people. It is possible to observe a change in the epidemiological profile in the country, thus evidencing the increase in the wild and rural air cycle, thus, there is greater difficulty in its control.

The North Region was the second region with more notifications (77) in the period studied. Lack of information, basic sanitation and an inadequate health structure contributed to the outbreaks. The predominance of cases in rural areas, probably due to outbreaks with exposure to *D. rotundus* bats in the Brazilian Amazon in 2006 and 2009.^{11,12} In addition, there was a growing deforestation in the regions, the impacts of this activity brought the bats closer to the communities. The main factors that contribute for rabies in Brazil to spread insidiously and worryingly among herbivores are: disorderly occupation, characterized by macro environmental changes, such as deforestation, construction of highways and hydroelectric plants, which have altered the environment in which bats they lived, forcing them to look for new areas and other sources of food.¹³

In Northeastern Brazil, rabies is endemic, with cases of human rabies being registered in all of these federative units.¹⁴ Therefore, it was possible to observe that this was the region that had the most cases of human rabies in these 20 years in Brazil. For the control of rabies in herbivores to be effective, it is important that the State Service for Animal Health Defense maintain a routine of registration of refuges/shelters of *Desmodus rotundus*, with monitoring at least once a year, respecting the regional characteristics of each state. The epidemiological surveillance strategy and work plan adopted should be reviewed annually or whenever necessary. The development of prophylactic measures will certainly bring positive results, given recent exposures to the virus.¹⁵

A large and important tool for epidemiological surveillance is antigen typing by indirect immunofluorescence (IIF) using AcM, which is a rapid specific te-

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chnique, and genetic characterization by RT-PCR and nucleotide sequencing. RT-PCR also the hemi nested-RT-PCR (hnRT-PCR) has been used with good sensitivity and specificity, confirming the diagnosis of DIF in a short period of time.^{17,18} Research carried out based on molecular biology has been of great importance, not only to complement the knowledge about the pathogenesis and immunology of rabies infection, but also to determine the genetic variability of VRab, including between strains and also to clarify the mechanisms of viral replication and transmission.¹⁹

Every suspected human case of rabies requires immediate and compulsory notification at the municipal, state and federal levels. The notification must be registered in the Notifiable Diseases Information System (Sinan), by completing and sending the Rabies Investigation Form.²⁰ Despite the cure of an angry patient in^{21,22,23} showed that there are possibilities for treating the disease, correct and timely human anti-rabies prophylaxis remains the most efficient way to prevent human deaths due to the disease.²⁴ In view of this, there is still a certain weakness in the control of human rabies in the North region, as there is a certain weakness in carrying out compulsory notifications that are made at the municipal level, thus hindering the actions of the Ministry of Health. In addition, there are few epidemiological bibliographic reviews of human rabies in the North region, which was carried out in the present study.

CONCLUSION

Thus, this study was able to reinforce the presentation of the human rabies virus in an endemic way, with sporadic outbreaks that may be related to factors such as climate, temperature, as well as continuous modifications in the urban space. The results presented allow us to observe that, given the complexity of epidemiological processes, understanding the occurrence of outbreaks in favora-

ble regions becomes a major challenge for vector surveillance and control, since human rabies is characterized by as a serious public health problem, especially in isolated areas where the poverty rate is high, in addition to the lack of informa-

tion and basic sanitation, which contributes to the worsening in the northern region. In addition, a probable cause for the spread of the disease is the growing deforestation in the affected regions, facilitating the contagion with humans and

other animals. Among the challenges to be faced, the need to optimize disease control by encouraging the adoption of regulatory and preventive resources in rabies surveillance and control actions stand out.■

REFERENCES

1. Brasil. Ministério da Agricultura, Pecuária e Abastecimento. Controle da raiva dos herbívoros : manual técnico 2009 / Ministério da Agricultura, Pecuária e Abastecimento. Secretaria de Defesa Agropecuária. – Brasília : Mapa/ACS, 2009. 124 p. ; 18 cm.
2. Who – World Health Organization. Expert Consultation on Rabies: First Report (WHO Technical Report Series). Geneva, Switzerland: World Health Organization, 2004, n. 931, 121 p.
3. Chalmers, A.W.; SCOTT, G.R. Ecology of rabies. *Tropical Animal Health and Production*, v. 1, p. 33–55, 1969.
4. Chorino, N, C. Caracterização molecular e filogenética de isolados do vírus rábico (lyssavirus – rhabdoviridae) em espécimes clínicos de herbívoros no estado do Rio de Janeiro. Tese. Centro de Ciências e Tecnologias Agropecuárias da Universidade Estadual do Norte Fluminense Darcy Ribeiro. Rio de Janeiro. 2009.
5. Schneider MC, Souza LM, Moraes NB, Diaz RC. Controle da raiva no Brasil de 1980 a 1990. *Revista de Saúde Pública*. 1996; 30(2):196-203.
6. Belotto A, Leanes LF, Schneider MC, Tamayo H, Correa E. Overview of rabies in the Americas. *Virus Research*. 2005; 111(1):5-12.
7. Schneider MC, Belotto A, Adé MP, Hendrickx S, Leanes LF, Rodrigues MJF, et al. Current status of human rabies transmitted by dogs in Latin America. *Cadernos de Saúde Pública*. 2007; 3(9):2049-2063.
8. Melo-Filho DJ. Reorganização das práticas e inovação tecnológica na vigilância em Saúde e os 20 anos do SUS. Texto elaborado como subsídio à sistematização do Relatório da SVS (Gestão 2007–2008). Brasília: Ministério da Saúde; 2008. 10. Laguardia J, Domingues CMA, Carvalho C, Lauerman CR, Macário E, Glatt R. Sistema de Informação de Agravos de Notificação (Sinan): desafios no desenvolvimento de um sistema de informação em saúde. *Epidemiologia e Serviços de Saúde*. 2004; 13(3):135-147.
9. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Doenças infecciosas e parasitárias: guia de bolso, 8ª edição. Brasília: Ministério da Saúde, 2010.
10. Silva, R, R. Bacha, C, J, C. Acessibilidade e aglomerações na Região Norte do Brasil sob o enfoque da Nova Geografia Econômica. *Nova Economia*. Belo Horizonte_24 (1) 169-190.
11. Rosa EST, Kotait I, Barbosa TFS, Carrieri ML, Brandão PE, Pinheiro AS, et al. Bat-transmitted human rabies outbreaks, Brazilian amazon. *Emerg Infect Dis* [Internet]. 2006 Aug [cited 2019 Feb 26];12(8):1197-202.
12. Mendes WDS, Silva AAM, Neiva RF, Costa NM, Assis MS, Vidigal PMO, et al. An outbreak of bat-transmitted human rabies in a village in the Brazilian Amazon. *Rev Saúde Pública* [Internet]. 2009 Dec [cited 2019 Feb 26];43(6):1075-7.
13. Novais, B. A. F., & Zappa, V. (2008). Raiva em bovinos—revisão de literatura. *Revista Científica Eletrônica de Medicina Veterinária Da Faculdade de Medicina Veterinária e Zootecnia de Garça*, 10.
14. Alves, Thiago Willame Barbosa et al.. "Perfil de acometidos por raiva humana no nordeste brasileiro entre os anos de 2001 a 2017: um estudo documental". *Anais CONADIS... Campina Grande: Realize Editora*, 2018. Disponível em: <<https://editorarealize.com.br/artigo/visualizar/50800>>. Acesso em: 23/10/2020.
15. Brasil. Ministério da Agricultura, Pecuária e Abastecimento. Controle da raiva dos herbívoros : manual técnico 2009 / Ministério da Agricultura, Pecuária e Abastecimento. Secretaria de Defesa Agropecuária. – Brasília : Mapa/ACS, 2009.
16. Brasil. Ministério da Saúde. Raiva in: Guia de vigilância epidemiológica / Ministério da saúde, Secretaria de Vigilância em Saúde. 6. ed. –Brasília, 2005. 603-632.
17. Araújo, D, B. Langoni, H. Almeida, MF, Megid, J. Heminested reverse-transcriptase polymerase chain reaction (hnRT-PCR) as a tool for rabies vírus detection in stored and decomposed samples. *BMC Research Notes*, 2008 1:17,.
18. Heaton, P. R.; Johnstone, P.; Mcelhinney, L.M.; Cowley, R.; O'sullivan, E.; Whitby, J.E.. Heminested PCR assay for detection of six genotypes of rabies and rabies-related viruses. *Journal of Clinical Microbiology*, Vol. 35, n. 11, nov. 1997, 2762–2766.
19. Wunner, W.H.; Larson, J.K.; Dietzschold, B.; Smith, C.L. The molecular biology of rabies viruses. *Reviews of Infectious Diseases*, 10: 771-84.
20. Kotait, I., Takaoka, N.Y., Carrieri, M.L., 2009: Manual Técnico Instituto Pasteur. Raiva – Aspectos gerais e clínica. São Paulo: Instituto Pasteur.
21. Wada, M. Y., S.M. Rocha, A.N.S. Elkhoury, 2011: Situação da Raiva no Brasil 2000 a 2009, *Epidemiol. Serv. Saúde*, Brasília, out-dez;20 (4):509-518.
22. Ministério da Saúde, 2009b: I Protocolo para Tratamento de Raiva Humana no Brasil. Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica. *Epidemiologia e Serviços de Saúde*, 18 (4):385-394.
23. Bourhy, H., 2010: Rabies, still neglected after 125 years of vaccination. *PLoS neglected tropical diseases*, 11 (4): 839.
24. Bourhy, H., 2010: Rabies, still neglected after 125 years of vaccination. *PLoS neglected tropical diseases*, 11 (4): 83