


Epidemiology of human rabies in the state of Ceará, Brazil, 1970 to 2019*

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Abstract

Objective: To describe cases of human rabies in Ceará State, Brazil between 1970 and 2019. **Methods:** This was a descriptive study using secondary data from the Ceará State Department of Health and the state reference hospital. **Results:** Of 171 cases, 75.7% occurred in males, 60.0% in <19-year-olds, and 56.0% in urban areas. Rabies was transmitted by dogs in 74.0% of cases, marmosets in 16.7% and bats in 7.3%. Between 1970 and 1978, there was an increase of cases (using the Joinpoint Regression Program, annual percentage change [APC] = 13.7 – 95%CI 4.6;41.5), while between 1978 and 2019 there was a decrease (APC = -6.7 – 95%CI -8.8;-5.9). There was a reduction in transmission by dogs (71 cases, last case in 2010) and an increase by sylvatic animals (5 cases since 2005). **Conclusion:** This study demonstrates changes in rabies transmission dynamics during the period studied, with a reduction in transmission by dogs and an increase of transmission by sylvatic animals.

Keywords: Zoonoses; Rabies; Epidemiological Monitoring; Public Health; Epidemiology, Descriptive.

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Introduction

Human rabies is an anthroozoonosis transmitted to humans by inoculation of the virus present in the saliva and secretions of infected mammals, mainly by biting.¹ Every year, some 60,000 deaths are reported worldwide, with most victims being children under the age of 15 and the highest concentration of deaths in Africa and Asia.^{2,3}

In Brazil, due to the implementation of public policies to improve epidemiological surveillance actions, human rabies transmitted by dogs has declined progressively. However, rabies carried and transmitted among wild mammals (mainly canids, bats, and marmosets) deserves special attention from the authorities, especially in the North and Northeast regions of the country.

In Brazil, due to the implementation of public policies to improve epidemiological surveillance actions, human rabies transmitted by dogs has declined progressively. However, rabies carried and transmitted among wild mammals (mainly canids, bats, and marmosets) deserves special attention from the authorities, especially in the North and Northeast regions of the country.⁴ From 2002 to 2012, 126 cases of human rabies were reported in Brazil, with wild mammals being responsible for 65.1% of these cases, and 3.2% transmitted by unknown species; the urban cycle accounted for 31.7% of cases.⁵

In 2004 and 2005, hematophagous bats caused most of the cases of rabies virus transmission to humans in Latin America, with 46 and 52 records, respectively. In that period, Brazil stood out with the highest number of cases, accounting for 86.5% of the total in the region.⁶

In 2010, only three cases of human rabies were reported in Brazil, all in the Northeast region, two of them in Ceará alone: one transmitted by a dog (*Canis lupus familiaris*) and the other by a marmoset (*Callithrix jacchus*). In 2013, five deaths from human

rabies were registered, three caused by dogs and two by marmosets. In 2015, there were two deaths from human rabies, one transmitted by a dog and the other by a cat; and in 2016, two more deaths, one in the state of Roraima, transmitted by a cat (*Felis catus*), and the other in the state of Ceará, transmitted by a hematophagous bat.⁷ In 2017, three cases of human rabies transmitted by cats were registered in the states of Pernambuco, Tocantins, and Bahia; and three cases in the state of Amazonas, which were transmitted by hematophagous bats.⁸

In the state of Ceará, from 2003 to 2013, 219,504 mammal attacks on humans with risk of rabies were recorded on the Notifiable Health Conditions Information System (SINAN), with dogs being the main aggressor, followed by cats (*Felis catus*).⁹ Bats appear as the main carriers of the rabies virus in Ceará as of 2011, when surveillance began.¹⁰ The viruses identified in human cases in Ceará are related to the variants carried by dogs, bats and other wild mammals.¹¹ The most recent death from human rabies in that Northeastern state occurred in 2016, in the rural area of Iracema.^{12,13}

It is relevant - and necessary - to provide health professionals with detailed and timely information, contributing to the development of actions to improve care, surveillance and control of rabies, and prevention of new cases. This study aimed to describe the epidemiology of human rabies cases in the state of Ceará, from 1970 to 2019.

Methods

A descriptive study based on secondary data was conducted covering the state of Ceará. Located in the Northeast region of Brazil, Ceará is bordered to the north by the Atlantic Ocean, to the west by the state of Piauí, to the east by the states of Rio Grande do Norte and Paraíba, and to the south by the state of Pernambuco. Ceará has a population of approximately nine million inhabitants and an area of 149,000 km², over which 184 municipalities are distributed.¹⁴

The study included all the cases of human rabies that occurred in Ceará from 1970 to 2019. The analysis was based on secondary data, available at the Department of Epidemiological Surveillance and Health Prevention (COVEP) and at São José Hospital of Infectious Diseases (HSJDI), both public agencies,

subordinated to the Ceará State Health Secretariat. COVEP technical reports resulting from investigations of cases and deaths from human rabies, available since 1990, were reviewed. HSJDI medical records and records of discharges and deaths retrieved from the medical archive, available since 1970, were reviewed. Data compilation suffered some limitations: from 1970 to 1973, the information obtained referred only to the number of cases; from 1974 to 1985, there was information on the number of cases, the municipality of occurrence, age, sex, and area of residence (rural or urban); from 1986 onwards, all the previous information was available, as well as the species of the aggressor species, type of exposure, and the anatomical site of the attack. Therefore, not all information variables were available for all cases.

The trend analysis counted 'year of study' as an independent variable and 'number of human rabies cases' as a dependent variable.

A database was built using Excel 2010 to organize, sort and categorize the information.

The time trend analysis was executed by the Joinpoint Regression Program version 4.7.0.0 (US National Cancer Institute, Bethesda, MD, USA), available via open access (<http://surveillance.cancer.gov/joinpoint/>), and by the Excel application, with production of tables and graphs, and presentation of data in absolute and relative numbers.

To calculate the annual percentage change (APC) of the proportion of human rabies cases, a trend analysis was performed through continuous linear regression, with inflection points. This method allows the time series data to be adjusted, based on the minimum number of inflexion points, as well as enabling it to be determined whether the inclusion of more inflexion points is statistically significant. The time series is represented by APC graphs and indicators. Each significant point indicates a change, either of an increase or a decrease in cases. A 5% significance level was used. Heteroscedastic errors were taken into account, and regression coefficients were estimated by weighted least squares. In view of the above and the temporal evaluation of the data, an adjusted model of autocorrelation of errors based on the data was also used. APC 95% confidence intervals (95% CI) were calculated by the empirical quantile method. A maximum of three inflection points was considered in the analysis for the periods.

The spatial distribution of the cases was described on maps, produced by the QGIS version 2.18.18 software.¹⁵

The study was submitted to Plataforma Brasil and approved by three Research Ethics Committees (CEP): the CEP of the Federal University of Ceará, through Certificate of Submission for Ethical Appraisal (CAAE) No. 13466719.6.0000.5054, on May 30, 2019; the CEP of the Ceará State Health Secretariat, CAAE No. 13466719.6.3001.5051, on July 11, 2019; and the CEP of HSJDI, CAAE No. 13466719.6.3002.5044, on July 3, 2019.

Results

In all, 171 cases of human rabies were identified in the state of Ceará, in the period 1970-2019, 46 of them coming from the COVEP database and 125 (prior to 1990) from the medical archive of São José Hospital of Infectious Diseases - HSJDI.

Most of the cases were male (106/140; 75.7%) and resident in urban areas (56.0%). The most affected age group was from 0 to 19 years old, with 84 cases (60.0%), followed by 20 to 39 years old, with 26 (18.6%) (Table 1).

Dogs were responsible for the transmission of the virus in almost 75% of the cases, followed by marmosets and bats (Table 1); of the two remaining cases, one was transmitted by a cat and the other by a raccoon. Biting was the form of exposure in almost all attacks. The hands were the part of the body with the highest record of attacks among affected people, followed by the head/neck and lower limbs (Table 1). Two trends can be observed in the epidemiology of human rabies in Ceará: a rapid growth in the number of cases between 1970 and 1978 (APC = 13.7; 95%CI 4.6;41.5) and then a gradual decline between 1978 and 2019 (APC = -6.7; 95%CI -8.8;-5.9). In this second period, a more intense reduction was observed up until 2002. In 2003, there were a total of seven cases, a higher quantitative value than in the following periods, from 2004 to 2019, when the downward trend was less marked, adding a total of six cases and a maximum value in 2010: two cases (Figure 1).

Dogs were the most frequent aggressor species, accounting for 74.0% of cases. The years with the highest number of cases transmitted by dogs were 1980 (8), 1989 (7) and 2003 (7) (Figure 2). The last case of dog transmission in Ceará occurred in 2010. Between 1991 and 1998, there were nine cases of transmission by marmosets, with 1991 standing out with four records.

Table 1 – Distribution of human rabies cases according to demographic characteristics, aggressor species and exposure to infection, Ceará, 1970-2019

Variables	N
Sex	
Male	106
Female	34
No information	31
Age group (in years)	
0-19	84
20-39	26
40-59	16
≥60	14
No information	31
Area of residence	
Urban	65
Rural	51
No information	55
Aggressor species	
Dog	71
Primate (marmoset)	16
Chiroptera (bat)	7
Cat	1
Raccoon	1
No information	75
Type of exposure to infection	
Scratch	2
Bite	61
No information	108
Affected body part	
Hands	23
Head/neck	10
Lower limbs	10
Upper limbs	8
Torso	3
No information	117

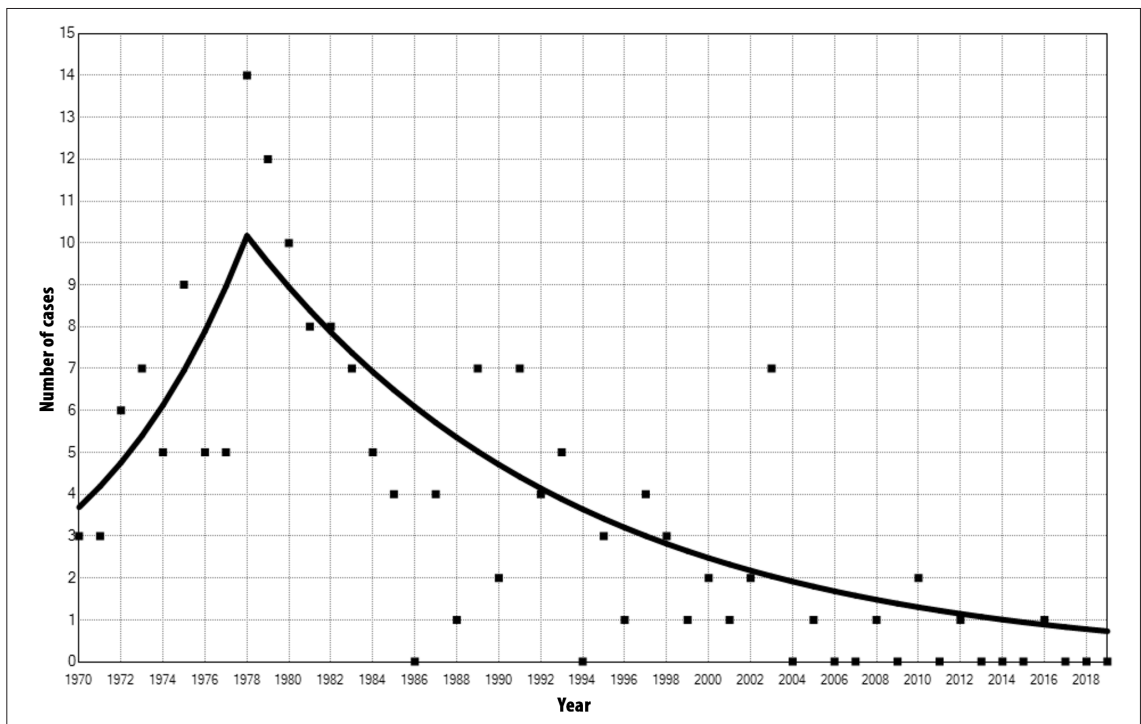
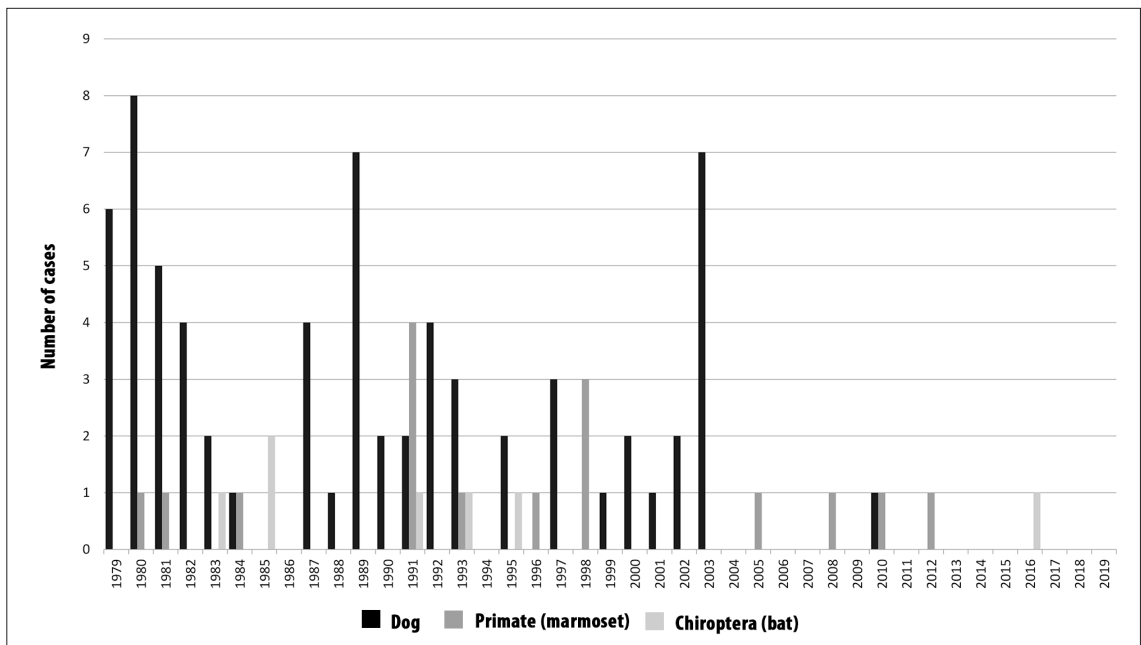


Figure 1 – Distribution of the number of human rabies cases per year, Ceará, 1970-2019



Note: a) Information on the aggressor species available only as from 1979.

Figure 2 – Distribution of the number of human rabies cases according to the transmitting animal, Ceará, 1979-2019^a

The seven cases of transmission by bats occurred between 1983 and 2016, almost always one case per year, with the exception of 1985, with two cases. The only case with a record of an attack by a cat occurred in 1979, and only one caused by a raccoon, in 1997.

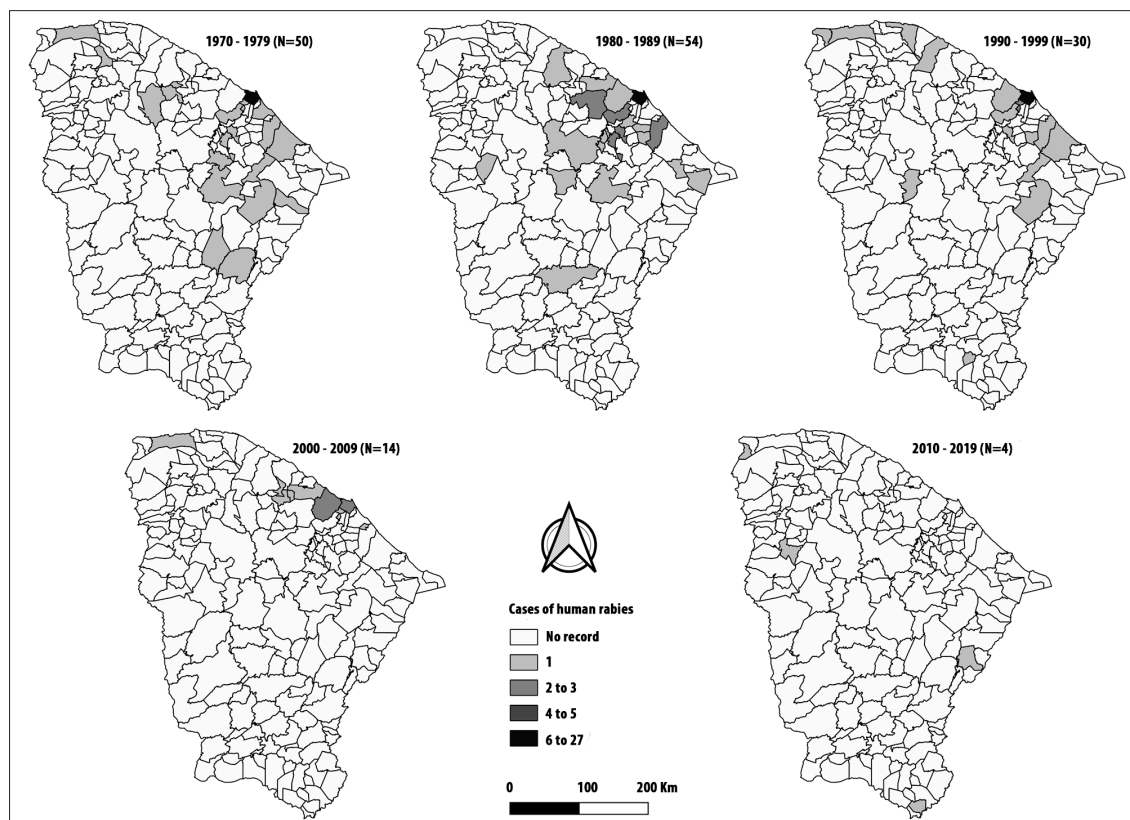
Of the 184 municipalities in Ceará, 48 (26.0%) confirmed cases of human rabies. Over the entire study period, the state's mesoregion with predominance of cases was the metropolitan region of Fortaleza, with 85 (49.7%), followed by the Northern region of Ceará (23.9%). The city with most records of cases was the capital of the state, Fortaleza, with 64 cases (37.4%) and most records of transmission by dogs until 2003. Next came the municipalities of Caucaia, Maranguape and Cascavel, with six cases (3.5%) each, and Maracanaú and Redenção, both with five cases (3.0%) (Figure 3). In the rest of the state, no defined pattern was observed, with 41 municipalities presenting between one and three cases. In Fortaleza,

among the cases information available about the aggressor species, 94.2% were attributed to attacks by dogs, one by a cat and one by a bat.

The decade with the greatest predominance of records was from 1970 to 1979, with 69 cases (40.4%) (Figure 3). From 1980 to 1989, 54 cases (31.6%) were registered, from 1990 to 1999, 30 cases (17.5%), from 2000 to 2009, 14 cases (8.2%), and from 2010 to 2019, a total of four cases (2.3%). In all periods analyzed, except for the last decade (2010 to 2019) when there were no cases, Fortaleza predominated with the highest number of human rabies deaths in the state of Ceará.

Discussion

This study is the largest time series of human rabies cases in the state of Ceará documented to date. It highlights changes in the dynamics of human rabies transmission and in the profile of aggressor species.



Note: a) From 1970 to 1979, 19 cases without information from the municipality of occurrence.

Figure 3 – Spatial distribution of reported human rabies cases (N=171), Ceará, 1970-2019^a

Since the 1980s, a decline in the number of cases has been observed, in addition to the fact that, in the last ten years, wild mammals, especially marmosets and bats, have become the most frequent aggressor species, replacing dogs.

The study has limitations. The main one is the use of secondary data. For the first years of the survey, there was a scarcity of data available, especially on the species of aggressor species. In addition, it was not possible to locate all the medical records and most of the information was collected from hospital discharge and death records. It should be noted that, before the present study, the only available information on human rabies cases in Ceará dated from 1990 to 2019, with only 46 confirmed cases.¹⁶

The explanations for the decline in the number of cases, pointed out in this study, are suggested as follows. In Brazil, the National Program for Prevention of Human Rabies was instituted in 1973, although it was only in 1977 that it was established in all states, through an agreement between the Ministries of Health, Agriculture and the Pan American Health Organization (PAHO).¹⁷ This chronology justifies, in part, the greater occurrence of human cases in Ceará in the period from 1970 to 1979. The inexistence of surveillance, prevention and control actions also explains the fact that most of the cases registered until 2003 were attributed to dog attacks. At the state level, it was only from 2005 onwards that Ceará started to perform canine rabies vaccination with coverage above 80%, meeting the goal recommended by the Ministry of Health.¹⁸ Therefore, the reduction in cases of rabies transmitted by domestic dogs from 2003 onwards was probably due to the implementation and strengthening of rabies surveillance actions and canine rabies vaccination.¹⁹

Another possible explanation for the reduction of the incidence of human rabies in Ceará is the introduction of the vaccine produced in human diploid cell culture, for prophylaxis purposes in humans. This product replaced the human rabies vaccine produced in the brain of newborn mice (Fuenzalida & Palacios vaccine), in order to be more effective, capable of inducing a better immune response in an earlier and longer lasting way, besides causing fewer adverse events.²⁰

Despite the control actions carried out, Ceará recorded human rabies cases transmitted by dogs up until 2010. The presence of dog vaccination programs

in an expanded form leads to a reduction in the incidence of human exposure to the rabies virus and, consequently, a reduction in the number of cases, provided that the population has access to post-exposure prophylaxis in a timely and opportune manner.² Studies conducted in other regions of Brazil also point to a reduction in cases of rabies transmitted by dogs and a change in the epidemiological characteristics of the disease from the 2000s onwards.^{21,22} However, in several countries in Africa and Asia, the presence of human rabies is still of concern, given the difficulties and challenges for infection surveillance and control programs in these countries.^{23,24}

In opposition to the reduction in cases of rabies transmitted by dogs, there was an increase in cases involving wild animals, such as bats and marmosets, which have become the main species transmitting the rabies virus to humans in Ceará.¹⁶ The marmoset, popularly known as 'soim', is a wild animal, misguidedly bred in captivity by the state's rural population, due to its being unaware of the disease's wildlife cycle. Hence the risk that the habit of breeding marmosets at home represents for the transmission of rabies to humans. Another study conducted in Ceará presents marmosets as animals of potential risk for the occurrence of accidents with humans and other mammals. Marmosets are a species of great epidemiological importance in the rabies wildlife cycle transmission chain, which reinforces the need for health education in the state. In the state of Amazonas, however, another study on animal involvement has identified the hematophagous bat as being responsible for the largest number of human cases of the disease.^{22,25,26}

The profile of the 'sex' and 'age group' variables of the people affected, according to this study, matches the findings of other studies in Brazil, United States and India. Males, children and adolescents were the most commonly affected groups, which can be explained by their coexistence and greater contact with domestic animals.^{22,23} The results of this study on the epidemiology of human rabies in Ceará differ from those reported in another survey conducted in 2013 in Sri Lanka,²⁷ where the majority of rabies victims were individuals over the age of 40 - probably due to most family members taking more care of children, and adults not giving due importance to being attacked

and therefore not seeking medical assistance to receive post-exposure prophylactic measures.

This study also reveals a greater proportion of human rabies cases in urban areas (metropolitan region of Fortaleza and northern region of Ceará), differently from the results found for Ecuador, where a predominance of cases was observed in rural areas.²⁸ Aspects related to culture, habits, production processes, migration and interaction with nature, according to the different regions and countries that were the object of analysis, may explain this difference between the conclusions of the two studies.

Achieving satisfactory coverage of dog vaccination and timely and complete post-exposure prophylaxis are essential for reducing the incidence of the disease worldwide.²⁹ In Latin America, between 1982 and 2003, the number of human rabies cases decreased from 355 cases to 35, representing a 91.0% decrease, and dog rabies cases decreased from 15,686 to 1,131, representing a 93.0% reduction.³⁰

It is concluded that greater attention by the authorities to the implementation of human rabies surveillance actions is necessary, with emphasis on addressing the wildlife cycle and educating the affected population, focused on transmission by wild animal species.

Authors' contributions

Duarte NFH, Alencar CH and Heukelbach J participated in the study concept, data analysis and interpretation, discussion of results, drafting and reviewing the manuscript. Pires-Neto RJ and Sousa AQ participated in the concept, discussion and review of the manuscript. Viana VE, Abreu KG and Melo IMLA participated in data collection and literature review. Feijão LX participated in the production and analysis of the data. All authors contributed to the preparation and final review of the manuscript and declare themselves to be responsible for all aspects of the work, ensuring its accuracy and integrity.

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