EPIDEMIOLOGICAL PANORAMA OF HUMAN RABIES IN NORTHEASTERN REGION OF BRAZIL FROM 2013 TO 2017

Panorama epidemiológico da raiva humana na região Nordeste do Brasil de 2013 a 2017

Short title: Rabies in Northeastern from 2013 to 2017

Camila Joyce Alves da Silva, Natanael da Silva Bezerra Júnior, Lucas Soares Bezerra, Isvânia Maria Serafim da Silva Lopes

ABSTRACT

Objectives: This study aimed to report the number of cases of human rabies from 2013 to 2017 in the Northeast region of Brazil and identify factors correlated to the distribution in the epidemiological panorama. **Methodology:** The data were collected from the Notifiable Diseases Information System. **Results:** The Northeast region accounted for over half of confirmed cases of human rabies in Brazil (67%). Most cases affected men (89%) aged from 20 to 39 years (56%), residents of urban areas (56%), and originated from aggressions by unvaccinated animals (80%). **Conclusion:** The incidence of human rabies in the Northeast region seems to be related to low development rates, lack of information regarding infection pathways and disease severity, inadequate post-exposure prophylaxis, and discontinuation of treatment. In addition, underreporting of suspected cases impairs the actions of local health authorities.

Keywords: Brazil; Epidemiology; Rabies.

RESUMO

Objetivos: Relatar o número de casos da raiva na região Nordeste no período de 2013 a 2017 e identificar aspectos correlacionados ao panorama epidemiológico de sua distribuição. **Metodologia:** Os dados foram coletados do Sistema de Informação de Agravos de Notificação. **Resultados:** A região Nordeste foi responsável por mais da metade dos casos confirmados de raiva humana no Brasil (67%). A maioria desses casos acometeu homens (89%), entre 20 e 39 anos (56%), residentes de áreas urbanas (56%), e originadas de agressões por animais não vacinados (80%). **Conclusão:** A incidência de raiva humana no Nordeste parece estar atrelada a baixos índices de desenvolvimento humano, falta de informações a respeito das vias de infecção e da gravidade da doença, profilaxia de pós-exposição inadequada e interrupção do tratamento. Além disso, a possível subnotificação de casos suspeitos dificulta as ações das autoridades de saúde locais.

Palavras-chave: Brasil; Epidemiologia; Raiva.

INTRODUCTION

Rabies is an anthropozoonotic viral disease transmitted to humans from saliva and secretions of infected animals through scratches, contact with mucous membranes, open wounds, and especially by bites. The fatality rate is near 100%, becoming a serious public health issue worldwide[1-3].

In Brazil, rabies is an endemic disease with a highly heterogeneous epidemiological distribution associated with socioeconomic and cultural conditions, with cases registered in Southeast and Central-West regions and predominantly in the North and Northeast regions[4, 5].

Rabies is a neurotropic virus of the genus *Lyssavirus*. The virus replication in neurons causes a characteristic clinical presentation of acute encephalomyelitis, with the formation of cytoplasmic inclusion bodies named Negri bodies[1, 2]. Clinical signs are highly variable and depend on the affected region since the virus replicates in any region of the nervous system. The incubation period is 12 days on average, with animal death five days after the onset of clinical signs. As a public health issue or event, rabies has mandatory notification by physicians and healthcare professionals, according to ordinance nº. 204/2016 of the Brazilian Ministry

of Health[6, 7].

Only mammals are transmitters and develop the disease of rabies virus, becoming vectors. Rabies presents three transmission cycles: urban, wild, and rural. Domestic (mainly dogs and cats) or wild (bats, monkeys, and foxes) animals are the major viral reservoirs and transmit the disease to humans and large animals, such as cattle and horses[1, 8, 9]. In Brazil, bats are key agents in the wild cycle, while in municipalities, dogs are the main cause of infections[5, 10].

Human rabies is a lethal disease since treatment is nonspecific. However, unlike other zoonoses, human rabies could be fully prevented with the control of animal reservoirs. In Brazil, over 2,500,000 doses of Fuenzalida & Palacios-type and cell culture vaccines are administered annually for post-exposure treatment and immunization of professionals at-risk[8, 11, 12].

The control of domestic animals comprehends the reduction of directly involved reservoirs and vaccination of susceptible individuals, especially in endemic areas, following recommendations of the World Health Organization (WHO). Thus, rabies associated with wildlife and non-hematophagous bats cannot be prevented[13, 14]. An extensive vaccination program reduced the incidence of rabies transmitted by dogs in Brazil; however, rabies transmitted by bats (particularly *Desmodus rotundus*) remains endemic, mainly in the Northern and Northeastern regions[15-17].

In 1973, the National Program for Human Rabies Prophylaxis was created in Brazil to reduce the number of human cases by controlling zoonosis in domestic animals and performing post-exposure prophylaxis in individuals bitten and in contact with infected animals. A main objective was to keep 70% of dogs vaccinated, the minimum percentage to interrupt the epidemiological chain of disease transmission[12, 18].

Rabies in Brazil demand improvement of surveillance measures for the urban cycle, implementation in the wild and aerial cycles, and reinforcement of the importance of human prophylaxis to prevent new cases[12, 14]. Changes in habitat and food availability for bats, disordered occupation by human action, and low adherence to vaccination are considered risk factors. The creation of programs focused on rabies control is associated with different animal species infected by the virus and is responsible for its dissemination. In most Brazilian cities, 80% of cases in the urban cycle are sustained by dogs[6].

The United Against Rabies Initiative of 2018, a collaboration between the WHO, the Food and Agriculture Organization of the United Nations, the World Animal Health Organization, and the Global Alliance for Rabies Control, launched a global strategic plan to cease human deaths from canine rabies until 2030[19,20]. This study aimed to report the number of cases of human rabies from 2013 to 2017 in the Northeast region of Brazil and identify factors correlated to the distribution in the epidemiological panorama

METHODS

The present study consisted of a descriptive analysis of epidemiological data on human rabies in the Northeast region of Brazil from 2013 to 2017. The database from the Notifiable Diseases Information System (SINAN) [21], managed by the Brazilian Ministry of Health, was accessed using the search terms “region/state of notification” and “year of first symptoms”. The search terms “age group”, “sex”, and “residence area” were also included in the analysis for individuals with a positive diagnosis.

The “Brazil in Synthesis” database, managed by the Brazilian Institute of Geography and Statistics[22], was accessed to evaluate the relevance of the socioeconomic factors according to the Human Development Index (HDI) of regions affected by human rabies. Populational and territorial information was retrieved from the 2010 Census.

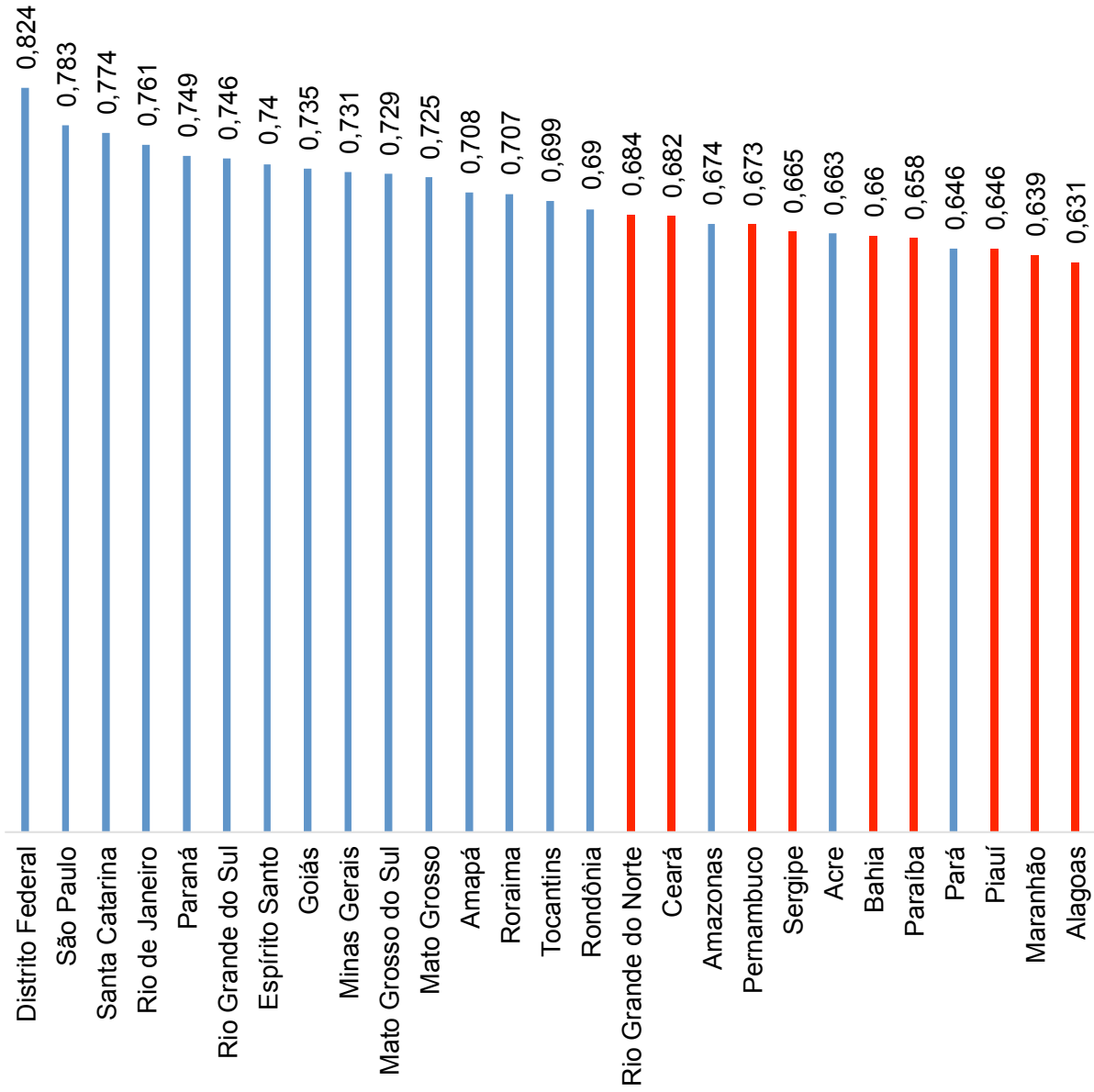
RESULTS

According to the WHO[20], rabies is responsible for 59,000 human deaths per year worldwide, especially in Asia (35,172) and Africa (21,476), affecting mainly low-income populations from rural areas.

The Northeast region of Brazil has over half the confirmed cases of human rabies, in-

cluding nine states: Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, and Sergipe. This region is the third-largest, with a territory of 1,302,679 km^2, and has the second-largest population, with 49,963,590 inhabitants. However, Northeastern states occupy the lowest ranks according to HDI (Figure 1), which assesses the progress of a population considering family income, education, and health[23].

Figure 1. Brazilian ranking of Human Development Index (HDI) by state.



The HDI values are presented on top of the bars corresponding to each state. The bars representing the Northeastern states are highlighted in red). Source: IBGE, 2010.

According to the SINAN database (2018)[21], between January 2013 and December 2017, 15 cases were confirmed in Brazil, with nine (60%) in the Northeast, five (33%) in the North, and one case (7%) in the Central-West region; the South and Southeast regions did not report human cases. According to these results, the Northeast region comprised over half the confirmed cases. The distribution of cases is shown in Table 1.

Table 1. Distribution of confirmed cases of human rabies in the Northeast region of Brazil.

State	Year of the last case before 2013	Number of cases					Total
		2013	2014	2015	2016	2017	
Maranhão	2012	3	-	-	-	-	3
Piauí	2001	2	-	-	-	-	2
Ceará	2012	-	-	-	1	-	1
Rio Grande do Norte	2010	-	-	1	-	-	1
Pernambuco	2008	-	-	-	-	1	1
Bahia	1999	-	-	-	-	1	1
Total	-	5	-	1	1	2	9

Source: SINAN (2018).

The Maranhão state was the most affected, with three cases in 2013, without further cases until 2017. Of the three cases, two were registered in the municipality of Humberto de Campos and one in the capital, São Luís. Before the analyzed period, two cases were confirmed at São Luís in 2012.

The Piauí state registered two cases in 2013, with one case at the municipality of Parnaíba and the other at the capital, Teresina. Until 2013, the last confirmed cases occurred 12 years before at the municipalities of Anísio de Abreu and Bonfim do Piauí, one case each.

The Ceará state had one confirmed case of human rabies at the capital, Fortaleza, in 2016[21]. Before this, the last case was in 2012 in the municipality of Barbalha.

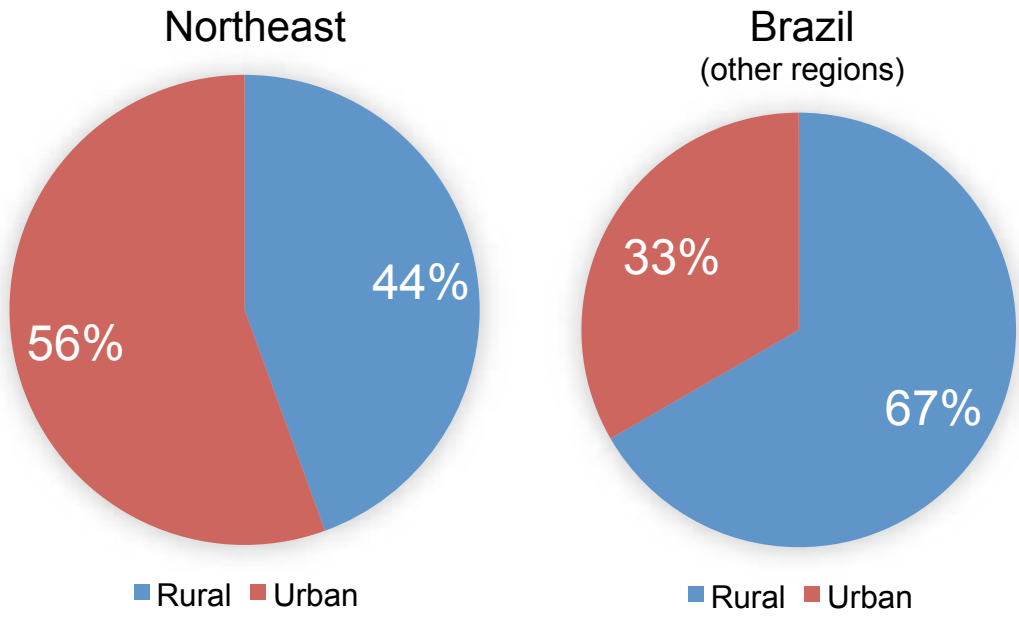
The Rio Grande do Norte state registered one case in 2015 at the capital, Natal. Before this episode, the last confirmed case was at the municipality of Frutuoso Gomes in 2010.

The Pernambuco state had one case of human rabies registered in 2017 at the capital, Recife that progressed to death. Before 2017, the last case was also registered at Recife in 2008.

Similarly, the Bahia state reported one confirmed case in 2017 in the municipality of Paramirim. Until 2017, the last three registered cases were at the municipalities of Dias d'Ávila, Itororó, and the capital, Salvador, in 1999.

Concerning the area of residence of infected individuals, from the nine cases in the Northeast region, four (44%) were registered in rural and five (56%) were in urban areas. A different proportion compared with other cases in Brazil; from six cases, four (66%) were registered in rural areas, and two (33%) were in urban areas (Figure 2).

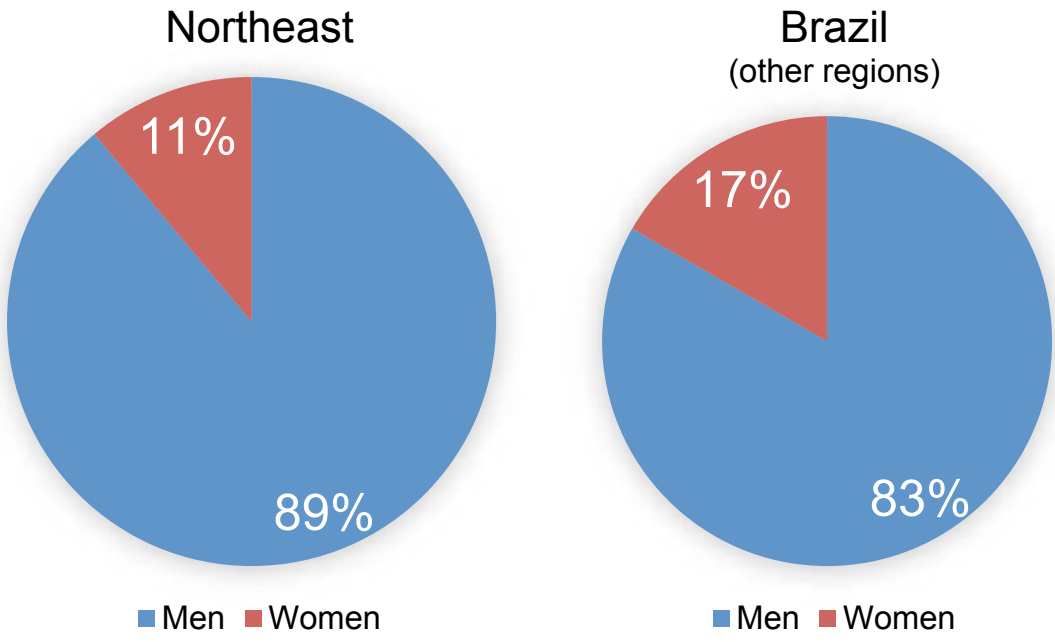
Figure 2. Percentages of confirmed cases of human rabies by area of residence in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).



Source: SINAN (2018).

Regarding sex, the Northeast region showed a significant disparity between men and women. Only one woman (11%) was diagnosed with human rabies in the municipality of Recife in 2017; the other eight cases (89%) were registered in men. This predominance in men was similar in other regions, with five (83%) cases in men and one case (17%) in a woman (Figure 3).

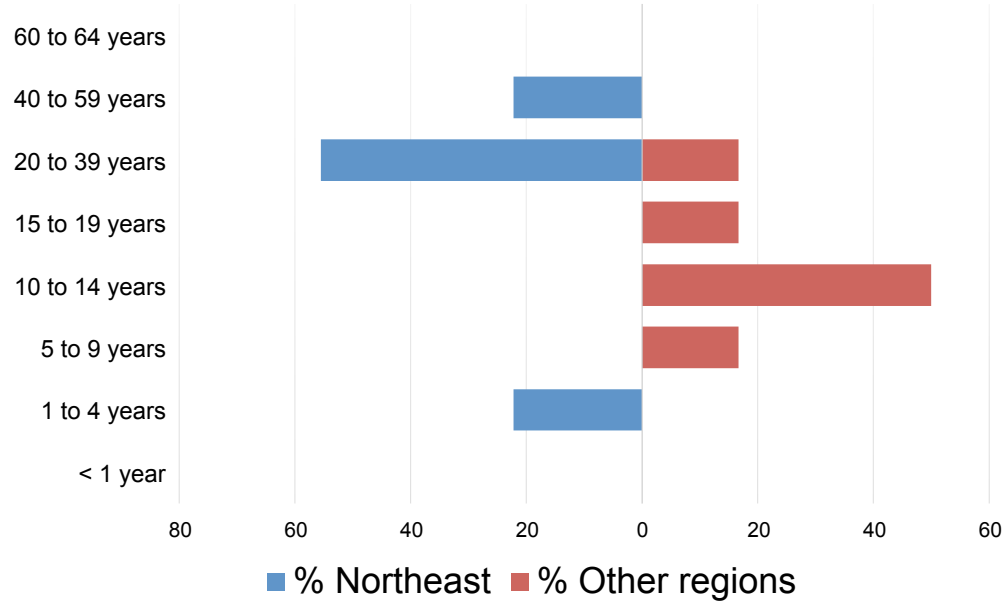
Figure 3. Percentage of confirmed cases of human rabies by sex in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).



Source: SINAN (2018).

The age group analysis showed that most cases in the Northeast region were in individuals aged 20 to 39 years, with five confirmed cases (56%). Additionally, two cases (22%) were registered in individuals aged from one to four years and two (22%) in the age group of 40 to 59 years. The other Brazilian regions had most cases between 10 and 14 years, encompassing three cases in the Amazon region and one confirmed case in the age groups of 5 to 9 years, 15 to 19 years, and 20 to 39 years (Figure 4).

Figure 4. Percentages of confirmed cases of human rabies by age group in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).



Source: SINAN (2018).

Last, from nine confirmed cases in the Northeast region, five acquired rabies from unvaccinated animals, and the other four did not have this information. This pattern was reflected in other regions of Brazil; from six cases of human rabies, four were acquired from unvaccinated animals, and the other two cases the immunization status was unknown.

DISCUSSION

A significant reduction in cases of human rabies was observed in Brazil over the past decades, considering absolute numbers. In 1990, 70 cases were registered, which was 467% higher than the total cases between 2013 and 2017[18]. This reduction reflects public health policies such as the implementation of vaccination programs for dogs and cats and administration of post-exposure prophylaxis24.

Otherwise, on the expressive reduction in notification numbers, this study observed that between 2013 and 2017, considering the confirmed cases, 60% occurred in the Northeast region, a percentage close to the 50% observed from 1996 to 2001[25]. This result highlights that human rabies remains a challenge for the health authorities of this region.

A control measure against rabies dissemination is the immunization of dogs and cats identified as potential domestic transmitters. Thus, some states in the Northeast region emphasized that vaccination campaigns met the goals for national immunization. Indeed, from 1982 to 2003, a reduction of 91% of human rabies cases transmitted by dogs in Latin America was observed due to efforts between countries[24]. Changes in the epidemiological transmission pattern of rabies in Latin America were evidenced in 2004 since hematophagous bats (Desmodus rotundus) were the primary transmitters to humans[24]. In this context, the present cycle of human rabies in the Northeast region of Brazil may be maintained by synanthropic animals, such as hematophagous and insectivorous bats, whose presence was

documented in several municipalities of this region[26].

Regarding the residence area of infected individuals, the number of cases in rural areas of the Northeast equaled other Brazilian regions (four cases). This finding corroborates previous studies, which documented human rabies in rural areas in the Maranhão state16. Additionally, researchers alerted on the circulation of rabies virus in the semiarid region of Paraíba, involving cattle, horses, goats, and foxes[27-29]. A study documented the presence of the same rabies virus lineage in livestock and in hematophagous and insectivorous bats in Maranhão e Paraíba states, suggesting bat attacks on herds and subsequent infection[30].

Moreover, the higher number of cases of human rabies in urban areas in the Northeast region (five cases) compared with other Brazilian regions (two cases) is noteworthy. This finding might arise from bats in large urban centers, where they adapt to urban conditions, find refuge and food, and increase their contact with humans and domestic animals, raising the chances of infection[26]. However, a greater population of bats does not reflect an increase in rabies dissemination, which is conditioned to virus circulation in the environment[31].

The socioeconomic development could be correlated to the higher prevalence of human rabies in the Northeast regions. Studies demonstrated an increased transmission of rabies in regions of greater social vulnerability, which is associate with lower levels of education on preventive measures and, consequently, more susceptibility to infections[25, 31]. Additionally, underreporting may occur since the population does not recognize licks and scratches as infection pathways, and inadequate conduct on post-exposure prophylaxis of healthcare professionals is also an issue[32, 33].

Most diagnoses in the Northeast region were in adults aged from 20 to 39 years (five cases), corroborating a previous study in the Pernambuco countryside[34]. The exposition during work and discontinuation of post-exposure prophylaxis may explain the higher prevalence in adults[35, 36]. This proportion differs from other Brazilian regions that showed a higher prevalence in children aged from 10 to 14 years (three cases), resembling indicators of the 1990s, probably linked to greater exposure to animals during plays[18].

Regarding sex, the data indicate a high incidence of rabies in men in all Brazilian regions. This finding differs from the literature, which showed homogeneous post-exposure prophylaxis percentages between men and women[36]. However, a higher number of interruptions in post-exposure prophylaxis in men may explain this result[36].

In the Northeast and other regions of Brazil, most transmissions were from unvaccinated animals (55% and 67%, respectively), and in the remaining cases, the immunization status was unknown (45% and 33%, respectively). This demonstrates that, despite high vaccination coverage, animals lack immunization, and patients report insufficient information to healthcare systems regarding the immunization status of domestic animals responsible for aggressions, which would facilitate the implementation of post-exposure prophylaxis[37].

CONCLUSION

The higher prevalence of human rabies in the Northeast region comprehends a multifactorial approach. Lower levels of socioeconomic development, lack of information on rabies transmission and disease lethality, underreporting of suspected cases, inadequate prophylactic care by healthcare professionals, and discontinuation of voluntary immunization schedules may be responsible for the numbers observed.

Moreover, since most cases in the Northeast region were from rural areas, it is crucial to emphasize to these populations the measures to handle animals that are economically valuable and discourage the breeding of wildlife, which may be infected and responsible for transmission to humans.

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