Received: 24 February 2017

DOI: 10.1111/zph.12444

ORIGINAL ARTICLE

WILEY

Characterization of rabies post-exposure prophylaxis in a region of the eastern Amazon, state of Pará, Brazil, between 2000 and 2014

N. S. De Paula[1] | E. A. Saraiva[1] | I. M. Araújo[1] | K. K. G. Nascimento[1] | D. A. Xavier[1] | K. S. Santos[2] | E. M. N. Abreu[3] | R. J. P. S. Guimãraes[2] | I. Abel[1]

[1]Laboratório de Epidemiologia e Geoprocessamento (EpiGeo), Programa de Pós-Graduação em Saúde Animal na Amazônia, Universidade Federal do Pará (UFPA), Castanhal, PA, Brasil

[2]Laboratório de Geoprocessamento do Instituto Evandro Chagas (IEC), Ananindeua, PA, Brasil

[3]Secretaria de Estado de Saúde Pública do Pará (SESPA), Belém, PA, Brasil

Correspondence
Isis Abel Bezerra, Laboratório de Epidemiologia e Geoprocessamento (EpiGeo), Programa de Pós-Graduação em Saúde Animal na Amazônia, Universidade Federal do Pará (UFPA), Castanhal, PA, Brasil.
Email: isisabel@ufpa.br

Funding information
PROPESP/UFPA

Summary

Animal bites are a serious public health issue, and prevention strategies have been consistently documented worldwide. The aim of this study was to characterize human anti-rabies treatment in 11 counties of the Salgado microregion, Pará state, Brazil, which borders the Bragantina microregion, where exposures of human rabies were reported in 2004 and 2005. A descriptive retrospective study was conducted using anti-rabies treatment notifications registered in the Information System for Notifiable Diseases (SINAN) database of the State Department of Public Health of Pará (SESPA) from January 2000 to December 2014. In this period, 13,403 exposures were reported, with a growing annual trend ($Y = 68.571x + 344.96$). The years 2012 and 2013 presented the highest exposure incidence. Salinópolis was the county with the highest average annual incidence per 10,000 persons (62.83), followed by São João de Pirabas (43.28) and São Caetano de Odivelas (41.27). Most patients were males (59.6%) and were 1–19 years old (48.7%). The main species involved in aggressions were dogs (74.1%), followed by bats (13.1%) and cats (7.4%). Biting was the most common kind of exposure, mostly on the lower limbs (39.6%). This study shows that aggression by bats was the second most common cause of demand for the service in the region for the past 14 years. The low quality of records may increase the difficulty of rabies surveillance in Pará.

KEYWORDS

bites, epidemiological surveillance, post-exposure prophylaxis, rabies, SINAN

1 | INTRODUCTION

Animal bites are a serious public health issue, and prevention strategies have been extensively documented worldwide (Masthi, Narayana, Kulkarni, & Gangaboraiah, 2014). Attacks inflicted by mammals may pose risks to human health, including the transmission of the rabies virus by contact with contaminated material, and typically saliva, through biting, scratching or licking by an infected animal (World Health Organization, 2014). In addition, such injuries may cause permanent disfiguration of the victim; however, such attacks are rarely fatal (Tenzin et al., 2011).

Rabies control in urban environments, where it is transmitted by dogs and cats, is possible with the adoption of prevention measures, such as vaccination of pets and post-exposure prophylaxis (PEP) in humans (Shim, Hampson, Cleaveland, & Galvani, 2009; Tenzin et al., 2011). After any kind of aggression, the exposed person should be examined by a health professional who can decide whether PEP is required. PEP includes three main procedures: immediate wound cleansing, rapid administration of immunoglobulin and a complete rabies vaccination protocol based on cell culture vaccines (Weant and Baker, 2013). However, the recommendation of PEP is also influenced by other factors, such as aggressor animal observation (Dodet, 2007).

In Brazil, human anti-rabies attendance is one of the compulsory notifications that must be registered in the Information System for Notifiable Diseases (SINAN). An epidemiological investigation using this system is conducted after any exposure of humans to a species that transmits the rabies virus (Oliveira et al., 2012). The analysis of SINAN records is a practice that may enable the implementation of dynamic diagnosis of the event in a population. This instrument can provide support for causal explanations of exposures or exposures of disease and can indicate the risks to people, thereby contributing to the identification of the epidemiological scenario of a given geographical region (Ministério da Saúde, 2009).

In Brazil, bats are primarily responsible for maintaining the rabies virus wild cycle, whereas dogs remain the major source of infection in the urban cycle in certain states (Saraiva, Thomaz, & Caldas, 2014). Between 2004 and 2005, 22 human rabies exposures were reported in northeast Pará state, with hematophagous bat species playing an important role in transmission of the disease (Fernandes, Costa, Andrade, & Silva, 2013).

The Salgado microregion is adjacent to the Bragantina microregion, where rabies exposures were reported in humans in 2004 and 2005. The populations of both municipalities live by the riverside, and artisanal fishing is the subsistence economic activity as well as maintenance of small vegetable gardens for their own consumption and engagement in a few extractivist practices. Thus, a more refined approach to animal aggressions is of fundamental importance given the habits and attitudes of the populations of these regions and their distribution between urban and rural areas.

The objective of this study was to characterize the anti-rabies treatment offered to inhabitants of the microregion of Salgado, state of Pará, eastern Amazon, Brazil, between 2000 and 2014.

Impacts

- After a 14-year retrospective study, notifications of anti-rabies treatment in the microregion of Salgado, state of Pará, Brazil, showed a growing linear trend.
- This is the first report in Brazil in which bats have been found to be the second most common species connected with human anti-rabies treatment.
- The populations affected are located on the edges of forest fragments or mangroves, live near rivers and fish for subsistence using the natural environment and seem to ignore rabies and prophylaxis measures.

2 | MATERIALS AND METHODS

A descriptive retrospective study was conducted based on anti-rabies treatment notifications registered in the SINAN database of the State Department of Public Health of Pará (SESPA). The exposures included were reported in the Salgado microregion between January 2000 and December 2014. This microregion covered an area of 5,784,461 km^2 and had 238,830 inhabitants as of 2010 (IBGE, 2010). The microregion is formed by 11 municipalities, namely, Colares, Curuçá, Magalhães Barata, Maracanã, Marapanim, Salinópolis, São Caetano de Odivelas, São João da Ponta, São João de Pirabas, Terra Alta and Vigia (Figure 1).

Variables considered in the survey process were (i) the municipality where the rabies exposure was reported, (ii) the age of the patient, (iii) the aggressor animal, (iv) the type of exposure to the virus, (v) the site and number of injuries, (vi) the condition of the animal, (vii) the treatment prescribed, (viii) any previous anti-rabies treatment taken by the patient, (ix) the time elapsed between the aggression and the demand for care, (x) the prescription of equine immunoglobulin rabies (ERIG), (xi) adverse reactions and (xi) data on discontinuation of treatment.

Certain variables had to be created: the time elapsed until medical assistance (=the day of attendance at the healthcare unit—the day of aggression), the reaction to treatment (ERIG + vaccine or only ERIG or only vaccine) and the number of doses applied (based on observation of the dates when the doses were applied). For the variable "site of injury," the category "more than one site" was created to organize all exposures with more than one site of aggression.

As SINAN was updated in 2006, for the variable aggressor species, which was assessed via a closed-ended question on both the older and the newer form, a category named "other" was created; this category included livestock animals, foxes and primates. These animal species were present in this category on the form used until 2005. Other non-specified animals were also included in this category.

All data were collected using TabWin 32 (version 3.6; DATASUS, Brasilia/DF, Brazil) and organized using Microsoft Office® Excel 2013, in which temporal trend analysis was conducted by linear regression. A trend was considered significant when the estimated regression model had $p \leq .05$. The data were then exported to the software SPSS® v.20.0 for a descriptive statistical analysis of the variables selected. The chi-square test at a 95% confidence interval was used to evaluate differences.

The spatial distribution of rabies exposures was assessed using the Brazilian Institute of Geography and Statistics Cartographic Bases (IBGE; http://www.ibge.gov.br), which was exported to and stored in the geographic information system (GIS) ArcGis v.10 for visualization, processing and analysis of the data. Demographic data obtained from the IBGE database were also considered to estimate the incidence of rabies exposures.

This research used secondary data, without access to the participants' identity. There was no risk to the analysed population.

3 | RESULTS

In total, 13,403 anti-rabies notifications were reported in the region during the period considered, with 893 exposures per year on average. The number of exposures varied between 187 in the year 2000

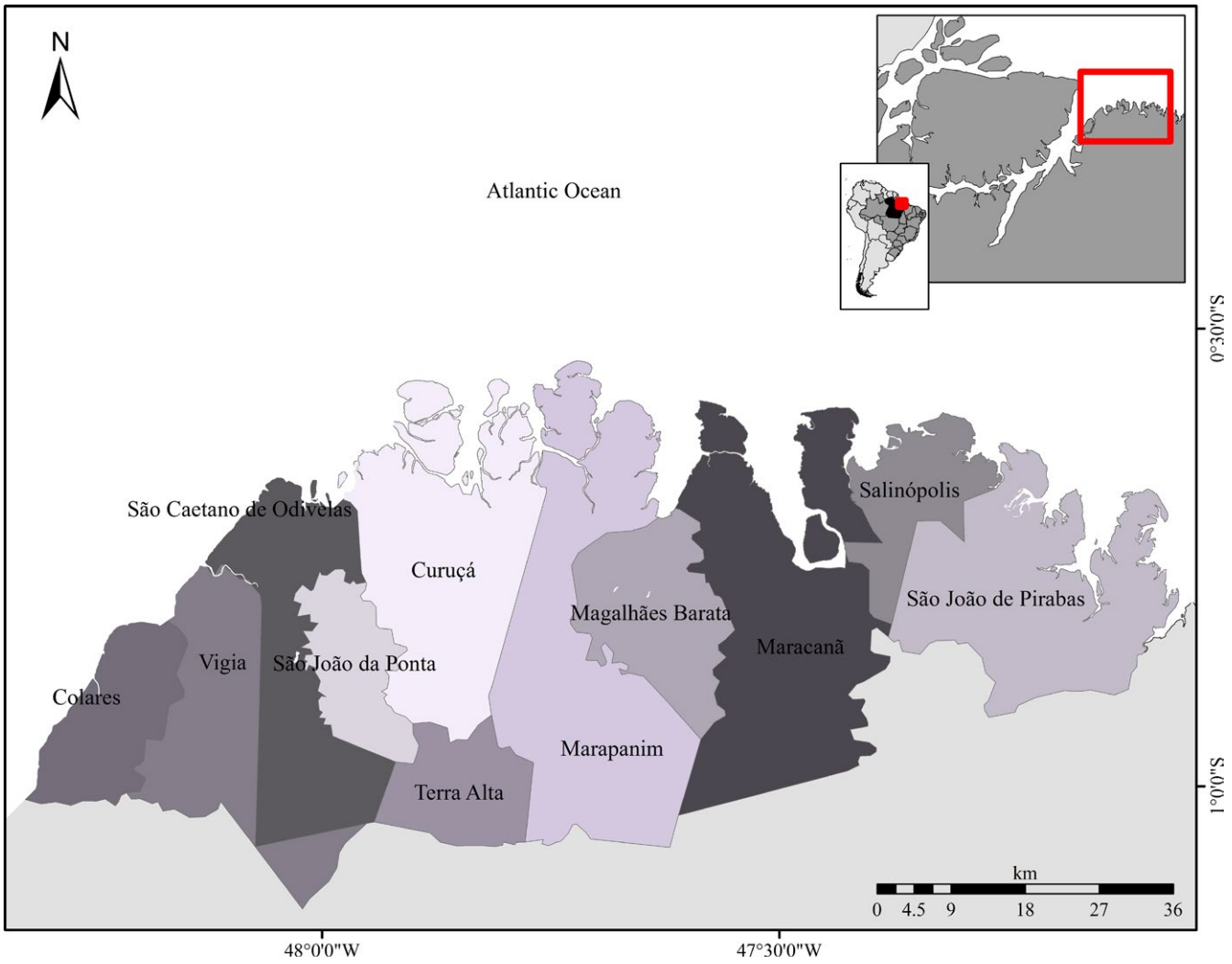

FIGURE 1 Salgado Paraense microregion, Pará, Brazil. [Colour figure can be viewed at wileyonlinelibrary.com]

and 13,312 exposures in 2012. Regression analysis revealed a growing linear trend, with increases in 68.57 new notifications per year (linear coefficient R^2 of .66 and p = .03).

The yearly distribution of notifications based on the species involved in the attacks is presented in Figure 2. Until 2001, no attack by hematophagous bats had been reported in any of the municipalities considered. However, in 2002, 81 attacks by bats were recorded, all of which occurred in the m1'unicipality of São Caetano de Odivelas. The number of exposures reported increased gradually with time, reaching significant values in the years 2004, 2005 and 2006. Hematophagous bats were the second most common aggressor species during this 3-year period, accounting for 32.4% (457/1,412) of exposures.

In the 14-year period covered in this study, in general, the main aggressor species was dogs (74.1%), followed by bats (13.1%) and cats (7.4%). Other species, such as primates, cattle, coati (*Nasua* sp), paca (*Cuniculus paca*), foxes and rodents, together represented 5.2% of notifications. The variable animal aggressor was considered as ignored on the remaining forms (0.2%). When the data were analysed by county, the annual incidence average per 10,000 persons varied from 19.33 in Maracanã to 62.83 in Salinópolis. Until 2004, the Salgado microregion showed a low aggression incidence. After that, the incidence increased and was maintained at the elevated level during the entire studied period, with some municipalities standing out, but without a geographical pattern (Figure 3).

The data obtained also revealed that 2012 and 2013 were the years when most exposures of anti-rabies treatment were notified. In every county, dogs were the main animals implicated, followed by cats. The exception was the municipality of Curuçá, where bats were the second most common major aggressor species, accounting for 10.4% of exposures (189/1,821), lending strength to informal reports of epidemiological surveillance regarding aggression by bats among humans in these municipalities.

Concerning the gender and age of the patients, most exposures occurred in men (59.5%) compared with women (40.5%) (χ^2 = 458.88, p < .01). People in the 1–19 age group represented 47.1% of the exposures reported. Children in the 5–9 age group (16.8%) were the most affected, followed by the 10–14 age group (13.8%) (Figure 4).

Most people who sought treatment had been bitten (79.8%, 10,591/13,266), followed by those who reported having experienced more than one type of exposure (9.5%, 1,267/13,266) and those who

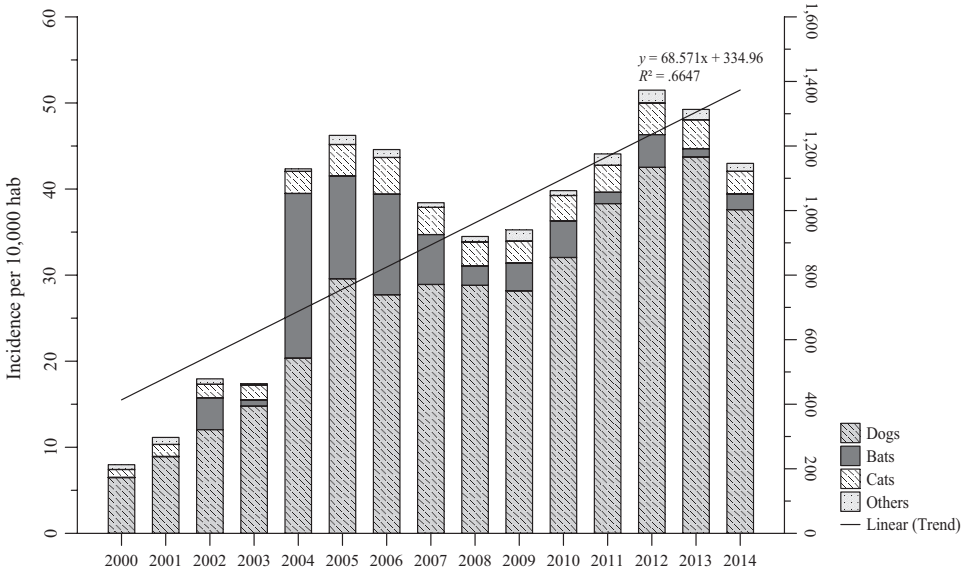

FIGURE 2 Incidence of bites per year of notification and the species involved for 10,000 inhabitants in the Salgado Paraense microregion, Pará, Brazil, from 2000 to 2014

had been scratched (6.4%, 854/13,266). The lesions reported during the period considered in this study were most commonly located on the lower limbs (39.5%, 5,240/13,260), hands and feet (28.1%, 3,729/13,260), and upper limbs (11.2%, 1,485/13,260). Concerning the size and type of wounds, most exposures reported included a single injury (56.2%), followed by surface wounds (49.5%). Certain patients reported having more than one wound (6.9%, 866/12,774) (Table 1). Considering these exposures and those in which the patients had been bitten, 77.9% of the patients did not receive a vaccine or ERIG.

Most people exposed to bats lived in rural areas (66.1%). The exposures reported in urban and peri-urban areas were less numerous, at 18.4% and 1.9%, respectively. However, this information was lacking in 13.6% of the notifications.

Several boxes were left blank on the 13,403 notification forms analysed. The main variables lacking proper information included the duration of previous treatment (if it ended before or after 90 days) (96.7%), active searching for the patient when the treatment was interrupted (92.3%), the reason for interruption of treatment (88.8%), prescription of equine rabies immunoglobulin (ERIG) (43.5%) and treatment interruption (43.3%). When these boxes were filled considering the initial 3-year period in which the vaccine used was suckling mouse brains (SMB) (n = 746), ERIG was not applied in any of the individuals. In the subsequent years in which the cell culture vaccine was used (n = 6,108 filled forms), 86.1% of the subjects received less than five vaccine doses, of which only 4.9% received ERIG. Also calls our attention the number of individuals who received 5–10 doses (n = 844), and in that category only 27% received ERIG (Table 2).

Importantly, no information about prescription of ERIG was provided in 52.2% of the reports of attacks by chiropterans throughout the study period. When this variable box was filled, the results revealed that 89.7% of patients received virus post-exposure treatment, whereas 9.8% received pre-exposure treatment and 0.4% received re-exposure treatment.

Data on the time elapsed between the attack and the provision of health care indicated that 93.2% of patients sought medical assistance after 0–10 days following the attack; 2.7%, after 10 days; and 4.1%, after 30 days. However, of the individuals who started treatment 30 days after the attack, 71.1% were bitten by bats, whereas dogs were the attacking species in 28.9% of exposures (χ^2 = 1749.97, p < .001).

4 | DISCUSSION

Notifications of rabies exposures are necessary for rabies surveillance. Here, we analysed a databank based on a 14-year period of anti-rabies treatment in the Salgado microregion, an area adjacent to the Bragantina microregion, where human rabies outbreaks occurred in the same period. To organize and analyse Brazilian surveillance data, the SINAN system was implemented gradually, starting in 1993; it was only in 1998 that the system became fully operational (Ministério da Saúde, 1998, 2007). Even so, in certain remote Brazilian areas, this system could not be accessed because of a lack of computational infrastructure in health units. This information may justify the low number of exposures reported in the first few years considered in this study, especially during the biennium of 2000–2001.

Spatiotemporal analysis demonstrated no geographical pattern. This finding was expected because most of the exposures involved dogs as the aggressor species. In general, the counties studied encompass large rural areas where dogs roam free, leading to conditions conducive to aggressions. However, in contrast to previous studies in the country, the present study demonstrated that bats are the second most common aggressor species in the region.

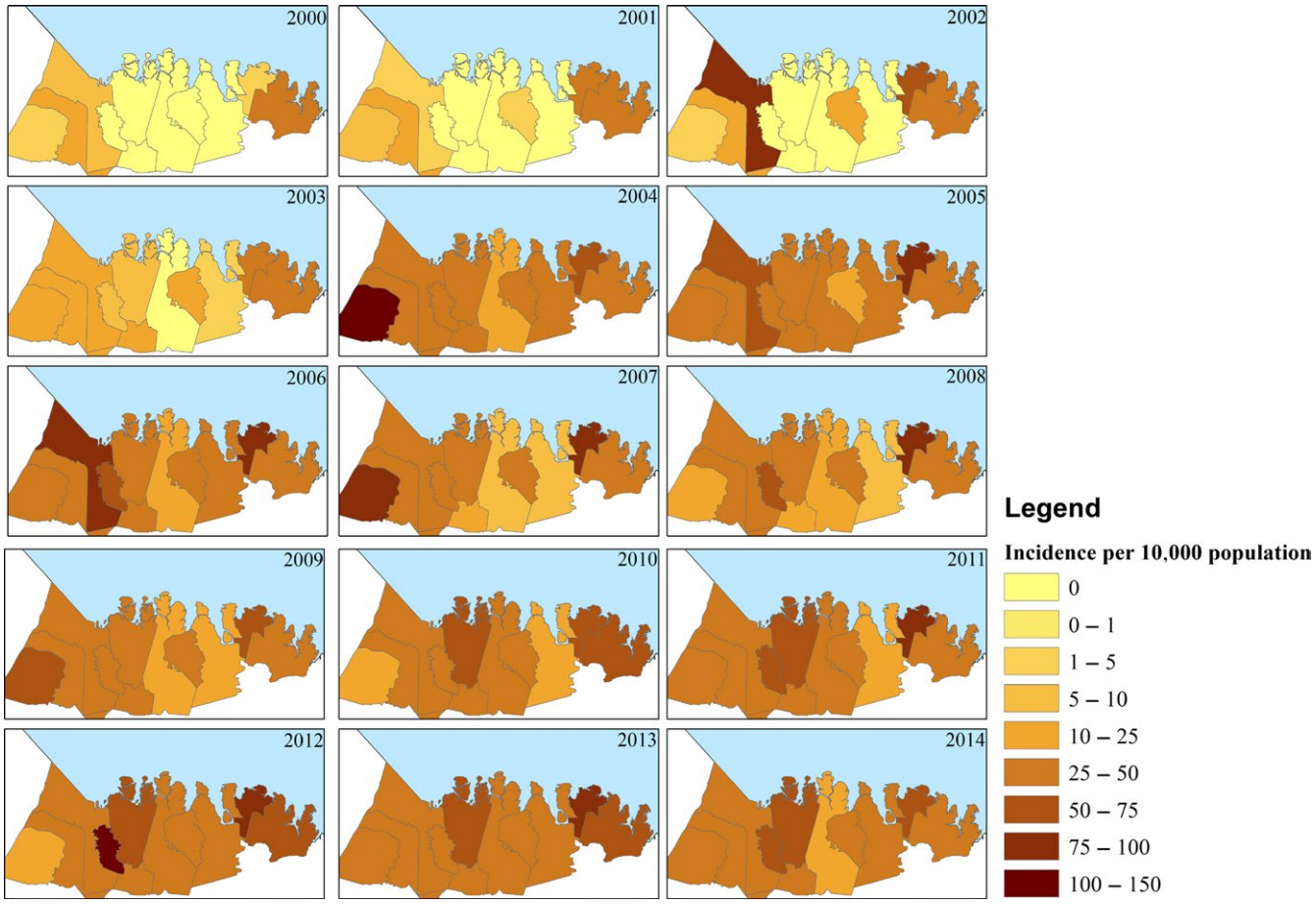

FIGURE 3 Spatiotemporal distribution of anti-rabies treatment in the Salgado Paraense microregion, Pará, Brazil, from 2000 to 2014. [Colour figure can be viewed at wileyonlinelibrary.com]

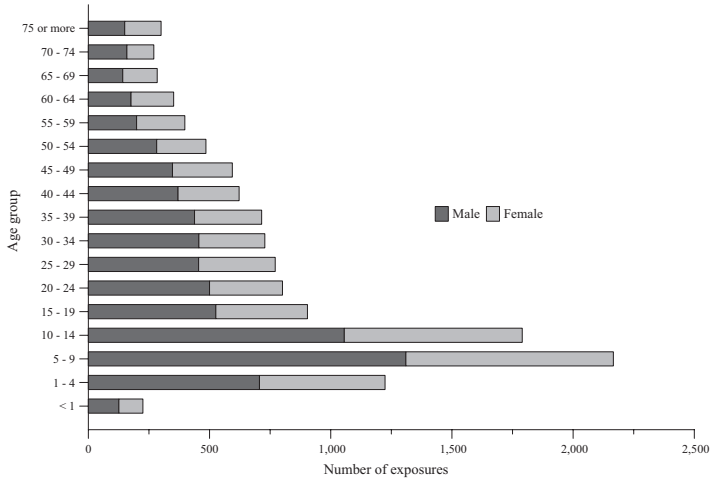

FIGURE 4 Distribution of anti-rabies treatment according to age and sex, in the Salgado Paraense microregion, Pará, Brazil, from 2000 to 2014

In 2004 and 2005, the state of Pará was the site of the largest human rabies outbreak caused by hematophagous bats ever recorded. The outbreak occurred in rural areas within extremely low-income populations (Schneider et al., 2009). In addition to the short distance between the region where outbreaks have been recorded and the area covered in the present study, the increase in reported exposures may also have been due to greater awareness concerning rabies and the implementation of educational measures underlining the importance of medical assistance after contact with potentially infected animals.

Studies covering the entire Brazilian territory (Veloso, Aerts, Fetzer, Anjos, & Sangiovanni, 2011; Saraiva et al., 2014; Oliveira et al., 2012) as well as other nations (Han et al., 2012; Shim et al., 2009; Song

TABLE 1 Characterization of wounds in patients of anti-rabies treatment in microregion Salgado Paraense, Pará, Brazil, from 2000 to 2014

	N	%
Kind of exposure		
Bite	10,591	79.8
More than one type	1,267	9.6
Scratch	850	6.4
Indirect contact	140	1.1
Licking	121	0.9
Other	38	0.3
Not informed	257	2.0
Total	13,266	100
Site of injury		
Lower limbs	5,240	39.6
Hand/foot	3,729	28.1
Upper limb	1,485	11.2
Head/Neck	925	6.9
Torso	547	4.1
More than one site	898	6.8
Mucosa	127	1.0
Not informed	309	2.3
Total	13,260[a]	100
Degree of injury		
Surface	6,322	49.5
Deep	4,794	37.5
More than one degree	886	6.6
Gash	665	5.2
Not informed	107	0.8
Total	12,774[a]	100
Kind of injury		
Single	7,345	56.2
Multiple	5,345	42.6
No injury	52	0.4
Not informed	115	0.9
Total	13,078[a]	100

[a]The total value differs for variables because of information missing in the report form.

et al., 2014) have indicated that cats are the second most common species involved in post-exposure rabies prophylaxis in humans under 19 years old. Attacks by chiropterans only account for approximately 0.5% of exposures in other Brazilian regions. Although worldwide dogs remain as the main organism that transmits rabies to humans, bats have been playing an increasingly prominent role in transmission (WHO, 2014). This finding was observed in the present study, which is the first report in Brazil in which bats have appeared as the second most common species connected with human anti-rabies treatment. This result underscores the importance of monitoring these exposures with consideration of the history of rabies transmission to humans by chiropterans in the region.

After 2004 and 2005, notifications of rabies exposures continued to occur. It seems that people are primarily concerned about the relationship between rabies and dogs, although the smaller number of notifications in which bats are the aggressor species indicates that more information is necessary to prevent another outbreak.

This study also detected an increase in notification by 2012 and 2013. Although the Brazilian Health Ministry had increased efforts to regulate epizootics and rabies as diseases with compulsory notification, no changes in technical standards related to rabies prevention in the human population that could justify this notification increase were reported (Ministério da Saúde, 2006, 2010).

Biting was the main type of exposure to the rabies virus, which is similar to previous findings observed in other Brazilian states, according to which 87.4% of patients were also exposed by being bitten (Veloso et al., 2011). However, the records analysed in the present study indicate that the number of patients who reported more than one type of exposure (9.5%, 1,267/13,266) was remarkably higher than the values observed in previous research, in which <5% of exposures were caused by more than one type of exposure (Han et al., 2012). These results shed light on the risk faced by individuals exposed to one contact with an infected animal once saliva is the most common and important transmission route of the rabies virus (Shim et al., 2009).

The analysis of the most frequent types of exposure to the rabies virus (bite) and wound extent (superficial) indicates that the attacks reported were mild to moderate (Ministério da Saúde, 2011). However, wounds are considered superficial only when no blood is present and deep when they are accompanied by blood, that is, when they cross the dermis barrier (World Health Organization, 2014). Therefore,

TABLE 2 Distribution of anti-rabies treatment according to the number of doses of SMB vaccine (until the year 2003) or cell culture vaccine with or without the application of ERIG in microregion Salgado Paraense, Pará, Brazil, from 2000 to 2014

Number of doses	SMB vaccine[a]	ERIG	Culture cell vaccine[b]	ERIG
0[c]	682 (91.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<5	52 (7.0%)	0 (0.0%)	5259 (86.1%)	256 (4.9%)
5–10	9 (1.2%)	0 (0.0%)	844 (13.8%)	228 (27.0%)
>10	3 (0.4%)	0 (0.0%)	5 (0.1%)	1 (20.0%)
Total	746 (100%)		6108 (100%)	

[a]Missing data—*n* = 588.
[b]Missing data—*n* = 5961.
[c]Dispense of treatment.

wounds caused by winged mammals (which have extremely sharp teeth) and those inflicted by dogs (which most often give rise to injuries with a dot shape) are both considered deep. Thus, the responsible health professional who completed the records may not have been informed about this issue.

An important fact to be considered is that the SINAN report form does not have specific questions about the evolution of a given case, which makes it impossible to evaluate whether the attack caused disfigurement or death for those patients with more than one wound.

In the rural areas of the counties studied, homes are often not surrounded by fences or walls, and animals roam freely, increasing the possibility of contact between children and dogs. Children are the main victims of dog bites and are not treated in most exposures because their exposure record is not declared or is unknown. Thus, many attacks remain unnoticed by parents or custodians (Hampson et al., 2008). In this sense, the results of the present study are similar to the findings published by Song et al. (2014), who reported 5,088 exposures of human rabies in China in children under the age of 15. These exposures represented 21.3% of the total number of rabies notifications from 2003 to 2009. The authors also observed that most children affected lived in rural areas, where guard dogs are normally kept by families.

The large number of attacks by bats analysed in the present study may be explained by the fact that the communities included are located on the edges of forest fragments or mangroves. In these environments, natural structures, such as hollow tree trunks, which bats use as shelter, are very common. The fact that children aged 5–9 years represent 13.2% of the victims of attacks by bats also lends strength to this hypothesis, given that children in this age group that remain inside the home at night.

The SINAN record form includes questions about the geographic coordinates of the home of the person attacked. However, no such information is considered when attacks occur in places other than the home. The populations studied often go fishing and hunting overnight, at locations distant from their homes, where they may become prey to vampire bats. This information is highly important in epidemiological analysis and could shed new light on the aerial cycle of transmission of the rabies virus, which requires special control measures. However, on all report forms analysed, the boxes reporting the geographic coordinates of the home of the victim and the destination were left blank. Such information does not provide details about the attack, but it would have been significantly useful in a spatial analysis, which could have been conducted in the present study.

The large amount of data omitted from the form may be explained by the fact that filling in the boxes is not compulsory or that the boxes do not have to be completed because they are defined by default in the pre-structured SINAN form. It should be emphasized that the form is confusing, given that certain boxes must be filled in by the health service attendant. Therefore, the results of the present study suggest the need to keep detailed records in epidemiological monitoring programmes, as discussed by other authors (Veloso et al., 2011; Oliveira et al., 2012).

PEP is a viable alternative in the effort to reduce the number of deaths associated with the rabies virus (Dodet, 2007). However, studies have shown that certain patients who died from rabies were infected with the *Lyssavirus* due to problems with healthcare (Han et al., 2012) or a delay before seeking medical assistance. In this context, the forms analysed in the present study indicate that most patients sought health care in due time. As the SINAN form does not register information about the address of the healthcare unit where the patient was attended, we could not identify the healthcare units' distribution. However, it is possible that patients who sought medical assistance after 10 days faced greater difficulties in reaching a healthcare unit because they lived in rural areas. In addition, given that PEP includes a long regimen of vaccines and ERIG via several visits to a healthcare unit, many patients feel discouraged from proceeding with treatment out of fear of missing a day of work (Masthi et al., 2014). It is possible that in many of these exposures, the treatment was interrupted by the health unit or abandoned by the patient. However, when analysing the prescription of ERIG and the number of vaccine doses applied the possibility of prescribing ERIG without necessity cannot be ruled out. Also, although we do not know what was prescribed, it is possible that there was a failure in the conduct, especially when the doses were applied above the recommended dose, without applying the ERIG, indicating that it was a serious case (Ministério da saúde 2002, 2011). As human deaths caused by rabies were attributed to the non-use of ERIG in the treatment, despite the vaccine protocol (Hampson et al., 2008), this analysis reinforces the need for training of health professionals for both adequate care and completing the form.

The fact that 52.5% of the records in which the aggressor species was a bat did not have information on ERIG use challenges the notion that bat bites pose serious health hazards and require treatment with ERIG, independently of the chiropteran species involved (Ministério da Saúde, 2011).

Over the years, updates in SINAN research records have resulted in an overload of data, causing system problems as well as a lack of reviewing of routines and correction of inconsistent records (Ministério da Saúde, 2007, 2009). We noticed that the report form for anti-rabies treatment in humans was modified when the SINAN database was transferred from a Windows platform (1998–2007) to a net platform (2007 to the present day). This transfer increased the number of boxes on the non-standardized report form that were left blank or indicated as not available (Ministério da Saúde, 2007). Ultimately, this lack of information rendered these forms useless in the present analysis. Moreover, the format of certain variables underwent important changes. For example, in the net version of SINAN, a box for indicating the date of vaccination is not provided, making it more difficult to count the doses administered and discover whether the treatment prescribed included a delayed vaccine protocol. Another important point is that the SMB

vaccine used until 2002 was replaced by a cell culture vaccine in 2003, which is administered according to a different dosage system. Given that in the present study, the SMB vaccine was used for only 4 years and the cell culture vaccine was used for 11 years, it was impossible to compare adverse reactions related to these treatments.

The results of the present study highlight the need to intensify prevention measures against biting by animals, to implement appropriate treatment of victims and to ensure completion of notification forms with all required information to improve monitoring of attacks and the risk of human rabies reemergence in the region.

5 | CONCLUSION

The present study shows that the number of notifications of antirabies treatment in the Salgado Paraense microregion, state of Pará, Brazil, currently follows a growing linear trend. Attacks by bats were the second most common reason for which patients sought healthcare in the region in the past 14 years. Attacks were essentially superficial in character: mostly children and adult men were affected primarily on the lower limbs, hands and feet. The low quality of the records may increase the difficulty of rabies surveillance in the Pará state.

ACKNOWLEDGEMENTS

We thank PROPESP for financial support; the Epidemiological Surveillance Coordinator Secretaria de Saúde Pública do Estado do Pará (SESPA) BS Cardoso for sharing the database; and the researchers GRC Rivero, VD Cerqueira, JG Barreto and CCG Moraes for their valuable contributions.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ORCID

I. Abel http://orcid.org/0000-0002-3720-7457

REFERENCES

Dodet, B. (2007). An important date in rabies history. *Vaccine*, *25*(52), 8647–8650. https://doi.org/10.1016/j.vaccine.2007.10.004

Fernandes, M. E. B., Costa, L. J. C., Andrade, D. E. F. A. G., & Silva, L. P. (2013). Rabies in humans and non-human in the state of Pará, Brazilian Amazon. *Brazilian Journal of Infectious Diseases*, *17*(2), 251–253. https://doi.org/10.1016/j.bjid.2012.10.015

Hampson, K., Dobson, A., Kaare, M., Dushoff, J., Magoto, M., & Sindoya, E. (2008). Rabies exposures, post-exposure prophylaxis and deaths in a region of endemic canine rabies. *PLoS Neglected Tropical Diseases*, *2*(11), e339. https://doi.org/10.1371/journal.pntd.0000339

Han, M. G., Ryou, J. S., Jeong, Y. E., Ju, Y. R., Cho, J. E., & Park, J. S. (2012). Epidemiologic features of animal bite cases occurring in rabies-endemic areas of Korea, 2005 to 2009. *Osong Public Health and Research Perspectives*, *3*(1), 14–18. https://doi.org/10.1016/j.phrp.2012.01.002

Instituto Brasileiro de Geografia e Estatística (IBGE), Censo Demográficoi (2010). Disponível em http://www.ibge.gov.br/home/estatística/população/censo2010/populaçãopormunicipiozip.htm. Acesso em: 02/07/2014.

Masthi, N. R. R., Narayana, D. H. N., Kulkarni, P., & Gangaboraiah, A. B. (2014). Epidemiology and prevention of animal bite and human rabies in a rural community-One health experiment. *Asian Pacific Journal of Tropical Disease*, *4*, 486–490. https://doi.org/10.1016/S2222-1808(14)604495

Ministério da Saúde, Fundação Nacional de Saúde (1998). *Portaria n.º 73, de 9 de março de 1998. Constitui comissão para desenvolver os instrumentos, definir fluxos e no novo software do SINAN*. Brasília-DF: Boletim de Serviço da Funasa.

Ministério da Saúde (2002). *Normas Técnicas da Profilaxia da Raiva Humana*. Brasília-DF.

Ministério da Saúde, Portaria n. 5, de 21 de fevereiro de (2006). *Inclui doenças na relação nacional de notificação compulsória, define doenças de notificação imediata, relação dos resultados laboratoriais que devem ser notificados pelos Laboratórios de Referência Nacional ou Regional e normas para notificação de casos*. Disponível em http://tinyurl.com/jvhzjpv. Acesso em: 18 agosto de 2017.

Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica (2007). *Sistema de Informação de Agravos de Notificação (SINAN)*. 2.ª edição Série A. Brasília-DF: Normas e Manuais Técnicos.

Ministério da Saúde, Organização Pan-Americana da Saúde Fundação Oswaldo Cruz (2009). *A experiência brasileira em sistemas de informação em saúde*. vol *1*, Brasília, DF.

Ministério da Saúde, Portaria MS nº. 2472 de 31 de agosto de (2010). *Relação de doenças, agravos e eventos em saúde pública de notificação compulsória – Gabinete do Ministro*. Brasilia-DF.

Ministério da Saúde (2011). *Normas Técnicas da Profilaxia da Raiva Humana*. Série A-1ª edição. Brasília-DF: Normas e Manuais Técnicos.

Oliveira, V. M. R., Pereira, P. L. L., Silva, J. A., Miranda, C. F. J., Rodrigues, K. O., Rodrigues, T. O., & Moreira, E. C. (2012). Mordedura canina e atendimento antirrábico humano em Minas Gerais. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, *64*(4), 891–898. https://doi.org/10.1590/S0102-09352012000400016

Saraiva, D. S., Thomaz, E. B. A. F. T., & Caldas, A. J. M. (2014). Raiva humana transmitida por cães no Maranhão: Avaliação das diretrizes básicas de eliminação da doença. *Cadernos Saúde Coletiva*, *22*(3), 281–291. https://doi.org/10.1590/1414-462x201400030010

Schneider, M. C., Romijn, P. C., Uieda, W., Tamayo, H., Silva, D. F., Belotto, A., … Leanes, L. F. (2009). Rabies transmitted by vampire bats to humans: An emerging zoonotic disease in Latin America? *Revista Panamericana de Salud Pública*, *25*(3), 260–269. https://doi.org/10.1590/S1020-49892009000300010

Shim, E., Hampson, K., Cleaveland, S., & Galvani, A. P. (2009). Evaluating the cost-effectiveness of rabies post-exposure prophylaxis: A case study in Tanzania. *Vaccine*, *27*(51), 7167–7172. https://doi.org/10.1016/j.vaccine.2009.09.027

Song, M., Tang, Q., Rayner, S., Tao, X. Y., Shen, X. X., & Liang, G. D. (2014). Factors influencing the number of rabies cases in children in China. *Biomedical and Environmental Sciences*, *27*(8), 627–632. https://doi.org/10.3967/bes2014.095

Tenzin, D. N. K., Gyeltshen, T., Firestone, S., Zangmo, C., Dema, C., Gyeltshen, R., & Ward, M. P. (2011). Dog bites in humans and estimating human rabies mortality in rabies endemic areas of Bhutan. *PLoS neglected tropical diseases*, *11*(5), e1391. https://doi.org/10.1371/journal.pntd.0001391

Veloso, R. D., Aerts, D. R. G. de C., Fetzer, L. O., dos Anjos, C. B. dos., & Sangiovanni, J. C. (2011). Perfil epidemiológico do atendimento antirrábico humano em Porto Alegre, RS, Brasil. *Ciência & Saúde Coletiva*, *16*(12), 4875–4884. https://doi.org/10.1590/S1413-81232011001300036

Weant, K. A., & Baker, S. N. (2013). Review of human rabies prophylaxis and treatment. *Critical Care Nursing Clinics of North America*, *25*(2), 225–242. https://doi.org/10.1016/j.ccell.2013.02.001

World Health Organization (WHO). (2014). Retrieved from http://www.who.int/mediacentre/factsheets/fs099/en/ (Accessed October 13 2014).

How to cite this article: De Paula NS, Saraiva EA, Araújo IM, et al. Characterization of rabies post-exposure prophylaxis in a region of the eastern Amazon, state of Pará, Brazil, between 2000 and 2014. *Zoonoses Public Health*. 2018;65:395–403. https://doi.org/10.1111/zph.12444