

## Research Article

# Human Anti-Rabies Treatment in the Mucuri Valley, Brazil, 2017 – 2019

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## Abstract

**Background:** We aimed to describe the profile of people involved in accidents with potentially rabid-transmitting animals, and characterize the spatial distribution and temporal trend of post-exposure human anti-rabies treatments.

**Methods:** We carried out a descriptive cross-sectional study including all post-exposure human anti-rabies care and the respective prophylactic conducts reported in the Notifiable Diseases Information System of the Brazilian Ministry of Health that took place in the 23 municipalities of Mucuri Valley, Minas Gerais State, Brazil, in the period from 2017 to 2019.

**Results:** 3,691 notifications of human anti-rabies care were registered, with an average of 102.5 per month. Canine and feline species were the main aggressors. There was a progressive increase of the notifications in the period, and a heterogeneous spatial distribution of incidence with a greater concentration of care in the municipalities located in the north of the region.

**Conclusions:** Our data show a higher incidence of cases when compared to other regions of Brazil. In addition, they can serve as a parameter to stimulate new research in the area and support the decision-making of public health managers in the region, aiming at the timely prevention and control of these neglected conditions.

**Keywords:** Incidence; Post-exposure prophylaxis; Rabies; Health services; Brazil

## Introduction

Rabies is an anthroponosis characterized as progressive and acute encephalitis that has high case fatality. It is transmitted to humans by the inoculation of the rabies virus present in the saliva and secretions of an infected animal, mainly by biting and scratching. All mammals are susceptible to the rabies and, therefore, are possible transmitters [1].

According to the World Health Organization, there are 55,000 estimated human deaths due to rabies *per year* worldwide, and approximately 40% are children under 15 years old [2]. Geographically, it is observed that about 99% of deaths occur in Asia and Africa and dog is the main transmitter [3]. In Brazil, from 2010 to 2020, 38 cases of human rabies were recorded. Of these, the dog was the aggressor animal in nine, bats in 20, non-human primates in four, and felines in another four, and in one of these, it was not possible to identify the aggressor animal [4].

The reduction in the number of human rabies cases in Brazil is due to the structuring of a surveillance system with a group of

actions of animal vaccination and post-exposure vaccination in humans [5]. Since 2013, there is no human rabies cases reported in the state of Minas Gerais, despite the reports of anti-rabies care are among the three most reported in the country [6]. Due to difficulties to implement agricultural defense actions, some regions of the state have frequently registered cases of rabies in cattle, as is the case of the 23 municipalities that compose the Mucuri Valley region. The last case of human rabies in Mucuri Valley took place in 1999 in the municipality of Fronteira dos Vales. However, until 2004 there were still cases of rabies in dogs and cats in this region [7].

Comprehensive national epidemiological studies on human rabies prophylaxis are scarce [8]. Among the studies carried out so far, the studies by Mota et al. (2016) [9] in Rio Grande do Sul, by Benedetti et al. (2020) [10] in Roraima; by Rigo & Honer (2005) [11] in Campo Grande, by Veloso et al. (2011) [12] in Porto Alegre and by Nascimento et al. (2019) [6] in Rio de Janeiro. Between 2007 and 2015, studies in Ceará evaluated the

completeness of notifications, the profile, the temporal trend, and the prevalence of inadequate post-exposure anti-rabies care [13-16]. And there was a prescription of 95.8% for inappropriate conduct, which also suggested the need to improve the quality of health service records. On the other hand, some studies point to levels above 90% of adequately indicated care in the cities of Porto Alegre (2006), Curitiba (2010), and Maringá (1997) [12,17,18].

Among the limited number of studies carried out on the subject in Minas Gerais, the study by Oliveira et al. (2012) [19] described and evaluated aspects of human anti-rabies care in Minas Gerais, from 1999 to 2004. Two other published studies were carried out in the capital Belo Horizonte, the first was conducted by Oliveira (2013) [20] who evaluated the spatial-temporal distribution of cases of canine aggression between 2007 and 2011; and the second by Cabral (2015) [21] who showed that among the post-exposure care associated with accidents with dogs between 2011 and 2012, the human anti-rabies care was inadequate in 32.7%, excessive in 21.2% and insufficient in 11.5%. To date, there are two studies published on the subject in Minas Gerais, one deals with the assessment of the potential risk of human rabies from canine aggression in Muzambinho - MG between 2005 and 2009, and the other on the compliance of human anti-rabies care in the south of Minas Gerais in 2015 [22,23].

Post-exposure human anti-rabies care in the municipalities of Mucuri Valley follows the Technical Standards for Human Rabies Prophylaxis [24,25]. The teams perform the primary care of each case, notify and, when necessary, prescribe and refer the patient to a referral unit or hospital to access the vaccine or serum. Since the Ministry of Health has recommended the centralization of vaccines, alteration of the vaccination schedule of 5 to 4 doses, and use of the intradermal route, preferably, for strategic reasons of the economy given the shortage of immunobiological [26,27].

Among the factors that possibly interfere with the efficiency of post-exposure human anti-rabies care in this region, we highlight the lack of knowledge for prophylaxis by part of the affected population, difficulty in accessing health services, operational problems caused by the lack of basic items such as: teams duly trained to conduct the prophylactic scheme; doctors in some units to prescribe the specific therapy, the vaccine in some reference units, the active surveillance of those who are absent from treatment, forecasting and provision of material resources that make timely and adequate care unfeasible. Furthermore, there is a considerable number of municipalities in the region that remain silent on human anti-rabies care since the lack of adequate notification of professionals involved in surveillance and rabies control can lead to failures in these activities [19,28].

Considering that the studied region has faced weaknesses due to the reduced availability of the human rabies vaccine, combined with the heterogeneous pattern of animal vaccination coverage in recent years and the deficient physical-operational structure installed in its health equipment, it was necessary to seek to understand the characteristics of people involved in accidents with animals potentially transmitting rabies, in addition to characterizing the spatial distribution and temporal trend of post-exposure human anti-rabies care that took place Mucuri Valley, Minas Gerais, Brazil, from 2017 to 2019.

## Methods

This is a descriptive cross-sectional study with a quantitative approach. All post-exposure human anti-rabies attendance and the respective prophylactic measures adopted were reported to the Notifiable Diseases Information System, of the Brazilian Ministry of Health.

The Mucuri Valley mesoregion is one of the 12 political-administrative divisions that make up the State of Minas Gerais in Brazil. It is located in the northeast region of the state and borders the states of Bahia and Espírito Santo to the east, the Jequitinhonha Valley mesoregion to the north and west, and the Rio Doce Valley mesoregion to the south. It comprises 23 municipalities with a population of approximately 397,096 inhabitants [29]. It is considered one of the poorest regions of the state, with a medium municipal Human Development Index (HDI) of 0.68. This mesoregion concentrates the largest number of illiterate adults over 25 years of age (33.42%) and has a rate of 34.4% of people with the lowest *per capita* household income in the state (less than US\$ 29,20), according to the Minas Gerais Social Responsibility Index [30].

Teófilo Otoni is the largest municipality in the mesoregion with approximately 141,502 inhabitants, in an area of 3,242 km<sup>2</sup> and a population density of 43.64 per km<sup>2</sup>, 445 km away from the state capital; the smallest municipality in the mesoregion is Umburatiba, with about 2,718 inhabitants. Teófilo Otoni is also the headquarters of the Regional Health Superintendence of the State of Minas Gerais, which is responsible for managing, planning, and supervising the health of 23 municipalities, which have a population of approximately 507,788 inhabitants (Figure 1).

The data source was based on the investigation forms of human anti-rabies attendance used throughout the Brazilian territory. This form consists of 60 variables referring to general data on victims of animals potentially transmitting rabies, in addition to epidemiological information on the exposure and on the human anti-rabies care adopted.

The sociodemographic variables included in this study were:

- a) Municipality where the injury occurred;
- b) Sex (male/female);
- c) Skin Color (brown/white/black/indigenous/Asian);
- d) Education (illiterate/elementary school I/primary school II/high school/higher education);
- e) Age group (0 to 4 years old, 5 to 19 years old, 20 to 59 years old, 60 years old and over);

The age groups of the people involved were divided according to the stages of human development (children/adolescents, adults, and elderly), respecting the classification based on the Children and Adolescents Statute and the World Health Organization.

- a) Area of residence (urban/rural/peri-urban);

The variables referring to the characteristics of exposure and injury were:

- a) Type of aggression (bite/scratch/lick/indirect contact/other)

- b) Presentation of the lesion (single/multiple/no lesion);
- c) Depth of the lesion (superficial/deep/lacerating);
- d) Anatomical region of the lesion (lower limbs/hands-foot/upper limbs/head-neck/trunk/mucosa);

Variables referring to the characteristics of the aggressor animals:

- a) Species of the aggressor animal (dog/cat/bat/non-human primates/domestic herbivores and foxes);
- b) Initial physical condition of the animal, therapeutic conduct in human victims and reason for interrupting treatment, and classification of the severity of the cases;

The incidence coefficient of human anti-rabies care was calculated from the number of cases multiplied by 10,000 and divided by the population of each municipality that makes up the Mucuri Valley. The estimated resident population for each year came from the Department of Informatics of the Unified Health System [29].

Data were exported and analyzed using Stata software version 11.2 (Stata Corp LP, College Station, TX, USA) [31]. The attendances analyzed were characterized according to the variables described. For the time trend analysis, simple linear regression was used, with the months of the year as an explanatory variable and the monthly incidence of human anti-rabies consultations per 10,000 inhabitants as the outcome. The equation and its statistical significance were calculated, as well as the coefficient of determination. The spatial distribution was evaluated with crude and smoothed data. The monthly incidence of human anti-rabies care was subjected to a smoothed analysis to remove the effect of instability and reduce the risk of the occurrence of a certain event in a small population. The spatial distribution analysis was performed using the Terra View 4.2.2 software. The tables containing the crude and smoothed indicators were imported to the ArcGIS 9.2 program, for making the maps.

The research was conducted by the ethical precepts of the National Health Council Resolutions nº 466/2012, 510/2016. The authors did not have access to data that would allow the identification of subjects. Secondary data were obtained with authorization from the Regional Health Superintendence of Teófilo Otoni, belonging to the Health Department of the State of Minas Gerais.

## Results

In the evaluated period, 3,691 notifications of human anti-rabies care were registered, with an average of 102.5 per month. There was a predominance of cares in males (2,012; 54.5%), of brown-skinned color (2,712; 73.5%), aged between 20 and 59 years old (1,756; 47.6%), of elementary school (587; 16.0%) and residents of the urban area of these municipalities (2,904; 78.7%). There was a low-quality level of information regarding the education variable, since the notifications showed a considerable index of the field selected in "not applicable/blank" (2,026; 54.8%). Exposure by biting was the most responsible for anti-rabies care, with 3,291 (89.2%) notifications, followed by exposure by scratching (553; 15.0%) and licking (99; 2.7%). The most affected body sites were the lower limbs (1,492; 40.4%), hands/feet (1,427; 38.7%) and upper limbs (525; 14.2%). Single lesions (2,415; 65.4%), multiple lesions (1,187; 32.2%), and superficial lesions (2,150; 58.2%) were the most frequent. It is

emphasized that all the fields on the characteristics of the exposure and the wound were duly filled in (Table 1).

**Table 1:** Distribution of post-exposure human anti-rabies care according to sociodemographic characteristics and exposure and injury characteristics, in Mucuri Valley, Minas Gerais, Brazil, 2017-2019 (N=3,691).

Variables	n	%
Sex		
Male	2,012	54.5
Female	1,679	45.5
Ethnicity/skin color		
Brown	2,712	73.5
White	600	16.3
Black	289	7.8
Indigenous	53	1.4
Asian	21	0.6
Ignored/Blank	16	0.4
Level of schooling		
Illiterate	170	4.6
Elementary school I	587	16
Elementary school II	324	8.8
High school	437	11.8
Higher education	147	4
Not applicable/Blank	2,026	54.8
Age group (years)		
0-4	276	7.4
5-19	1,008	27.3
20-59	1,756	47.6
≥60	641	17.4
Ignored/Blank	10	0.3
Area of residence		
Urban	2,904	78.7
Rural	726	19.7
Peri-urban	20	0.5
Ignored/Blank	41	1.1
Type of aggression		
Bite	3,291	89.2
Scratch	553	15
Licking	99	2.7
Indirect contact	52	1.4
Other	33	0.9
Lesion		
Single	2,415	65.4
Multiple	1,187	32.2
No injury	26	0.7
Ignored/Blank	63	1.7
Type of Lesion		
Superficial	2,150	58.2
Deep	1,369	37.1
Lacerating	205	5.6
Lesion Location		
Lower Limbs	1,492	40.4
Hands/Feet	1,427	38.7
Upper Limbs	525	14.2
Head/Neck	279	7.6
Trunk	161	4.4
Mucosa	76	2.1



In 2,311 (62.2%) of the cares, the animal was declared healthy at the time of exposure. Of the total number of aggressions by dogs and cats, 3,561 (96.5%) were subject to observation. However, the most prevalent type of treatment indicated was observation together with the vaccine, with 1,422 records (38.5%); followed by vaccine (894; 24.2%) and observation of the animal (857; 23.2%). It is observed that 6.0%, 221 notifications of people who were exposed to this condition had already received post-exposure rabies prophylaxis (Figure 2). It was observed that (1,772; 48%) of the undergoing anti-rabies care were not interrupted, unlike others 343(9.3%) interrupted ones. It is also noted that in 1,576 notifications (42.7%) the treatment interruption field was not filled in.

The canine aggression was the most predominant (3,036; 82.2%), followed by the feline (525; 14.2%) and *Chiroptera* (32; 0.9%). Aggressions caused by non-human primates, domestic herbivores and foxes accounted for 10(0.3%), 4(0.2%) and 2(0.1%) cares, respectively.

There was a progressive increase in the incidence each year (2017: 26.0 attendances per 10,000 inhabitants), (2018: 31.3 attendances per 10,000 inhabitants.), with emphasis on the year 2019 (35.9 attendances per 10,000 inhabitants). The temporal trend indicated a statistically significant increase in incidence in the period with a coefficient of determination of 43.9% ( $p < 0.001$ ). A higher incidence was observed in January, March, and August in 2017; in 2018 the highlight months were January, March, and July, and in 2019, the highlight was in January, April, August, and December. February remained with a low incidence in the three years evaluated (Figure 3).

The municipalities of Umburatiba and Fronteiras dos Vales, located in the northern region of the mesoregion, had the highest levels of average incidence of human anti-rabies care per 10,000 inhabitants throughout the evaluated period (191.3 and 145.5, respectively). The lowest coefficient occurred in the municipality of Ataleia, located in the southern region of the mesoregion, with 18.2 attendances per 10,000 inhabitants (Figure 4).

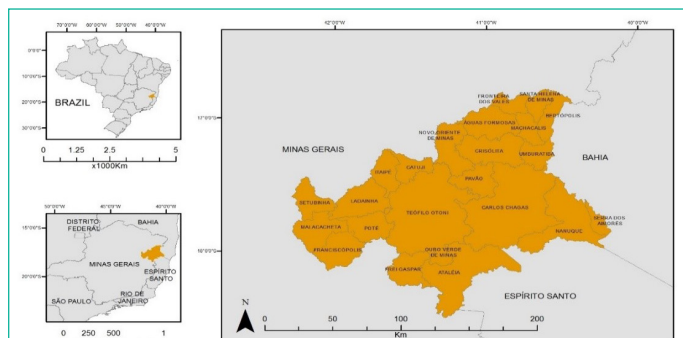


Figure 1: The geographical location of the municipalities that make up the Mucuri Valley mesoregion, Minas Gerais, Brazil.

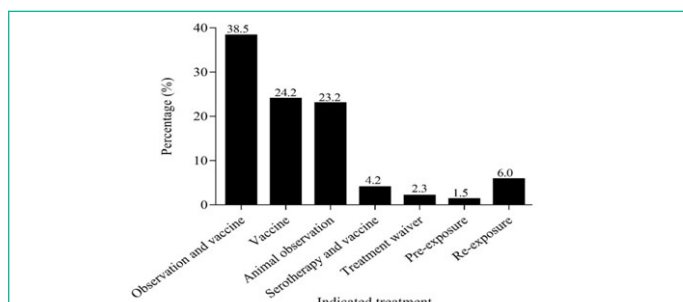


Figure 2: Distribution of frequencies of treatments indicated in post-exposure human anti-rabies care, Mucuri Valley, Brazil, 2017-2019 (N=3,691).

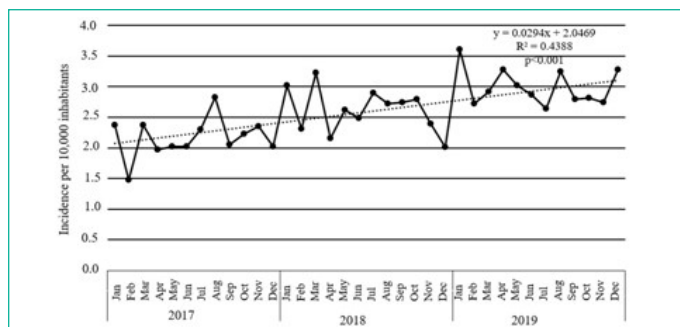


Figure 3: Temporal trend in the incidence of post-exposure human anti-rabies care (per 10,000 inhabitants) in the municipalities of Mucuri Valley, Minas Gerais, Brazil, 2017-2019.

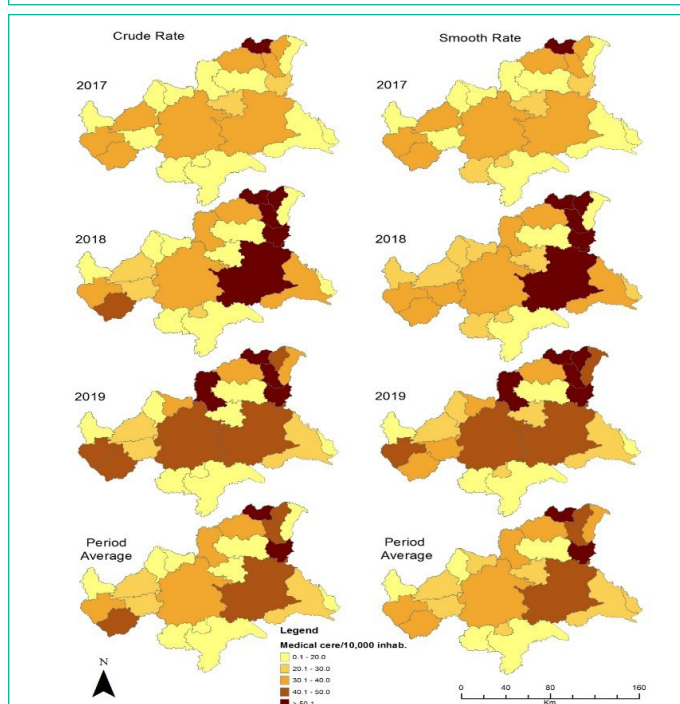


Figure 4: Spatial distribution of human anti-rabies attendance in the municipalities of Mucuri Valley, Minas Gerais, Brazil, 2017 to 2019. A- Crude Rate; B - Smoothed Rate.

### Discussion

This is the first study that describes the epidemiological situation of post-exposure human anti-rabies care in the 23 municipalities that make up the Mucuri Valley, making it possible to know through a sociodemographic approach the temporal trend and the spatial distribution of the identified cases will allow the prevention and control strategies of human rabies that take into account the fragility and potential of this region [12].

Although the population of the study region is predominantly female, it was shown that post-exposure human anti-rabies attendance was more frequent in males, a fact also observed in the state of Roraima, with 58.8% [10]. There was a higher proportion of brown-skinned, which is consistent with the ethnic composition of the region, which differs from a study in Rio de Janeiro whose results indicated a predominance of affected whites (70%) [6]. The participation of Maxakali indigenous people in attendance was 1.4%, and despite being higher than the national average of 0.5% [32], it is considered undersized because they are often affected by these animals, but rarely seek services, due to linguistic, cultural, and geographic barriers [33].

It appears that the educational level of the sample studied is compatible with incomplete elementary education, which is consistent with practically most of the studies consulted [14].

The age group that most underwent anti-rabies treatment was adults, in agreement with studies carried out in Salgueiro-PE, in 2007, where 47.9% of the consultations were in people between 20 and 59 years old [34]. As it affected more urban inhabitants, permanent surveillance is required, as this population group is more exposed to factors that increase the risk of exposure to this disease [35].

The biting pattern of this sample compared to other studies shows a higher level than that found in the state of São Paulo (80.5%) [36], but inferring the pattern found in Roraima, which was 93.0% [10]. The single lesion occurred in more than half of the aggressions, a result compatible with the study by Benedetti et al., 2020, with 54.1%, in Roraima, but contrary to the study by Santos, Melo, and Brandespim [37] which indicated a level of 58, 3% of multiple injuries. The superficial injury was the most prevalent, disagreeing with the result found by Carvalho and Silva [38] in a study also carried out in northeastern Brazil, in which they found a level of 77% of deep injuries. Most of those affected had their lower limbs affected, in agreement with the study by Cabral [21] carried out in Belo Horizonte from 2011 to 2012, which shows a proportion of 35.5%. On the other hand, it differs from most of the consulted studies that point to the predominance of hands/feet as the main place of exposure, according to a study in Chapecó-SC [39], in Ceará [14] and in Rio de Janeiro [6].

Observation together with the vaccine was the most frequent indicated type of treatment, in agreement with the studies carried out in Belo Horizonte with 57.2%, in Ceará with 49.9%, and in the mesoregion of Pernambuco with 70.4% [15,21,37]. In the study carried out in the state of Roraima, the vaccine alone was the most prevalent treatment with 41.6% [10]. The surveillance and control of this disease throughout the country over valueate vaccination to the detriment of animal observation, although there are studies in which the authors concluded that 93.9% of the consultations had the correct indication of treatment [40].

It is observed that the number of people who had previously received post-exposure rabies prophylaxis was higher than in the study carried out in Ceará, which accounted for an amount of almost 5% [15]. It is important to know if the person has already received previous prophylactic treatment to adopt the appropriate conduct, if the patient received complete treatment less than 15 days before the current accident, vaccination should be waived; if the previous regimen is incomplete, additional doses should be indicated [41].

It is observed that the number of post-exposure treatments in this region remains high, as in practically the whole country [42]. To reduce unnecessary prophylaxis, in addition to an increase in animal observation and integration of medical and veterinary health services are essential [12], a difficult challenge to be overcome by the lack of infrastructure in the health system and the low integration between the areas involved with the surveillance and control of these conditions in the evaluated municipalities.

It is worth mentioning the predominance of aggression caused by dogs. The lack of control and census of the canid and feline population is a challenge for the surveillance of this disease in the region. In addition, attention is drawn to the municipalities of Bertópolis and Santa Helena de Minas, which have the largest vulnerable population in the region, which is the Maxakali indigenous peoples, who, due to the habit of living with domiciled dogs and cats and domesticate wild animals

such as tamarins and bats are frequent victims of these aggressions that often go unnoticed by the region's health services, representing a serious problem of sanitary and environmental control [43].

There was a higher frequency of notifications in January of each year, a fact that may be related to the school vacation period and vacations of a considerable portion of the resident population. During this period, people are more exposed to animals, as the movement of individuals on public roads increases, which can increase the risk of this type of condition [19,39,44].

It is noted that the incidence of human anti-rabies attendance in some municipalities in the mesoregion exceeds the pattern found in the Kilifi municipality (Kenya), between 2006 and 2011 (30.2/10,000), that of the state of Roraima (54.4/10,000), considered the highest incidence in the country so far, surpasses that of Minas Gerais (12.2/10,000) in the period between 1999 and 2004, and also that of the state of São Paulo in the period from 2013 to 2017: (25.2/10,000) [10,19,36,45]. The municipalities with the highest incidence of attendance can be characterized by structural deficiencies: high turnover of health professionals, lack of health education, lack of animal control, or administration of vaccines in immunosuppressed animals [16].

Another issue to consider is that, in small territorial areas, inadequate social conditions can favor the spread of the rabies virus. Local social inequality increases contact between humans and domestic animals, characterizing a great risk to public health [6].

This study of human anti-rabies care in a low-income region in the state of Minas Gerais is pioneering because, for the first time, there is a parameter to analyze the performance of public health actions and services aimed at human anti-rabies prophylaxis and to discuss the epidemiological situation of this morbidity in this region, with the possibility of comparing the spatial and temporal trend of the incidence of this condition between the different municipalities of Mucuri Valley, with other mesoregions of the state and the country, given the considerable relevance of this theme for health public in the region.

Despite the limitation of secondary data, the present research becomes useful to broaden the debate on a neglected topic by Brazilian public health authorities and by the population itself. The use of secondary data did not influence the results, with the exception of the level of education variable, which was very poorly filled out.

## Conclusions

There was an increasing and significant trend in the incidence of post-exposure human anti-rabies care with a monthly fluctuation over the three years evaluated. Biting was the most prevalent type of aggression, with single and superficial wounds, and the lower limbs were the most affected. The urban area concentrated the largest number of cases with predominance in males.

There is a need to improve interventions to reduce the risk of rabies exposure in the municipalities in the northern of the mesoregion, which had higher incidences of anti-rabies care. Our data show a higher incidence of cases when compared to other regions of Brazil. This region needs to generate more epidemiological data to be processed, evaluated, and transmitted promptly to the health systems for timely decision-making.

## Author Statements

### Conflict of Interest

The authors declare that there is no conflict of interest.

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