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Research Article

Envenomings Caused by Venomous Animals in Roraima: A Neglected Health Problem in the Brazil's Northernmost State

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Abstract

Accidents caused by venomous animals are an important global neglected disease with high impact in Brazilian Amazon. The substantial numbers of envenomings registered in the Amazon region can be explained by the optimal conditions for the venomous fauna (*e.g* climate), however, the numbers are underestimated owing to extensive under-reporting. This study carried out an epidemiological study of envenomings caused by venomous animals in the state of Roraima, the Brazil's Northernmost state within a typical vegetation of Amazon rainforest. Envenomings by venomous animals between 2013 and 2016 were collected from 15 municipalities of Roraima and statistically analyzed using different parameters. Data were collected from the National Notifiable Diseases Information System (SINAN). During the studied period, Roraima presented 2,239 envenomings within venomous animals, with most of them registered in the capital Boa Vista. In addition, male victims between 20 and 39-years old prevailed. Regarding the length of time between the accident and therapy (*i.e* antivenom administration), 72.7% of the victims were treated in less than 6 hours. Fortunately, most of the Roraima envenomings were classified as mild, with exception to snakebites, in which victims were associated to present moderate envenomings, although deaths were considered rare. The high incidence of envenomings caused by venomous animals in Roraima, as well as the induced-moderate severity in victims of snakebites,contribute to the knowledge of the local reality, which is needed to advocate measures that aim to reduce the accidents by venomous animal attacks and promote therapeutic measures, such as supplying of specific antivenoms in places where they are most required.

Keywords: Amazon region; Epidemiological report; Envenoming; Roraima; Venomous animals

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Introduction

Accidents caused by venomous animals are considered a global public health problem due to high number of cases and the complexity of their clinical evolution [1]. Envenomings caused by these animals are classified as Neglected Tropical Diseases (NTD), since they affect almost exclusively low-income people, deprived of political power, and living in developing regions [2-4]. Snakebites leads the severity of envenomings, being responsible for most of disabilities and premature deaths worldwide. According to the World Health Organization (WHO), it is estimated that 7,400 people every day are bitten by snakes, resulting in 2.7 million cases of snakebite envenomings in the continent and about 81,000 to 138,000 deaths each year [4].

In Brazil, despite the magnitude regarding the incidence of the venomous animals' accidents, there is no uniformity of them through the regions [5]. While North and Central-West regions present snakebite prevalence, in the Northeast and Southeast regions scorpion stings prevailed [6,7]. On the other hand, in the South region, spiders are responsible for the highest number of accidents [5]. These geographic variations reflect the different degrees of human occupation in each region, the ecological imbalance caused by disordered urban growth, and the particular habitat that the animal can be adapted (*e.g Tityus serrulatus* scorpion demonstrated easy adaptation with high proliferation in most of Brazilian urban areas) [8-10]. It is important to note that only after June 1985 (during a high crisis and low production of antivenoms in the country), the notification of accidents with snakes became mandatory in the country. Later (1988), reporting scorpionism and araneism also became mandatory, which results in the National Program for Control Accidents by Venomous Animals (*Programa Nacional de Controle de Acidentes por Animais Peçonhentos*) [11].

The state of Roraima is the Brazil's Northernmost state, presenting a typical vegetation of Amazon rainforest, besides being able to encompass favorable climatic conditions (equatorial and tropical) to shelter a wide biodiversity in almost all its territory, similar to the other Brazilian states of the North region [5,12,13]. Together, all these conditions possibly justify why the Amazon region presents the highest incidence of snakebites. Interestingly, the Amazon stable temperature during all the year (average of 27ºC) present relevant effect upon the reproduction of reptilians based on the inability of keeping themselves warm [14,15].

Despite the long history and high prevalence of accidents with venomous animals in Brazil, there are still few epidemiological studies regarding envenomings in the country [14,16], especially in the state of Roraima. Although underreported accidents are a problem in all Brazil, Roraima can be highlighted due to the scarcity of

research investments and high number of Indians (more than 40% of the state is considered Indian areas), which potentiate underreporting data. Thus, the real statistics that provide a complete understanding of the current picture of the venomous animals' accidents in Roraima is inconsistent and underestimated. In this sense, the present study describes an epidemiological analysis of venomous animals' accidents occurred in the Roraima state.

Materials and Methods

The epidemiological data on envenomings for the period from 2013 to 2016 were obtained from National Notifiable Diseases Information System (SINAN), a public information system, available online by the Ministry of Health (see http://portalsinan.saude.gov.br/). Different variations were analyzed including year of incidence (2013, 2014, 2015, and 2016), municipality's incidence (Alto Alegre, Amajari, Boa Vista, Bonfim, Cantá, Caracaraí, Caroebe, Iracema, Mucajaí, Normandia, Pacaraima, Rorainópolis, São João da Baliza, São Luiz and Uiramutã), age group of victims, sex of victims, venomous animal responsible for the accident (snake, spider, scorpion, caterpillar, bees, others, and unknown), number of snakebite accidents according to the genus (*Bothrops*, *Crotalus*, *Micrurus*, *Lachesis*, non-venomous snake and unknow), interval between accident and therapeutics (0-6 hours, 6-24 hours, and unknown), and envenoming severity (healing and deaths).

Data was obtained using Tabwin32 (version 4.14) and statistical analyzes were performed to verify the normal distribution (Shapiro Wilk's test) and homogeneity (Levene and Brown-Forsythe test) of the results, followed by parametric tests (in the presence of these conditions) or non-parametric tests (in the absence of these conditions).

Comparison between the different victims' age groups of accidents caused by venomous animals, different species of animals responsible for the accidents, and number of accidents caused by the different snake genus were performed by One-way of Analysis of Variance (ANOVA) followed by Tukey or Kruskal-Wallis test. The difference between the occurrence of accidents by venomous animals between the female and male patients was evaluated by Student's t-test for independent samples. Possible association between the type of accident and the time for the therapeutic intervention, as well as between the type of accident and the severity of the envenoming was evaluated by the Chi-Square or Fisher's Exact test. Statistical analysis was performed using the Excel Software (Microsoft Office 2013, Redmond, WA, USA), Graph Pad Prism 5.0 (La Jolla, San Diego, CA, USA), or Statistica 12.0 software (StatSoft). Statistical significance level was set at 5% ($p < 0.05$).

Results

During 2013 to 2016, a total of 2,239 cases of accidents involving venomous animals was reported in the state of Roraima. The 2014 year showed the highest number of accidents (589) followed by 2016, 2013, and 2015 with 583, 546, and 521 reported cases, respectively (Figure 1).

Concerning Roraima municipalities, the highest accidents numbers were registered in Boa Vista (state capital), which presented 1,048 victims through all the analyzed period, corresponding to 46.8% of the total number of accidents among the 15 municipalities analyzed (Table 1). Other municipalities also presented relevant number of envenomings during the four years analyzed, however presenting lower victims than the state capital. Alto Alegre was the second city with highest number of victims during the analyzed period, with a total of 434 cases, corresponding to 19.38%. Amajari (110 cases), Mucajaí (100 cases), Uiramutã (96 cases), and Rorainópolis (77 cases), also presented important relevance. On the other hand, Cantá, the municipality with the lowest envenoming victims, only held 5 cases during 2013. Interestingly, during the years of 2014, 2015, and 2016, Cantá did not registered any envenoming. The analysis of the victims' ages reveals that victims with 20 to 39-years old present the highest envenoming numbers (2013-192, 2014-186, 2015-199, and 2016-182 victims), followed by victims with 40 to 59 (2013-108, 2014-124, 2015-61, and 2016-118 cases), and with 15 to 19-years old (2013-65, 2014-77, 2015-66 and 2016-75 cases). Elderly group (*i.e* more than 70 years-old) presented fewest envenoming victims (Figure 2).

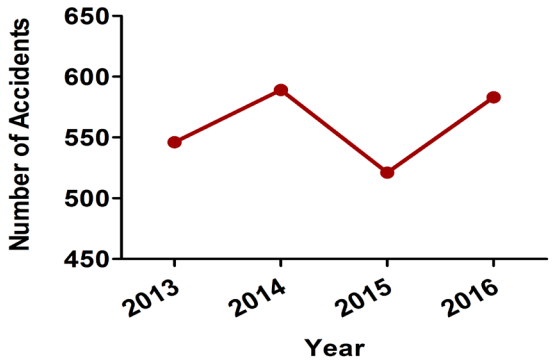

Figure 1: Envenomings in Roraima (2013-2016). This figure is in color in the electronic version.

Table 1: Distribution of envenomings by Roraima municipalities (2013-2016).

Roraima Municipalities	2013	2014	2015	2016	Total
Alto Alegre	95	108	115	116	434
Amajari	29	18	35	28	110
Boa Vista	250	262	263	273	1,048
Bonfim	10	21	4	9	44
Cantá	5	-	-	-	5
Caracaraí	19	21	11	12	63
Caroebe	15	16	10	12	53
Iracema	11	17	11	12	51
Mucajaí	20	23	17	40	100
Normandia	6	3	3	6	18
Pacaraima	22	13	15	13	63
Rorainópolis	22	35	5	15	77
São João da Baliza	18	13	8	10	49
São Luiz	7	7	8	6	28
Uiramutã	17	32	16	31	96
TOTAL	**546**	**589**	**521**	**583**	**2,239**

Regarding victim`s gender , there was a significant predominance ($p<0.05$) of men in all the analyzed years, presenting at least two-thirds of the total of the victims (2013-377 *versus* 169; 2014-377 *versus* 212; 2015-338 *versus* 183, and 2016-384 *versus*198 envenomings case, male and female, respectively) (Figure 3).

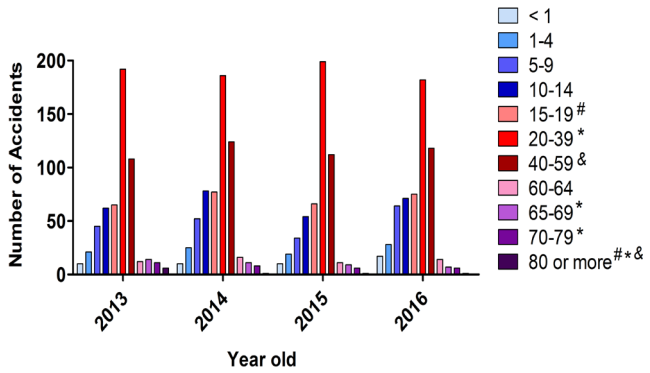

Figure 2: Roraima age-related number of envenomings (2013-2016)**.** Data was analyzed by Kruskal-Wallis test. Values of p<0.05 were considered statistically significant. Age range 15-19 was statistically significant with 80 or more (#). Age range 20-39 was statistically significant with 65-69, 70-79 and 80 or more (*). Age range 40-59 was statistically significant with 70-79 and 80 or more (&). This figure is in color in the electronic version.

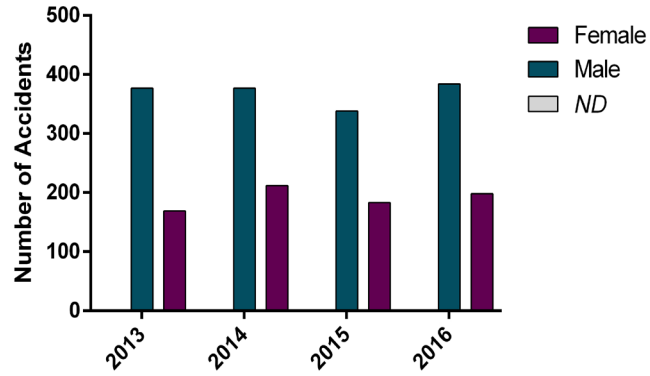

Figure 3: Roraima sex-related number of envenomings (2013-2016). Sex-related (male versus female) number of accidents were analyzed by Student's t-test. Values of p<0.05 were considered statistically significant (*). *ND* means not determined. This figure is in color in the electronic version.

Regarding the animals responsible for envenomings there were a significant predominance (p<0.05) of snakebites (2013-351, 2014-332, 2015-331, and 2016-326 cases) in comparison to other venomous animals. On the other hand, accidents triggered by scorpions appear in second position with more modest numbers than snakes (2013-62, 2014-80, 2015-81, and 2016-102 cases), followed by bees (2013-52, 2014-66, 2015-48, and 2016-81 cases), spiders (2013-22, 2014-27, 2015-23, and 2016-30 cases), and caterpillars (2013-9, 2014-11, 2015-4, and 2016-13 cases) (Table 2). In respect to snakes genera, *Bothrops* genus presented the highest number of envenomings (2013-247, 2014-233, 2015-119, and 2016-233 cases), followed by *Crotalus* (2013-34, 2014-22, 2015-26 and 2016-326 cases), *Lachesis* (2013-33, 2014-29, 2015-15 and 2016-22 cases), and *Micrurus* genera (2013-1, 2014-3, 2015-2 and 2016-4 cases) (Figure 4). Nevertheless, the statistical significance (p<0.05) was only observed between *Bothrops*, *Micrurus*, and non-venomous snakes. It is important to emphasize that in a high number of accidents the snake genus was not determined (unknown).

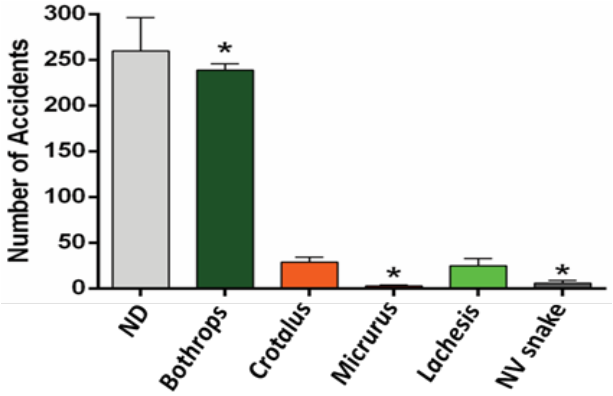

Figure 4: Total number of snakebites in Roraima according to the animal genus (2013-2016). Data was submitted to analysis of Kruskal-Wallis test. *indicates statistical difference (p<0.05) among them. *ND* means not determined. *NV* means non-venomous. This figure is in color in the electronic version.

The time between accident and medical care (antivenom therapy) was also evaluated. After excluding cases in which the venomous animal was not identified, a total of 1,319 (72.71%) victims were treated in less than 6 hours after the accident, meanwhile low number of victims were treated with more than 6 hours (21.3%) (Table 3). Interestingly, the statistical analysis demonstrated that ophidian accidents are associated with 78% of patients that received therapeutic intervention after 6 hours of the accident. On the other hand, accidents caused by spiders are associated with 6.2% of patients that received therapeutic intervention after 6 hours of the accident.

The victims' envenoming severity was also explored in this study. The analysis of all the reported cases (including those 198 cases where the severity was not stratified) reveals that 1,280 envenomings (57.1%) were classified as mild, 597 (26.6%) as moderate, and 164 (7.3%) as severe (Table 4). Notably, ophidian envenomings are high associated to the development of moderate pathological manifestations in victims, while other animals are associated to progress as mild envenomings (p<0.05).

Table 2: Number of envenomings in Roraima according to the different venomous animals (2013-2016).

Accidentyear	Snake	Spider	Scorpion	Caterpillar	Bees	Others	*ND*	Total
2013	351	22	62	9	52	36	14	546
2014	332	27	80	11	66	53	20	589
2015	331	23	81	4	48	32	2	521
2016	326	30	102	13	81	23	8	583
Total	**1,340[a]**	**102[b]**	**325[c]**	**37[b]**	**247[c]**	**144[b]**	**44**	**2,239**

Data was analyzed by ANOVA followed by Tukey's post hoc test. Values of $p<0.05$ were considered statistically significant. Different superscript letters indicate statistical difference. *ND* means not determined.

Table 3: Number of envenomings in Roraima concerning therapeutical intervention time (2013-2016).

Venomous Animal	0-6 Hours	6-24+ Hours	*ND*	Total
Snake	775	373	194	1,342[a]
Spider	52	30	20	102[a]
Scorpion	232	26	67	325[b]
Caterpillar	24	2	11	37[b]
Bee	147	28	72	247[b]
Others	89	17	37	143[b]
Unknown	17	2	24	43
Total	**1,336**	**478**	**425**	**2,239**

Data was analyzed by Chi-square test. Values of $p<0.05$ were considered statistically significant. Different superscript letters indicate statistical difference. *ND* means not determined.

Table 4: Roraima's envenoming clinical evaluation according to animal`s group.

Venomous Animal	Mild	Moderate	Severe	*ND*	Total
Snake	576	510*	157*	99	1342
Spider	76	14	2	10	102
Scorpion	272	26	2	25	325
Caterpillar	29	2	-	6	37
Bee	205	27*	-	15	247
Others	110	16*	2	14	144
Unknown	12	2	1	29	44
Total	**1,280**	**597**	**164**	**198**	**2,239**

Data was analyzed by Chi-square test.

*Indicates statistical difference ($p<0.05$) in comparison to the same venomous animal in the mild group. *ND* means not determined.

Clinical severity of envenoming (mild, moderate, or severe) was classified according to the Brazilian Health Ministry guidelines.

This peculiar distribution might be better observed once the cases are described as percentages, in which mild accidents represent 42.9% of the ophidian accidents. In addition, besides snakes present the highest numbers of moderate envenomings, they are also responsible to the most severe ones. For instance, the evaluation regarding type of accident and envenoming severity demonstrated that only ophidian accidents present a distinctive pattern of clinical evolution comparing to all analyzed peers. Meanwhile the specific statistical study demonstrated that, in exception to snakes, the other envenomings are prone to affect Roraima victims under the same clinical evolution (mild) since mild envenomings prevailed in spiders (74.5%), scorpions (83.6%), caterpillars (78.3%), and bees (82.9%).

Finally, the study of envenoming evolution, that is cure or death, reveals that 84.7% of victims evolved to cure, although 14.7% did not have their evolution registered (Figure 5A). Despite the high number of accidents in the state of Roraima, evolution to deaths is rare, and in the analyzed period there were only 9 deaths reported (2013-2, 2014-2, 2015-1, and 2016-4 deaths). Remarkably, 8 of the registered deaths were caused by snakebites (6 caused by *Bothrops*, 1 by *Crotalus*, and 1 by *Micrurus*) and one by another venomous animal genus (not mentioned in the database) (Figure 5B). Therefore, the presented panel suggests that, despite the accidents severity, time intervention of treatment is capable of preventing death in most of the envenomings in Roraima, leading to a very low lethality rate (0.004%).

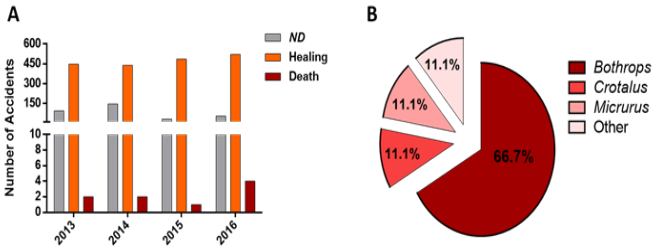

Figure 5: (A) Roraima envenoming evolution (cure versus deaths) (2013-2016); (B) Snakebite lethality distribution according to snake genus (2013-2016). *ND* means not determined. This figure is in color in the electronic version.

Discussion

Epidemiological data on envenomings within venomous animals are critical to reflect the real magnitude of these accidents. In Brazil, databases such as SINAN and National Poisoning Information System (*SINITOX, Sistema Nacional de Informações Tóxico-Farmacológicas*) are considered fundamental for the development of public health in the country, based on their analyzes it is possible to identify and quantify the antivenoms to be distributed into federated units. In other words, epidemiological studies can improve and strengthen production, supply, and distribution of life-saving antivenoms and other commodities in the country. Furthermore, based on the collected

data, government can determine strategic areas to be supervised, monitor and improve victims assistance in health units, as well as develop strategies to control envenoming accidents such as by prevention campaigns [17-20].

The present study analyzed epidemiological information on envenomings caused by venomous animals in Roraima state, the northernmost state of Brazil, with most of its area comprised of exuberant Amazonian rainforest sheltering ample biodiversity in almost all of its territory, similar to other Brazilian states of the North region [12,21]. Therefore, these factors express a great risk for the occurrence of envenomings, which possibly justifies the Amazon region having the highest incidence of ophidian accidents [14].

The number of envenomings caused by venomous animals in Roraima during the period 2013-2016 is low (less than 0.33%) compared to the numbers registered in Brazil (2013-159-597, 2014-168-399, 2015-172-014, and 2016-172-412) [22]. It is interesting to mention that in 2015, in the state of Roraima, there was a decrease in reported accidents. This occurrence could be a reflection of national public strategies to control these accidents such as:

i. Campaign to aware the population to avoid certain environments during rainy season, a season where snakes and other venomous animals usually leave their nests and invade urban areas [23-25];
ii. Propagation of the use of PPE (Personal Protection Equipment) to workers in specific areas, such as forests, open field, civil construction, and many others [26,27];
iii. Underreporting, incomplete registration, or omissions in data collection [16,18].

The distribution of accidents among municipalities reveals the highest number of notifications in Boa Vista, which was expected, since the capital presents most of the population of Roraima (63.5%), as well as concentrates the main health reference centers such as the General Hospital of Roraima (HGR, *Hospital Geral de Roraima Rubens de Souza Bento*) and the Children's Emergency Service (HCSA, *Hospital da Criança Santo Antonio*), besides the capital presenting the most health professionals trained to effectively report envenomings accidents compared to smaller municipalities. However, other municipalities such as Amajari, Mucajaí, Uiramutã, and Rorainópolis also present relevant contribution. These municipalities are located in forest boundaries, which could explain the high incidence of envenoming within venomous animals [21,28,29].

Regarding gender, it was reported highest number of envenomings with men in all age groups, especially males between 20 and 39 years old. This immediately suggests that accidents occur in economically active individuals and outside the home environment, probably due to working conditions that expose them to such risk (such as farming, hunting, etc) [30], which was previously observed [31-33]. Furthermore, this finding is in agreement with the national data [18,34].

Looking into the animal genera responsible for envenomings in Roraima, snakes predominated with nearly 60% of all accidents, which were especially caused by *Bothrops* (popular name *jararaca*) and *Crotalus* (rattlesnake, popular name *cascavél*) genera, which results can be supported by other studies [35,36]. The snakebite predominance can be justified by the fact that snakes have considerable preference for environments that are prone to rodent proliferation (*e.g* storehouses, barns, and rubble), located inside forests or surrounding forests, a very common places in the municipalities of Roraima [21,37-40]. Regarding rattlesnakes envenomings in the state, it is important to emphasize the *Crotalus durissus ruruima* species, which in Brazil can be found just in Roraima (although they habit southern Venezuela) [41]. Besides presenting particular components and high individual variation [42], the main problem is that *C.d. ruruima* venom is not used to produce anticrotalic antivenom in Brazil (horses are immunized with *C.d. terrificus* and *C.d. collilineatus* venoms, 50% of each) [43,44]. Indeed, antivenomic studies demonstrated that *C.d. ruruima* venom is not well recognized and neutralized by the Brazilian rattlesnake antivenom, recommending the use of botropic-crotalic antivenom for therapeutics of victims [41].

The scorpion envenomings reach the second position, being responsible for 14.51% of the total number of accidents in Roraima. Our findings differ from the epidemiological data from most of Brazilian states, such as São Paulo and Minas Gerais, where scorpionism leads [17,45,46]. One possible justification is the absence of *Tityus serrulatus* scorpion in Roraima, which is the species mainly responsible for the high scorpionism incidence in the country. In addition, Roraima presents low urbanized areas (*i.e* less populated state of Brazil), which results to lowland areas favorable to scorpion proliferation due to the low accumulation of debris, garbage, and insects [47].

During 2013 to 2016, 50.95% of the victims were treated in less than 6 hours after the accident, which suggest a positive scenario since only 7.42% of the envenomings were considered severe. Clinical severity of envenoming (mild, moderate, or severe) was classified according to the Brazilian Health Ministry guidelines [48]. Other study also analyzed the time interval in receiving assistance in Rondônia (other Amazon state), in which the time between the snakebite and arrival at the hospital was higher than 6 hours in 72.7% of patients [49]. According to studies conducted in the last 100 years in Brazil, the main challenge of treating envenoming patients is the delayed care, which will result in severe envenoming and difficulties to control venom effects into patient efficiently [18,50,51]. Thus, for the best prognosis and reduction of venom induced-sequelae, it is recommended that the victims are treated in the first 6 hours after the accident [50], which emphasizes that in Roraima state the envenomings are, in most of cases, being treated with less time delay. Notably, scorpions and caterpillars envenomings resulted in the earliest care (less than 1 hour), possibly because most of them occurred in urban areas, where access to treatment can be established earlier [28,52,53].

Although most of snakebites data were registered in Boa Vista, several happened in peripheric and/or rural areas, nearby cities, or even in Indian communities. Thus, a delay in the treatment is expected based on the distance from origin of the accident and the hospital. Moreover, Roraima habitants keep some traditional culture to treat envenomings and, in many cases, victims only look for properly medical care after using traditional medicines instead [54]. Indeed, a recent study demonstrated that only few native Indians were registered as having received treatment in Brazilian Amazon (6.88%) [33].

Despite the considerable number of accidents in Roraima state, evolution to deaths is rare, and in the analyzed period there were only 9 deaths (2013-2, 2014-2, 2015-1, and 2016-4 deaths). Out of the nine deaths, eight were caused by snakes, 75% affected by *Bothrops*, 12.5% by *Crotalus*, and 12.5% by *Micrurus genera*. Nevertheless, deaths from snakebites are known to be under-reported in the surveillance systems, which are estimated to be around 30% [55].

Beyond Brazil, other underdeveloped countries have also demonstrated high envenomings incidence within different numbers of mortality [56]. In Kenya, snakebites are considered a silent public health problem, presenting individual incidence between 2.7 to 6.7 per 100,000 inhabitants per year and 2.27% of mortality [57]. Although the country lacks a surveillance system to measure the incidence of snakebites, the Northern region of Cameroon presents 200 snakebites per 100,000 inhabitants [58]. In Costa Rica, there are reported 2 to 19 snakebite cases per 100,000 population per year [59]. On the other hand, Nigeria presents even higher snakebite incidence reaching 497 cases per 100,000 population per year and 12% of mortality. The high mortality in Nigeria can be explained by de low medical assistance, since only 8.5 % of snakebite victims attend hospitals in Nigeria [60]. Unlike underdeveloped countries, snakebite envenomings in developed countries are lower, as can be evidenced by Switzerland [61], France and Germany [62], Czech Republic [63], and USA [64-66]. Thus, a more detailed analysis of envenomings in underdeveloped countries is required, in order to design interventions that could reduce the impact of the public health problem in these countries.

Conclusion

The envenomings registered in Roraima consist a huge and largely neglected health problem in Brazil. The challenge of the region is to specify the requirements for antivenom production for the local necessities. In order to do this, it is essential to organize the collection of epidemiological data. Thus, this study outlined the Roraima epidemiological profile of envenomings, which demonstrated to be caused most by snakes (*Bothrops* and *Crolatus genera*), affecting mainly men aged 20 to 39 years. Furthermore, Roraima envenomings mostly presented mild evolution, with the majority of victims being treated in less of 6 hours, and rare deaths. Our results contribute to the knowledge of local reality, which is needed to advocate measures that aim to reduce the accidents by venomous animal attacks and to promote therapeutic measures, such as supplying of specific antivenoms in places where they are most required.

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