

ORIGINAL ARTICLE

Epidemiological and clinical aspects of snakebites in the upper Juruá River region, western Brazilian Amazonia

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ABSTRACT

This study addresses the clinical and epidemiological aspects of envenoming cases resulting from snakebites treated at a hospital in Cruzeiro do Sul, in the upper Juruá River region, western Brazilian Amazonia. The specific identity of snakes that caused the envenomings was inferred (a) from the diagnosis of patient symptoms and signs upon hospital admission, (b) by enzyme immunoassay for detection of *Bothrops atrox* and *Lachesis muta* venom from serum samples taken from patients before antivenom therapy, or (c) by direct identification of the snake, when it was brought along to the hospital or photographed. There were 133 snakebites (76.2 cases per 100,000 inhabitants) registered during one year (July 2017 to June 2018). Most snakebites (88.7%) were caused by *Bothrops* spp., and the rest by non-venomous snakes or dry bites. Snakebites tended to occur more often during the rainy season, coinciding with the period of greater reproductive activity of the snakes and greater availability of their prey. In addition, the increase in the water level of rivers and lakes during the rainy season tends to concentrate snakes in dry places and, thus, to increase encounters with humans. Information campaigns on prevention and first aid, specially among the most vulnerable groups (indigenous people, farmers, and children and teenagers in rural areas), and the importance of using protective equipment (boots, leggings, leather gloves) in certain high risk activities (e.g. agriculture and extractivism in forests) are fundamental for the reduction of snakebite morbidity.

KEYWORDS: venomous animals; snakes; envenoming; Acre; *Bothrops atrox*; enzyme immunoassay

Aspectos clínicos e epidemiológicos de acidentes ofídicos na região do Alto Juruá, oeste da Amazônia brasileira

RESUMO

Este estudo aborda os aspectos clínicos e epidemiológicos dos envenenamentos ofídicos tratados em um hospital em Cruzeiro do Sul, Acre, resultantes de acidentes que ocorreram na região do Alto Juruá, no oeste da Amazônia brasileira. A identidade específica das serpentes que causaram os envenenamentos foi inferida (a) pelos sinais e sintomas apresentados pelo paciente na admissão hospitalar, (b) por imunoensaio enzimático para detecção de veneno de *Bothrops atrox* e *Lachesis muta* em amostras de soro retiradas de pacientes antes da soroterapia, e (c) pela identificação direta da serpente, quando esta foi levada para o hospital ou fotografada. Houve 133 casos (76,2 casos por 100.000 habitantes) de acidentes ofídicos registrados durante um ano (julho 2017 a junho 2018). A maioria das picadas de serpentes (88,7%) foi causada por *Bothrops* spp., e o restante por espécies não peçonhentas ou “picadas secas”. Os acidentes ofídicos tenderam a ocorrer com maior frequência durante a estação chuvosa, coincidindo com o período de maior atividade reprodutiva das serpentes e maior disponibilidade de suas presas. Além disso, o aumento dos níveis de rios e lagos pode fazer com que esses animais procurem locais mais secos, aumentando a frequência de encontro com seres humanos. Campanhas educativas sobre prevenção e primeiros socorros, principalmente entre os grupos mais vulneráveis (indígenas, agricultores, crianças e adolescentes em áreas rurais), e sobre a importância da utilização de equipamentos de proteção (botas, perneiras, luvas de couro) em determinadas atividades de maior risco (e.g., agricultura e extrativismo em florestas), são fundamentais para reduzir a morbidade de picadas de serpentes.

PALAVRAS-CHAVE: animais peçonhentos; serpentes; envenenamentos; Acre; *Bothrops atrox*; imunoensaio enzimático

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INTRODUCTION

Snakebites are a neglected health problem on a global scale, specially in Africa, Asia, and Latin America (Gutiérrez 2014; Chippaux 2017; Williams *et al.* 2019). There are an estimated 2.7 million cases of snake envenoming per year on the planet, resulting in 81,000 to 138,000 deaths, and 400,000 cases of amputation and other permanent sequels (Williams *et al.* 2019). The envenomings are concentrated in rural areas, where hundreds of millions of people depend on agriculture or subsistence hunting and gathering to survive, living alongside snakes, and running the risk of suffering snakebites on a daily basis (Sharma *et al.* 2004; Rahman *et al.* 2010; Mise *et al.* 2019). In Latin America, despite considerable efforts in some countries to prevent and treat snakebites, and to train staff in the management of envenomings, there still remain major challenges to reduce snakebite morbidity (Gutiérrez 2014).

In Brazil, 406 species of snakes are known, of which 67 belong to the families Elapidae and Viperidae, which are considered to be venomous (Costa and Bérnills 2018; Bernarde *et al.* 2018) and are involved in cases of snakebites, which amount to approximately 28,000 cases per year (Bernarde 2014). The greatest diversity of venomous snakes in Brazil is found in the Amazon region (34 species) (Costa and Bérnills 2018; Bernarde *et al.* 2018a), where the highest incidence of snakebites is recorded, accounting for an average of 46.51 cases per 100,000 inhabitants per year during 2010–2015 (Magalhães *et al.* 2018). Snakebites are considered a neglected health problem in Brazilian Amazonia, where the great distance between the site of the snakebite and the nearest healthcare provider causes frequent delay in the administration of antivenom therapy, increasing the severity of the envenoming (Feitosa *et al.* 2015a; 2015b; Souza *et al.* 2018). Despite the advances in healthcare for snakebites in Brazil, availability and accessibility to antivenom is not uniform with respect to the most vulnerable parts of the population, particularly, those who live in remote areas in Brazilian Amazonia (Fan and Monteiro 2018). More realistic and comprehensive healthcare programs for the most vulnerable groups, such as indigenous groups in remote reserves, and the availability of the lyophilized form of antivenoms are needed in order to reduce the high morbidity and mortality rates associated with snakebites (Mendonça-da-Silva *et al.* 2017).

Bothrops Wagler, 1824 snakebites are the most frequent in Amazonia (81% of cases; Magalhães *et al.* 2018), being caused mainly by *Bothrops atrox* L. (Feitosa *et al.* 2015a). *Bothrops atrox* is the most abundant venomous snake, both in forested and anthropized environments (Cunha and Nascimento 1993; Oliveira and Martins 2001), which increases the encounter frequency and the probability of being bitten by this species (Pardal *et al.* 2004; Waldez and Vogt 2009; Roriz *et al.* 2018). The name attributed to *B. atrox* in the Brazilian state of Acre (“surucucu”) may cause an overestimation of cases of lachetic snakebites, because the same name is assigned

to the snake *Lachesis muta* L. (Bernarde and Gomes 2012; Mota-da-Silva *et al.* 2019a). Indeed, lachetic envenoming is the second most frequent in Amazonia (7.4%; Magalhães *et al.* 2018), accounting for 0.3% to 2.2% of cases in regional epidemiological studies (e.g., Pardal *et al.* 2004; Moreno *et al.* 2005; Lima *et al.* 2009; Roriz *et al.* 2018). The lower frequency of lachetic bites is probably due to the low population density of *L. muta*, which requires forested habitats and is less aggressive than *B. atrox* (Bernarde 2014). Crotalic snakebites, caused by the rattlesnake (*Crotalus durissus* L.), are the third most frequent (4.4%) in Amazonia (Magalhães *et al.* 2018). The latter species is rather associated with savanna habitats, which limits its distribution and occurrence in the Amazon region (Santos *et al.* 2019). The fourth type of envenoming in Amazonia is caused by coral snakes of the genus *Micrurus* Wagler, 1824, with a low frequency (0.3%; Magalhães *et al.* 2018), mainly due to the lower frequency of human encounters with coral snakes, due to their secretive habits and lower abundance and the lower inoculating capacity of the *Micrurus* bite (Bernarde 2014).

In the upper region of the Juruá River, a right-hand tributary of the Amazonas River in the extreme western part of the Brazilian Amazon, snakebites are a significant public health problem, as cases are frequent, mainly in rural and forested areas, during agriculture and extractivism activities (Pierini *et al.* 1996; Bernarde and Gomes 2012; Mota-da-Silva *et al.* 2019b). In the present study, we monitored snakebite cases treated over one year in a hospital in Cruzeiro do Sul, the main urban center in the upper Juruá region, and evaluated the clinical and epidemiological aspects of the envenoming.

MATERIAL AND METHODS

Study area

The study was conducted during a one-year period (July 1, 2017 to June 30, 2018) at the Juruá Regional Hospital in the municipality of Cruzeiro do Sul (Acre) (07°37'51"N, 72°40'12"W), located in the upper Juruá region in the western Brazilian Amazonia. This hospital regularly treats victims of snakebites from four municipalities (Cruzeiro do Sul, Mâncio Lima, and Rodrigues Alves in the state of Acre, and Guajará in the state of Amazonas), comprising an area of 24,806 km² (Figure 1). The upper Juruá region has over 90% primary forest cover (ACRE 2010). The region has a total population of 137,722 inhabitants, mostly concentrated in the urban area (72%), the rest living in rural areas, including forests (IBGE 2019). The main economic activities in the region are the production of manioc flour, extractivism of forest products (palm fruits), agriculture (corn, rice, beans, banana, watermelon and vegetables), livestock and fishing (ACRE 2010). The climate of the region is tropical, hot, and humid, with an annual average temperature of 24.5 °C (ACRE 2010), with the highest rainfall period from November to April (average annual rainfall of 2500 mm), coinciding with the period of the highest level of the Juruá River (Moreira *et al.* 2019).

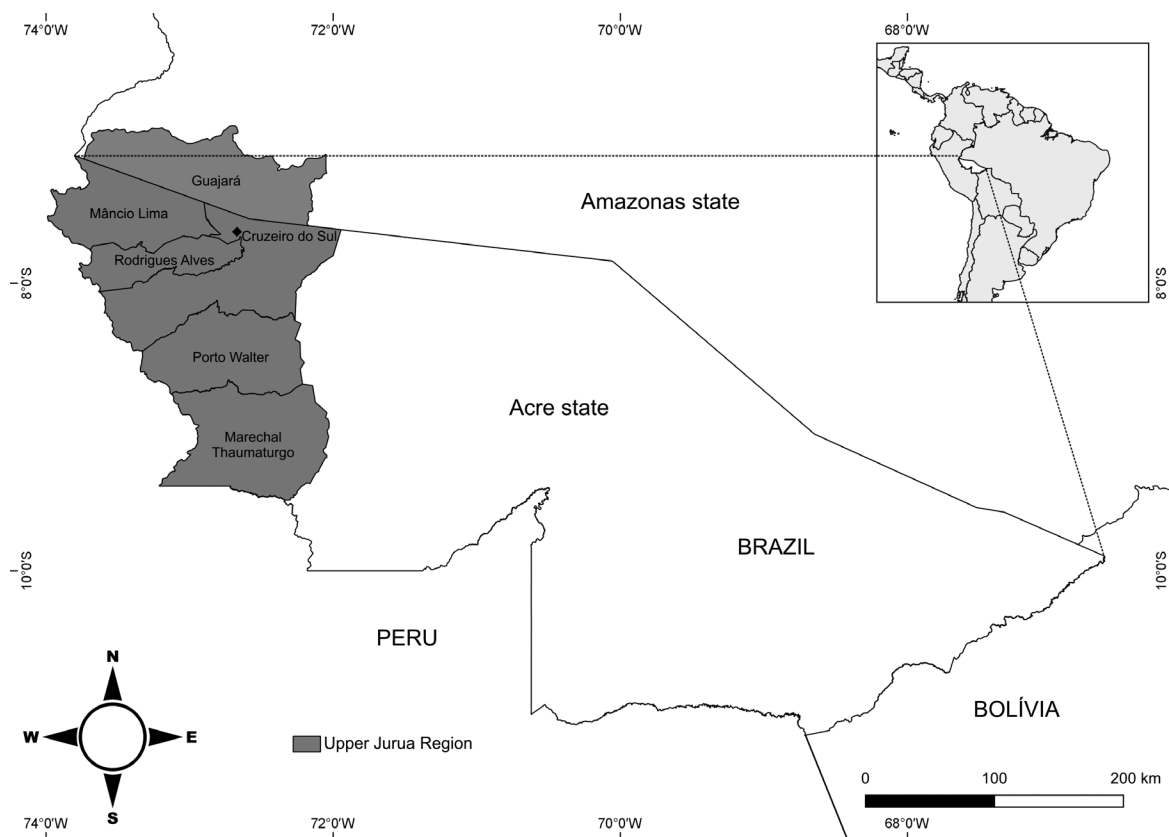


Figure 1. Location of the upper Juruá River region in Brazil. The municipalities belonging to the upper Juruá river are shown in gray.

Snake identification

The specific identity of snakes that caused the envenomings was obtained (a) from the diagnosis of patient symptoms and signs upon hospital admission, (b) by enzyme immunoassay for detection of *Bothrops atrox* and *Lachesis muta* venom from serum samples taken from patients before antivenom therapy, and (c) by direct identification of the snake, when it was brought along to the hospital or photographed.

The snakes, when taken to the hospital or photographed, were identified using a regional snake identification guide (Bernarde *et al.* 2017). When the snakes were not brought to the hospital, a panel containing photographs of snakes was shown to the patient to assess whether he or she recognized the species responsible for the envenoming. This was not a primary criterion for diagnosing the type of envenoming, but served as complementary information (see Mota-da-Silva *et al.* 2019a). The board contained color photographs of 17 common species in the upper Juruá region (Bernarde *et al.* 2017) featured in the following order of appearance: *Boa constrictor*, *Eunectes murinus*, *Bothrops bilineatus smaragdinus*, *Spilotes pullatus*, *Lachesis muta*, *B. atrox* (adult), *Corallus batesii*, *Micrurus lemniscatus*, *Oxyrhopus melanogenys*, *M. hemprichii*, *M. annellatus bolivianus*, *B. atrox* (juvenile), *Epicrates cenchria*, *Anilius scytale*, *Oxybelis fulgidus*, *M. surinamensis*,

Erythrolamprus aesculapii and *E. reginae*. In the panel, species were only indicated by letters from A to R. There were two contiguous photographs of each species on the panel, to test for consistency in the identification of the species. For *Bothrops atrox* there were four photographs (two of juveniles and two of adults). The snakebite cases in which the snake was not taken to the hospital and the patient was asymptomatic and had no change in blood coagulation time were considered “dry bites” or caused by non-venomous snakes (Silveira and Nishioka 1992; Nicoletti *et al.* 2010).

Clinical manifestations

The clinical and laboratorial data regarding the manifestations from the envenoming of the victims were obtained from the observation of patients and medical records. The Lee-White coagulation test was done in duplicate in a laboratory of the hospital.

The severity of bothropic envenomations was classified according to the following criteria (Ministério da Saúde 2016): mild (pain and edema of up to one segment, mild or absent bleeding, present or absent coagulopathy); moderate (two-segment pain and edema; mild or absent bleeding; present or absent coagulopathy); and severe (three-segment pain and edema or at least one of the following systemic complications: severe bleeding, hypotension / shock or acute renal failure, coagulopathy present or absent).

Venom-specific enzyme immunoenzymatic assays

Immunoenzymatic assays (ELISA) were used to identify and quantify circulating *Bothrops atrox* or *Lachesis muta* venoms in serum samples according to Pardal *et al.* (2004). Venom toxins present in the samples were captured with *Bothrops-Lachesis* antivenoms coated on ELISA plates. The plates were then incubated with a second antibody produced in rabbits for use in treating *B. atrox* venom or a specific mouse monoclonal antibody anti-*Lachesis muta* venom (Colombini *et al.* 2001) for reaction with bound toxins. This step was followed by incubation with anti-rabbit or anti-mouse IgG-peroxidase conjugates. Reactions were revealed by addition of the enzyme substrates (OPD plus H₂O₂) and recorded at 492 nm. Values were calculated using standard curves with known concentrations of *B. atrox* or *L. muta* venom. The cut-off level corresponded to the mean plus 2 SD values of negative samples obtained from volunteer donors accompanying the patients.

Statistical analysis

Monthly values of rainfall and water level of the Juruá River for the study period were obtained from the websites of the National Institute of Meteorology (INMET 2019) and the National Water Agency (ANA 2019), respectively, for a station in Cruzeiro do Sul. For statistical analysis purposes, only the cases that occurred in the municipalities that regularly send snakebite victims to the Juruá Regional Hospital were considered (Cruzeiro do Sul, Mâncio Lima, and Rodrigues Alves in the state of Acre, and Guajará in the state of Amazonas). The morbidity coefficient (cases per 100,000 inhabitants) was calculated by dividing the number snakebite patients during the study period by the number of inhabitants of the region and multiplying by 100,000. We used Pearson's correlation to analyze the relationship between the number of monthly snakebites with rainfall and river level. The association between variable categories (Table 2) was analyzed by cross-reference, calculating the Pearson Chi-square test (χ^2). The significance level for all analyses was set at $P \leq 0.05$.

Ethical aspects

This research is part of the project "Venomous snakes and snakebites in Cruzeiro do Sul region in the state of Acre" approved by the Committee of Ethics in Research with Humans of Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (Authorization nr. 2,084,630). All patients gave written consent to participate in the study.

RESULTS

During the study period, 133 snakebite cases were treated at the Juruá Regional Hospital (Table 1), with a morbidity coefficient of 76.2 cases per 100,000 inhabitants in the upper Juruá region. Most of the snakebites were classified as bothropic (118 cases, 88.7%). The remaining cases were attributed to non-venomous snakes or to dry bites. In 20 cases (15%), the snake that caused the bite was brought in with the patient or photographed

(13 *Bothrops atrox* and seven non-venomous snakes) (Figure 2). *Bothrops atrox* was recognized by 86.8% of the patients who saw the photo plates (79 of the 91 patients who saw the snake). Bothropic envenoming was confirmed by the enzymatic assay in 28 cases (29% of the cases, $n = 97$). Crotalic, lachetic, and elapidic envenoming were not recorded. One death was recorded in the period (0.7% lethality).

The cases treated at the Juruá Regional Hospital came mostly (86.4%) from the municipalities of Acre state (AC), mainly from Cruzeiro do Sul (54 cases, 45.8%), Mâncio Lima (21 cases, 17.8%), and Rodrigues Alves (17 cases,

Table 1. Clinical and epidemiological characteristics of snakebite cases ($n = 133$) treated in the Juruá Regional Hospital in the Municipality of Cruzeiro do Sul, in the upper Juruá River region (western Brazilian Amazonia), from July 2017 to June 2018. Sample size available for each parameter is indicated in parentheses in each case. N cases = number of cases.

Parameter	N cases	Frequency (%)
Type of snakebite (133)		
Bothropic	118	88.7
Non-venomous/dry bite	15	11.3
Season (120)		
Rainy (Nov to Apr)	79	65.8
Dry (May to Oct)	41	34.2
Type of land use		
Rural	114	85.7
Urban	19	14.3
Sex of snakebite victim		
Masculine	102	76.7
Feminine	31	23.3
Age group		
0 to 10	15	11.3
11 to 20	37	27.8
21 to 30	21	15.8
31 to 40	28	21.0
41 to 50	19	14.4
51 to 60	8	6.0
> 60	5	3.7
Occupation (133)		
Farmer	64	48
Student	33	25
Housewife	5	4.0
Other	31	23
Time to hospital (133)		
0 to 1 hour	16	12.0
1 to 3 hours	34	25.6
3 to 6 hours	29	21.8
6 to 12 hours	24	18.0
12 to 24 hours	15	11.3
> 24 hours	15	11.3

Table 1. Continued.

Parameter	N cases	Frequency (%)
Body part bitten (133)		
Foot	89	67.0
Leg	23	17.0
Thigh	2	1.6
Hand	13	10.0
Arm	2	1.5
Forearm	1	0.7
Head	1	0.7
Thorax	2	1.5
Level of bothropic envenoming (118)		
Mild	59	50.0
Moderate	43	36.5
Severe	16	13.5
Physical symptoms/complications (118)		
Pain	110	93.2
Edema	110	93.2
Bruising	15	12.7
Bleeding at site of bite	13	11.0
Blisters	12	10.2
Secondary infection	11	9.0
Cellulitis	8	6.7
Local lymphadenopathy	6	5.1
Necrosis	3	2.5
Abscess	2	1.7
Erysipelas	1	0.8
Compartment syndrome	1	0.8
Systemic symptoms/complications (118)		
Blood coagulation change (103)	85	82.5
Hemorrhages	26	22.0
Acute renal failure	6	5.1
Dyspnea	2	1.7
Hemorrhagic stroke	1	0.8
Septic shock	1	0.8
Death	1	0.8

14.4%) (Table 2). Thirteen cases were from Guajará (11%), in Amazonas state (AM), and some cases were transferred from more distant or difficult-to-reach municipalities, such as Porto Walter (AC) (4 cases, 3.4%), Tarauacá (AC) (4 cases, 3.4%), Atalaia do Norte (AM) (2 cases, 1.7%), Feijó (AC) (1 case, 0.8%) e Jordão (AC) (1 case, 0.8%).

Most snakebites (65.8%) occurred during the rainy season, but the correlations between the frequency of snakebites and rainfall and river level were non significant (respectively, $r = 0.337$; $P = 0.285$; $n = 12$; and $r = 0.497$; $P = 0.100$; $n = 12$). (Table 1, Figure 3). Snakebites occurred mostly in the rural area (85.7% of the cases). They were more frequent in males (76.7%), in the 11-20 years age group (28.7%). Bites were predominantly on the foot (67%) and the main victims were farmers (48%) and children and teenagers (39%) (Table 1).

Table 2. Clinical and epidemiological characteristics of cases of bothropic envenoming in the Juruá Regional Hospital, in the Municipality of Cruzeiro do Sul in the upper Juruá River region (western Brazilian Amazon), from July 2017 to June 2018, according to severity grade (mild, moderate or severe). Sample size is indicated in each case, in parentheses after the parameter. Data for number of ampoules are minimum - maximum followed by the average in parentheses. For other parameters values are the absolute numbers followed by the frequency (%) in parentheses.

Parameter	Mild	Moderate	Severe
Number of ampoules applied for antivenom therapy (103)			
	2 - 8 (4.5)	3 - 12 (6.7)	8 - 22 (12.5)
Time to hospital treatment (118)			
≤ 6 hours	43 (65.2)	20 (30.3)	3 (4.5)
> 6 hours	16 (30.8)	23 (44.2)	13 (25)
Ethnicity (118)			
Indigenous (7)	2 (28.5)	2 (28.5)	3 (43)
Non-Indigenous (111)	57 (51.3)	41 (37)	13 (11.7)
Municipality (118)			
Cruzeiro do Sul	28 (51.9)	21 (38.8)	5 (9.3)
Mâncio Lima	12 (57.1)	7 (33.3)	2 (9.6)
Rodrigues Alves	10 (58.8)	5 (29.5)	2 (11.7)
Porto Walter	0	03 (75)	1 (25)
Marechal Thaumaturgo	0	0	1 (100)
Tarauacá	4 (100)	0	0
Feijó	0	1 (100)	0
Guajará	5 (38.5)	5 (38.5)	3 (23)
Atalaia do Norte	0	1 (50)	1 (50)
Jordão	0	0	1 (100)
Type of land use (118)			
Rural	52 (48)	42 (38)	15 (14)
Urban	7 (78)	1 (11)	1(11)
Age group (118)			
0 to 10	7 (54)	2 (15)	4 (31)
11 to 20	24 (68,6)	9 (25.7)	2 (5.7)
21 to 30	6 (33.3)	10 (55.5)	2 (11.2)
31 to 40	10 (42)	11(46)	3 (12)
41 to 50	8(47)	7 (41)	2 (12)
51 to 60	4 (57)	3 (43)	0
> 60	0	1 (25)	3 (75)
Sex (118)			
Male	48 (50)	35 (37)	12 (13)
Female	11 (48)	8 (35)	4 (17)
Anatomical region bitten (116)			
Lower members	50 (51.5)	33 (34.1)	14 (14.4)
Upper members	6 (37.5)	9 (56.2)	1 (6.3)
Trunk	1 (50)	1 (50)	0
Head	0	0	1 (100)

The majority (59.4%) of snakebite cases were treated in less than six hours (Table 1). Pain and edema were the most frequent local manifestations (93.2% of cases), followed by ecchymosis (12.7%), bleeding at the site of the bite (11%), blisters (10.2%), secondary infection (9%), cellulitis (6%), regional lymphadenopathy (5.1%), necrosis (2.5%), abscess (1.7%), erysipelas (0.8%), and compartment syndrome

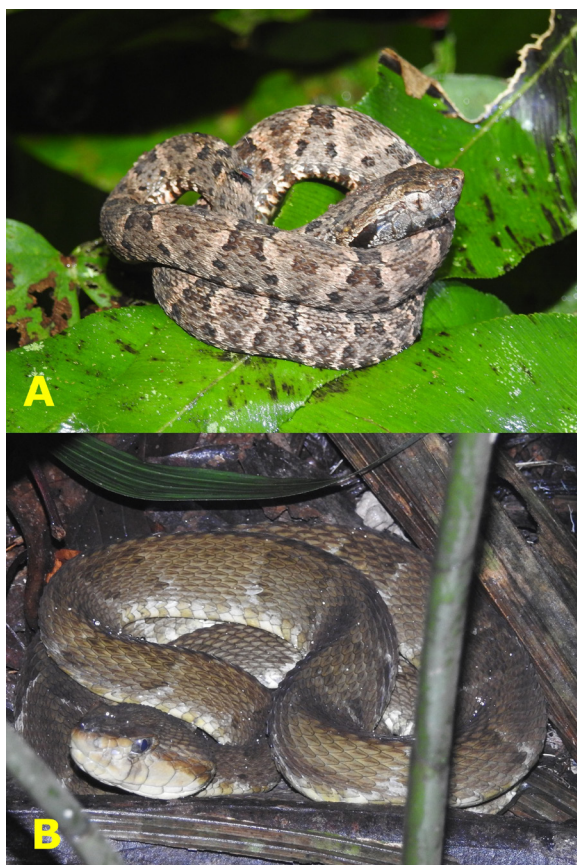


Figure 2. Jararaca or surucucu (*Bothrops atrox*), the snake responsible for envenomings in the present study in the upper Juruá River region. (A) Juvenile; (B) Adult. Credit: Paulo Sérgio Bernarde. This figure is in color in the electronic version.

(0.8%) (Table 1, Figure 4). The most frequent systemic manifestations and complications were changes in blood coagulation time (82.5% of 103 cases), bleeding (22%) followed by acute renal failure (5.1%), dyspnea (1.7%), septic shock (0.8%), and hemorrhagic stroke (0.8%) (Table 1).

Half of the cases were classified as mild, 36.5% as moderate and 13.5% as severe (Table 1). The severity of the snakebites was associated with the delay in receiving the antivenom therapy, as 65% of patients treated in less than six hours were mild cases, while almost 70% of patients treated in over six hours were moderate to severe cases (Table 2) (Chi-square test = 17.4, $P < 0.001$). There was a predominance of mild cases in patients from the urban area of Cruzeiro do Sul (78% of cases) compared to those in the rural areas (48%) (Table 2). The highest proportions of severe cases were observed in children aged 10 years or less (31% of cases) and in the elderly (75%) (Table 2) (Chi-square test = 27.94, $P = 0.006$). Indigenous patients ($n = 7$) were the predominant severe cases (43%) in relation to the non-indigenous population (11.7%), however, there was no significant difference between the proportions (Table 2) (Chi-square test = 5.52, $P = 0.063$).

Of the 118 bothropic envenoming patients, 15 did not receive antivenom therapy, either because it was a mild case, more than seven days had elapsed since the snakebite, or insufficient clinical background information was available. The mean number of serum ampoules used in treatment varied from 4.5 in mild cases, to 6.7 in moderate cases, and 12.5 in severe cases (Table 2).

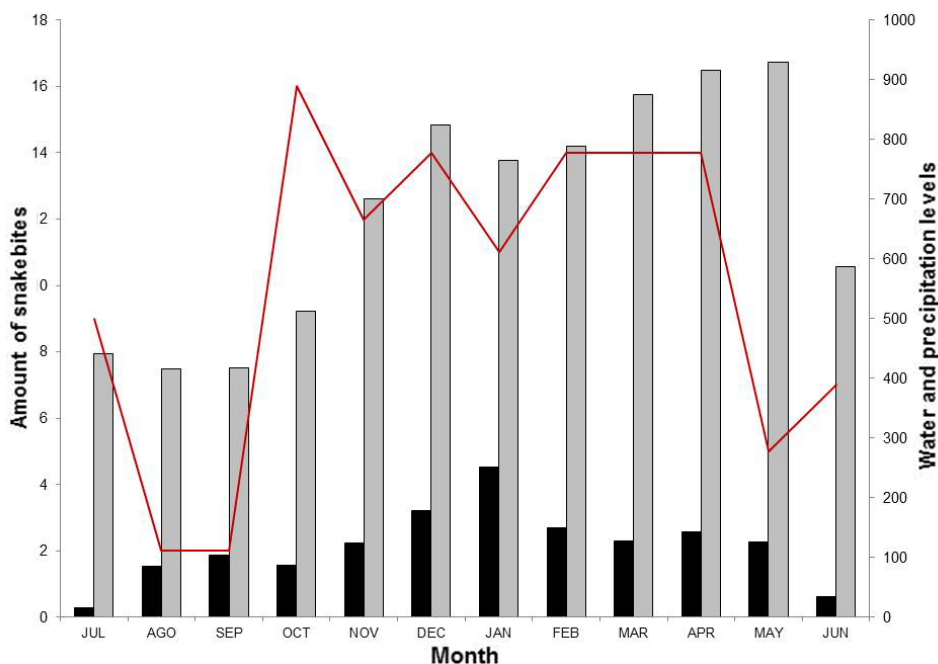


Figure 3. Monthly distribution of snakebites (red line), rainfall (black bars, values in mm), and water level of the Juruá River (grey bars, values in cm) from July 2017 to June 2018. This figure is in color in the electronic version.



Figure 4. Evolution of *Bothrops* snakebite wounds in this study: (A) Foot with edema, ecchymosis and bleeding; (B) Leg with edema in three segments; (C) Foot with edema and blister; (D) Leg with necrosis. Credit: Ageane Mota da Silva. This figure is in color in the electronic version.

DISCUSSION

The morbidity coefficient in this study (76.2 cases per 100,000 inhabitants) was higher than that recorded for the nine states comprising Brazilian Amazonia (ranging from 25.2 to 75.3 per 100,000 inhabitants in Roraima and Mato Grosso, respectively; Magalhães *et al.* 2018). In the Brazilian Amazon, some of the highest incidences of snakebites on Earth were registered (over 200 cases per 100,000 inhabitants; Feitosa *et al.* 2015a). We recorded a higher morbidity coefficient in the upper Juruá region than that recorded for Acre state as a whole, the northern Brazilian region, and Brazil (61.1, 56.1 and 14.7 cases per 100,000 inhabitants, respectively) (Chippaux 2015). This points to a high prevalence of snakebites in the upper Juruá region, as previously reported by Pierini *et al.* (1996)

Except for cases of snakebites by non-venomous snakes, the exclusive occurrence of bothropic envenoming in our sample confirms the low frequency of lachetic and elapidic bites in Amazonia (Pardal *et al.* 2004; Moreno *et al.* 2005; Oliveira *et al.* 2018; Roriz *et al.* 2018). Our study also suggests that the frequency of lachetic snakebites (51%) recorded in a previous study for Cruzeiro do Sul (Bernarde and Gomes 2012) was overestimated, probably due to that both *Bothrops atrox* and *Lachesis muta* are known by the common name “surucucu” in the region, which can lead health

professionals to mistakenly diagnose bothropic as lachetic envenomings (Mota-da-Silva *et al.* 2019a). *Bothrops atrox* is the main snake species involved in envenomings in the upper Juruá region, as it was identified by 86.8% of the patients through photographs, composed 66.6% of the specimens that caused envenomings that were brought to the hospital, and was confirmed in 29% of the immunoenzymatic assays performed on patients’ blood samples. This species presents a generalist diet, preying on various types of animals (rodents, amphibians, lizards, other snakes), and is the venomous snake most commonly found in forests, while also being the most tolerant to anthropized areas (pasture, agriculture) (Turci *et al.* 2009; Bernarde *et al.* 2017). The species had already been identified in other studies as the cause of most snakebites in the upper Juruá region (Pierini *et al.* 1996; Bernarde and Gomes 2012; Mota-da-Silva *et al.* 2019a).

Snakebites tended to occur more often during the rainy season, corroborating other studies in Amazonia (Moreno *et al.* 2005; Bernarde and Gomes 2012; Feitosa *et al.* 2015a; Roriz *et al.* 2018). The lack of correlation between snakebite frequency and rainfall or river level in our study may be owed to stochasticity, as we analyzed data for only one year. In a previous study conducted in this region over two years, a positive correlation between snakebites and rainfall was observed (Bernarde and Gomes 2012). The rainy months

coincide with the period of greater reproductive activity of the snakes (mating, birth of young; Martins and Oliveira 1998; Oliveira and Martins 2001; Almeida-Santos and Salomão 2002) and availability of their prey (Martins and Oliveira 1998; Oliveira and Martins 2001; Turci *et al.* 2009). At the same time, the flooding of rivers and lakes drives snakes to seek drier places, increasing encounters with humans, as certain human activities are also more frequent during this period (planting and harvesting, extractivism of forest products, hunting) (Pierini *et al.* 1996; Moreno *et al.* 2005; Waldez and Vogt 2009; Feitosa *et al.* 2015a; Mota-da-Silva *et al.* 2019b).

The general epidemiological profile of the victims registered in our study (the majority of victims were male, living in rural areas and were bitten on lower limbs) corresponds to what has been observed in other studies on snakebites in Amazonia (Moreno *et al.* 2005; Magalhães *et al.* 2018). The proportion of younger victims in our study (39% under 20 years of age) was higher than that recorded by Magalhães *et al.* (2018) for Brazilian Amazonia. The predominance of bites on the feet (67% of the cases) and on the legs (17%) reinforces the importance of the use of boots or leggings during rural and extractivist activities, as a preventative measure against snakebites (Oliveira *et al.* 2018). Snakebites involving the upper regions of the body (14.4% of cases), could be associated, in some cases, with the presence of *Bothrops bilineatus smaragdinus* and young *B. atrox* in the vegetation, the most frequently found *Bothrops* individuals in forested floodplains of the upper Juruá (Turci *et al.* 2009; Fonseca *et al.* 2019). As observed by Moreno *et al.* (2005) in the region of Rio Branco (capital of Acre state), the main snakebite victims in our study were farmers, highlighting the occupational correlate of snakebite morbidity with agriculture (Mise *et al.* 2019), and children and teenagers, confirming these groups as those at higher risk, and which should be primary targets of prevention campaigns.

The time elapsed between the snakebite and hospital care was lower in our study than that recorded by Bernarde and Gomes (2012) in previous years for the same region (53.6% treated in less than six hours and 27% after 24 hours, against 60% and 11.3%, respectively, in our study). This decrease in time to treatment may be due to the increase in the number of ambulances in Acre after 2015 (O'Dwyer *et al.* 2017), as well as to improvements in road infrastructure and telephone services, increasing the accessibility of patients to healthcare providers. The majority of mild cases in our study (43 of 59 cases, 73%) were among those treated in less than six hours, while 13 of 16 severe cases (81%) were among those treated after more than six hours had passed, which points to that longer delays in getting antivenom therapy are associated with an enhanced severity of symptomatology, including serious complications and death (Feitosa *et al.* 2015b; Mise *et al.* 2018; Roriz *et al.* 2018).

The frequency of mild, moderate and severe bothropic envenoming in our study (50, 36.5 and 13.5%, respectively), differed somewhat from that reported for the capital city of Acre state, Rio Branco (31.2, 48.6 and 20.2%) (Moreno *et al.* 2005). Severity frequencies were also reported for other Amazonian urban centers, such as Porto Velho (23.9, 26.1 and 50%), also in the southwestern Amazon (Roriz *et al.* 2018), Manaus (27.7, 54.2 and 18.1%), in the central Amazon (Oliveira *et al.* 2019), and Belém (58.1, 36.5 and 5.4%), in the eastern Amazon (Pardal *et al.* 2004). These figures depend on the criteria used to define severity grades and the local context of accessibility to healthcare (Feitosa *et al.*, 2015b), but may also be related to regional variations in the venom of *Bothrops atrox* (Núñez *et al.* 2009; Sousa *et al.* 2013; Del-Rei *et al.* 2019).

The most frequently observed symptoms in our study (pain and edema) are the most commonly observed in bothropic envenomings (Oliveira *et al.* 2018). Other symptoms and complications observed less frequently, such as hemorrhage, renal failure and septic shock, are also typical of bothropic envenoming (Souza 2002; Pardal *et al.* 2004; Oliveira *et al.* 2018; Roriz *et al.* 2018). Altered blood clotting time had been observed in 43.1% to 72.2% cases of *Bothrops* envenomings in the Brazilian Amazon (Souza 2002; Pardal *et al.* 2004; Moreno *et al.* 2005; Oliveira *et al.* 2019). The frequency in our study (82.5%) was more similar to that reported for Colombia (84.6%; Otero *et al.* 1996). In Ecuador, 95% cases were reported with altered blood clotting (Smalligan *et al.* 2004). These varying frequencies may owe to regional differences in *B. atrox* venom (Núñez *et al.* 2009; Sousa *et al.* 2013; Del-Rei *et al.* 2019) or that different *Bothrops* species were present in the study areas. For example, *B. atrox* and *B. bilineatus smaragdinus* caused, respectively, 45% and 36% of the envenomings in Pastaza (Ecuadorian Amazon), while *B. atrox* caused most of snakebites in other studies (Souza 2002; Pardal *et al.* 2004; Moreno *et al.* 2005; Roriz *et al.* 2018).

In the state of Amazonas, indigenous patients had higher lethality risk from snakebites than non-indigenous patients (Souza *et al.* 2018), a tendency which we also observed in our study. In addition to more precarious access to health services from indigenous communities, they probably also resort more frequently to traditional treatments instead of seeking medical attention (Pierini *et al.* 1996), and only look for a hospital when the snakebite symptoms get more serious.

CONCLUSIONS

Snakebite is a significant health problem in the upper Juruá region, reaching mainly farmers, children and teenagers in rural and forested areas. The main species of venomous snake involved in snakebites was *Bothrops atrox*, and snakebites occur more during the rainy season. The delay of the antivenom therapy due to the great distance of the localities where the bites occur and the hospital care was a problem associated with

the severity of the cases. It is suggested educational campaigns for populations most vulnerable to snakebites to reduce this degree of morbidity in the western Brazilian Amazonia.

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