Exploring snakebite epidemiology between 2010 and 2021 in Paraná, Brazil: introducing distribution patterns, clinical profiles, and sociodemographic factors

Explorando a epidemiologia dos acidentes ofídicos entre 2010 e 2021 no Paraná, Brasil: apresentando padrões de distribuição, aspectos clínicos e fatores sociodemográficos

Daniel José Scheliga¹, Adriano Akira Ferreira Hino², Marcia Olandoski³, Julio Cesar de Moura-Leite⁴, Emanuel Marques da Silva⁵, Selene Elifio-Esposito⁶

Abstract

Snakebite envenomation, although prevalent in rural and tropical areas, is often neglected as a public health issue. Paraná records fewer cases compared to other Brazilian regions, yet the epidemiology and factors affecting these incidents are not fully understood. This study aimed to describe the epidemiology of snakebite accidents in Paraná from 2010 to 2021 and identify factors associated with clinical outcomes. Data were sourced from the Notifiable Diseases Information System and Venomous Animals Notification System. Incident trends were analyzed using Joinpoint Regression, and highincidence regions were identified through spatial autocorrelation and hotspot analysis. Associations between factors and outcomes were assessed using logistic regression, Fisher's exact test, or the Chisquared test. Of 9,362 cases, 69.19% involved Bothrops spp., while Thamnodynastes spp., Dipsas spp., and *Philodryas* spp. were the main non-venomous snakes. Venomous snakebite incidence decreased by 7.74% from 2017 to 2021. Death was associated with age >65, illiteracy, delays ≥ 6 h, and local/systemic complications (p < 0.001). Non-venomous snakebite accidents rose by 6% since 2010. A case of acute renal failure was reported in an accident involving *Pseudablabes patagoniensis*. The study highlights snakebites as a significant public health issue due to their potential for severe complications. The findings enhance understanding of snakebite epidemiology in Paraná, aiding in the development of targeted interventions and prevention strategies.

Keywords: Snakebites; Envenomation; Neglected tropical diseases; Public health challenges.

¹ Mestrado em Ciências da Saúde pela Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil.

² Doutorado pelo Programa de Pós-Graduação em Educação Física da Universidade Federal do Paraná (UFPR), Curitiba, Paraná, Brasil. Professor Adjunto da Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil.

³ Doutorado em Ciências da Saúde pela Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil. Professora Adjunta da Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil.

⁴ Doutorado em Zoologia pela Universidade Federal do Paraná (UFPR), Curitiba, Paraná, Brasil. Professor Titular da Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil.

⁵ Mestrado em Saúde Pública pela Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro, Rio de Janeiro, Brasil. Biólogo da Seção de Vigilância Sanitária, Ambiental e Saúde do Trabalhador da 1ª Regional de Saúde - Paranaguá (1ª RS), Paranaguá, Paraná, Brasil.

⁶ Doutorado em Ciências (concentração em Bioquímica) pela Universidade Federal do Paraná (UFPR), Curitiba, Paraná, Brasil. Professora Titular da Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Paraná, Brasil. *E-mail*: selene.e@pucpr.br

Resumo

O envenenamento por serpentes, embora prevalente em áreas rurais e tropicais, é frequentemente negligenciado como um problema de saúde pública. O Paraná registra menos casos em comparação com outras regiões brasileiras, mas a epidemiologia e os fatores que afetam esses incidentes não são totalmente compreendidos. Este estudo teve como objetivo descrever a epidemiologia dos acidentes ofídicos no Paraná de 2010 a 2021 e identificar os fatores associados aos resultados clínicos. Os dados foram obtidos do Sistema de Informação de Agravos de Notificação e do Sistema de Notificação de Animais Peçonhentos. As tendências de incidência foram analisadas usando a regressão Joinpoint, e as regiões de alta incidência foram identificadas por meio de autocorrelação espacial e análise de hotspot. As associações entre fatores e desfechos foram avaliadas por meio de regressão logística, teste exato de Fisher ou teste de qui-quadrado. Dos 9.362 casos, 69,19% envolviam Bothrops spp., enquanto Thamnodynastes spp., Dipsas spp. e Philodryas spp. foram as principais serpentes não venenosas. A incidência de picadas por serpentes venenosas diminuiu 7,74% de 2017 a 2021. A morte foi associada à idade >65 anos, ao analfabetismo, a atrasos no atendimento ≥6 horas e a complicações locais/sistêmicas (p<0,001). Os acidentes com serpentes não venenosas aumentaram em 6% desde 2010. Um caso de insuficiência renal aguda foi relatado em um acidente envolvendo Pseudablabes patagoniensis. O estudo destaca as picadas de serpentes como um importante problema de saúde pública devido ao seu potencial para complicações graves. Os resultados melhoram a compreensão da epidemiologia do ofidismo no Paraná, auxiliando no desenvolvimento de intervenções direcionadas e estratégias de prevenção.

Palavras-chave: Picadas de serpentes; Envenenamento; Doenças tropicais negligenciadas; Desafios para saúde pública.

Introduction

Snakebites pose a significant public health concern and profoundly affect regions where access to timely and adequate treatment is limited or nonexistent. Annually, 1.8–2.7 million cases of snakebites are estimated to occur worldwide, resulting in up to 138,000 deaths.⁽¹⁾ A lack of proper treatment can lead to long-term physical and psychological disabilities among victims;⁽²⁾ however, the impact of snakebites extends beyond individual health, since treatment of snakebite victims imposes substantial costs on healthcare systems as well.⁽³⁾ Recognizing the severity of this issue, the World Health Organization classified snakebite envenomation as a neglected tropical disease in 2017.⁽⁴⁾

In Brazil, 29,543 snakebite accidents and 94 deaths were reported in 2022, most of which occurred in the northern region.⁽⁵⁾ In contrast to other regions, the southern region of Brazil exhibits a significantly lower incidence of snakebite accidents and fatalities, which is attributed to higher urbanization rates and well-equipped healthcare centers close to the affected areas.⁽⁶⁾ In Paraná, epidemiological surveillance is responsible for identifying the quantity of antivenom needed for each municipality. The municipalities are organized into 22 Health Regions, which are responsible for sending monthly reports on the antivenom stock. This process is supported by the Venomous Animal Information System (SINAP), which monitors occurrences by species in each region, allowing for a more precise allocation of the serums.⁽⁷⁾

In 2010, the accidents caused by venomous and poisonous animals became part of the Compulsory Notification List in Brazil, which is provided by the Notifiable Diseases Information System (SINAN) database. In the state of Paraná, the State Secretariat for Health maintains the SINAP database integrated to the Animal Taxonomy Laboratory (LabTax) within the Environmental Surveillance Coordination division. It aims to record the taxonomic identifications of animals using photographs archived in SINAP or samples sent to LabTax. The integration of data, which is essential to improve our understanding and responses to accidents involving venomous animals, was the motivation behind conducting this study. This can allow for a more comprehensive analysis of trends, geographical distribution, and taxonomy of the species involved. Additionally, the ability to include data on snakebites caused by species of relatively low importance to public health is of great relevance, given the scarcity of studies on this topic.

This study aimed to describe the aspects of the epidemiology of snakebite accidents in Paraná, including seasonal patterns, geographical distributions, and incidence rates in different municipalities. The factors associated with unfavorable outcomes of snakebite accidents, such as mortality, as well as local and systemic complications, were also examined. Identifying these factors offers valuable insights regarding the impact of snakebite accidents on victims, as well as their association with other related variables.

Methods

Study area

Paraná has an area of 199 299 km². The predominant biome is the Atlantic Forest,⁽⁸⁾ which can be divided into Dense Ombrophilous, Mixed Ombrophilous (or Araucaria Forest), and Seasonal Forests.⁽⁹⁾ It has an estimated 11 444 380 inhabitants. Of these, 86% live in urban areas); 3.9% are illiterate (considering those aged \geq 15 years); and 16.8% are \geq 60 years of age.⁽¹⁰⁾

Study design

This descriptive, observational, cross-sectional study included data on snakebite accidents in the state of Paraná, documented using code 41 of the Brazilian Institute of Geography and Statistics (IBGE), that occurred between 2010 and 2021. Over this period, 10596 accidents were reported in Paraná and registered in SINAN. Of these, 1228 were excluded: 39 because they occurred outside the state, 15 because they were duplicates, three because they were related to the *Lachesis* (a snake that is not found in Paraná), and 1176 because the snake was not identified.

Data sources

The clinical data of the snakebite cases were selected from the following SINAN categories: individual notification, epidemiological history, clinical data, accident data, treatment, and outcomes. Snake identification was performed using data from the SINAP database (http://201.77.19.16/zoonose/ login) that included family, genus, species, and corresponding SINAN medical record number. The estimated population of Paraná was imported from the IBGE population estimate.

Classification of snakes

The snakes responsible for the accidents were categorized as highly venomous public health significance (PHS) snakes (*Bothrops*, *Crotalus*, and *Micrurus*) and non-venomous snakes of low public health significance (LPHS). Recently, the genera *Thamnodynastes*⁽¹¹⁾ and *Philodryas*⁽¹²⁾ have undergone phylogenetic revisions, changing the taxa of some species. This study used the old classification of genera (*Thamnodynastes* and *Philodryas*), although the new classification was adopted when species were specified.

Spatial and statistical analysis

Joinpoint Regression software version 4.9. $1.0.^{(13)}$ was used to describe the temporal trends of snakebites, considering the annual incidence (cases/100 000 inhabitants) as a unit of analysis. The significance level for the temporal trend was set at p<0.05.⁽¹⁴⁾ Global spatial autocorrelation of Moran's analysis was performed to analyze the presence of clusters of municipalities with higher or lower snakebite incidences. The significance level for this aspect was set to p<0.0001. Local spatial autocorrelation analysis (i.e., hotspot analysis) was used to identify municipalities with high or low spatial clustering values. We included all 399 cities

in Paraná as the unit of analysis and adopted a firstorder contiguity matrix. This type of relationship considers any municipality that shares borders with neighboring ones.⁽¹⁵⁾ All analyses were performed using ArcGIS 10.2 software,⁽¹⁶⁾ and clustering values are presented as 90, 95, and 99% confidence intervals (CIs), using choropleth maps.

Fisher's exact or Chi-squared tests were performed to independently identify the factors associated with outcomes such as death, local complications, and systemic complications, by fitting binary logistic regression models and estimating odds ratio (OR) values at the 95% CI level. The basic unit for this analysis was one case. Factors with a frequency of zero in any of their classifications were analyzed using Fisher's exact or Chisquared tests. Cases registered as deaths due to other causes were excluded from the analysis. All tests were performed using Statistical Package for the Social Sciences software (SPSS; version 28.0), with the significance level set at p < 0.05.⁽¹⁷⁾ Graphs of the distribution of snakebites by seasonality, occurrence area, and snake genus were prepared using Prism-GraphPad version 9.5.1.⁽¹⁸⁾

Ethics approval

This project meets ethical guidelines and was approved by the Research Ethics Committees of the involved institutions under Plataforma Brasil CAAE 53321921.8.0000.002.

Results

Distributions of accidents by seasons, area of occurrence, and snake genera

In this study, we analyzed 9362 snakebite accidents that occurred in Paraná between 2010 and 2021. They occurred more frequently in the summer (43.55%) and spring (28.02%) (Figure 1A). Rural areas had the highest occurrence of snakebites (79.92%; Figure 1B). The accidents were mainly caused by *Bothrops* spp. (69.19%) and *Crotalus* (14.32%; Figure 1C, left). LPHS snakes accounted for 15.90% of the accidents, mainly caused by the genera *Thamnodynastes* (40.6%), *Dipsas* (16.4%), and *Philodryas* (8.9%; Figure 1C, right).



Figure 1 - Distribution of snakebite accidents by: (A) months and seasons; (B) area of occurrence;

Caption: PHS: public health significance snake; LPHS: low public health significance snake. **Source**: the authors.

The total incidence ranged between 5.7 and 7.9 cases per 100000 individuals. For PHS snakes, Joinpoint regression showed two points of change in the line, with statistical significance occurring between 2017 and 2021, showing a decrease of 7.74% (Figure 2A). Guaraqueçaba, the easternmost municipality in the state of Paraná, had the highest incidence (138 cases; Figure 2B). The identification of clusters in the PHS group was observed (Moran's Global Index: 0.32; Z-score: 11.13; p<0.0001), with 32 municipalities identified as critical points with a CI of 99%, as well as 20 and 12 municipalities with CI of 95% and 90%, respectively. In the cold spots, nine municipalities were identified with a 95% CI and 33 with a 90% CI (Figure 2C).

Figure 2 - Analysis of incidence in PHS snakes and LPHS snakes. (A) Temporal behavior of incidence; (B) Distribution of municipal incidences; (C) Distribution of hot spots and cold spots of incidence.



Caption: APC: annual percent change; PHS: public health significance; LPHS: low public health significance. *: indicates a significant change in APC. **Source**: the authors.

For LPHS snakes, there was a trend of a 6% increase in the incidence from 2010 to 2021 (Figure 2A). The municipality of Marquinho had the highest incidence in this group (14 cases; Figure 2B). The identification of clusters was also observed in the LPHS group (Moran's Global Index: 0.13; Z-score: 4.40; p<0.0001), with 16 municipalities as hot spots with 99% CI, as well as 10 and nine municipalities with 95% and 90% CIs,

respectively. In the cold spots, four municipalities were identified with 95% CI and 11 with 90% CI (Figure 2C).

Sociodemographic and clinical profiles of snakebite victims

The frequency of snakebite accidents was higher among males (76.2%) and people aged 16–

45 years-old (48.2%; Table 1). The most affected ethnicities were white (76.7%) and mixed-race

(18.1%). Most of the accidents involved literate individuals (96.9%).

Variables (valid n)	Frequency n (%)
Sex (9362)	
Male	7134 (76.2)
Female	2228 (23.8)
Pregnant (2228)	
Yes	40 (1.8)
No	2188 (98.2)
Age group (in years; 9343)	
0–15	1381 (14.8)
16–45	4507 (48.2)
46–65	2782 (29.8)
>65	673 (7.2)
Ethnicity (9036)	
White	6927 (76.7)
Black	273 (3.0)
Mixed-race	1639 (18.1)
Indigenous	145 (1.6)
Asian	52 (0.6)
Education (7070)	
Illiterate	219 (3.1)
Literate	6851 (96.9)
Occupation (6490)	
Rural	3042 (46.9)
Non-rural	3448 (53.1)
Work-related accident (8895)	
Yes	2519 (28.3)
No	6376 (71.7)
Formal occupation (2519)	
Rural worker	1502 (59.6)
Civil construction	74 (2.9)
Fisherman	17 (0.7)
Others	356 (14.1)
Unknown	570 (22.6)

Table 1	- Sociodemog	raphic char	acteristics	of snakebite	accidents that	occurred be	etween 2010	0 and 2021
	0	1						

Source: the authors.

In general, 1000 cases (10.9%) were classified as severe, of which 799 were caused by *Bothrops*, 177 by *Crotalus*, 21 by *Micrurus* spp., and three were caused by LPHS snakes (Table 2). Most of the victims recovered (99.6%), although 34 deaths were recorded, all of which were caused by *Bothrops* (22 cases, 64.7%; lethality within genus, 0.34%) and *Crotalus* (12 cases, 35.3%; lethality within genus, 0.90%). The lower limbs were the most affected body parts (70.5%). Most victims received medical attention within 6 h of being bitten (91.4%).

Table 2 - Clinical features and treatm	ent of snakebite accidents occ	curred between 2010 and 2021.
--	--------------------------------	-------------------------------

		LPHS snakes			
Variable	Valid n or n (%)	Bothrops n (%)	Crotalus n (%)	<i>Micrurus</i> n (%)	n (%)
Case classification	9136	6327 (69.2)	1296 (14.2)	52 (0.6)	1461 (16.0)
Mild	4941 (54.1)	2869 (45.4)	657 (50.7)	26 (50.0)	1389 (95.1)
Moderate	3195 (35.0)	2659 (42.0)	462 (35.6)	5 (9.6)	69 (4.7)
Severe	1000 (10.9)	799 (12.6)	177 (13.7)	21 (40.4)	3 (0.2)
Outcome	8718	6007 (68.9)	1227 (14.1)	49 (0.5)	1435 (16.5)
Recovered	8684 (99.6)	5985 (99.6)	1215 (99.0)	49 (100)	1435 (100)
Death	34 (0.4)	22 (0.4)	12 (1.0)	0 (0)	0 (0)
Bite site	9330	6454 (69.2)	1339 (14.3)	52 (0.6)	1485 (15.9)
Upper limbs	2565 (27.5)	1718 (26.6)	367 (27.4)	25 (48.1)	455 (30.6)
Lower limbs	6576 (70.5)	4616 (71.5)	950 (71.0)	24 (46.1)	986 (66.4)
Other sites	189 (2.0)	120 (1.9)	22 (1.6)	3 (5.8)	44 (3.0)
Time elapsed until treatment	9083	6279 (69.1)	1299 (14.3)	53 (0.6)	1452 (16.0)
<6 h	8301 (91.4)	5766 (91.8)	1164 (89.6)	47 (88.7)	1324 (91.2)
≥6 h	782 (8.6)	513 (8.2)	135 (10.4)	6 (11.3)	128 (8.8)
Local manifestations	8583	6202 (72.3)	1195 (13.9)	40 (0.5)	1146 (13.3)
Pain	8138 (94.8)	5959 (96.1)	1118 (93.4)	34 (85.0)	1027 (89.6)
Edema	6457 (75.2)	5134 (82.8)	795 (66.4)	21 (52.5)	507 (44.2)
Ecchymosis	1650 (19.2)	1477 (23.8)	113 (9.4)	4 (10.0)	56 (4.9)
Necrosis	219 (2.6)	200 (3.2)	12 (0.9)	1 (2.5)	6 (0.5)

Continues

<i>a</i> .	
Continuc	ition

Systemic manifestations	1480	869 (58.7)	517 (34.9)	23 (1.6)	71 (4.8)
Neuroparalytic	663 (44.8)	223 (25.7)	409 (79.1)	11 (47.8)	20 (28.2)
Vagal	430 (29.0)	278 (32.0)	118 (22.8)	9 (39.1)	25 (35.2)
Myolytic	316 (21.3)	169 (19.5)	146 (28.2)	0 (0)	1 (1.4)
Renal	157 (10.6)	101 (11.6)	53 (10.3)	1 (4.3)	2 (2.8)
Clotting time	8810	6124 (69.5)	1239 (14.1)	47 (0.5)	1400 (15.9)
Normal	2571 (29.2)	1819 (29.7)	401 (32.4)	16 (34.0)	335 (23.9)
Abnormal	1525 (17.3)	1239 (20.2)	246 (19.8)	7 (14.9)	33 (2.4)
Not performed	4714 (53.5)	3066 (50.1)	592 (47.8)	24 (51.1)	1032 (73.7)
Local complications	306	270 (88.2)	23 (7.5)	0 (0)	13 (4.3)
Secondary infections	172 (56.2)	148 (54.8)	12 (52.2)	0 (0)	12 (92.3)
Extensive necrosis	84 (27.4)	80 (29.6)	2 (8.7)	0 (0)	2 (15.4)
Compart. syndrome	12 (3.9)	12 (4.4)	0 (0)	0 (0)	0 (0)
Functional deficit	62 (20.2)	52 (19.3)	9 (39.1)	0 (0)	1 (7.7)
Amputation	8 (2.6)	7 (2.6)	1 (4.3)	0 (0)	0 (0)
Systemic complications	142	88 (62.0)	49 (34.5)	2 (1.4)	3 (2.1)
AKI ^(a)	104 (73.2)	59 (67.0)	43 (87.8)	0 (0)	2 (66.7)
Respiratory failure	45 (31.6)	26 (29.5)	16 (32.6)	2 (100)	1 (33.3)
Septicemia	8 (5.6)	5 (5.7)	3 (6.1)	0 (0)	0 (0)
Shock	27 (19.0)	21 (23.9)	6 (12.2)	0 (0)	0 (0)
Serotherapy	9146	6341 (69.3)	1290 (14.1)	51 (0.6)	1464 (16.0)
Yes	6656 (72.8)	5568 (87.8)	1024 (79.4)	28 (54.9)	36 (2.5)
No	2490 (27.2)	773 (12.2)	266 (20.6)	23 (45.1)	1428 (97.5)
Serums	6481	5487 (84.7)	936 (14,4)	27 (0.4)	31 (0.5)
SABr ^(b)	6481 5482 (84.6)	5487 (84.7) 5395 (98.3)	936 (14,4) 56 (6.0)	27 (0.4) 3 (11.1)	31 (0.5) 28 (90.3)
SABr ^(b) SACr ^(c)	6481 5482 (84.6) 868 (13.4)	5487 (84.7) 5395 (98.3) 47 (0.9)	936 (14,4) 56 (6.0) 818 (87.4)	27 (0.4) 3 (11.1) 1 (3.7)	31 (0.5) 28 (90.3) 2 (6.5)
Serums SABr ^(b) SACr ^(c) SABL ^(d)	6481 5482 (84.6) 868 (13.4) 13 (0.2)	5487 (84.7) 5395 (98.3) 47 (0.9) 11 (0.2)	936 (14,4) 56 (6.0) 818 (87.4) 2 (0.2)	27 (0.4) 3 (11.1) 1 (3.7) 0 (0)	31 (0.5) 28 (90.3) 2 (6.5) 0 (0)
Serums SABr ^(b) SACr ^(c) SABL ^(d) SAEla ^(e)	6481 5482 (84.6) 868 (13.4) 13 (0.2) 29 (0.4)	5487 (84.7) 5395 (98.3) 47 (0.9) 11 (0.2) 5 (0.1)	936 (14,4) 56 (6.0) 818 (87.4) 2 (0.2) 1 (0.1)	27 (0.4) 3 (11.1) 1 (3.7) 0 (0) 23 (85.2)	31 (0.5) 28 (90.3) 2 (6.5) 0 (0) 0 (0)

Caption: (a) AKI: Acute Kidney Injury; (b) SABr: Antibotropic Serum; (c) SACr: Anticrotalic Serum; (d) SABL: Antibotropic-laquetic Serum; (e) SAEla: Antielapid Serum; (f) SABC: Antibotropic-crotalic Serum. PHS: public health significance; LPHS: low public health significance. **Source**: the authors.

source:

Accidents involving PHS snakes caused local manifestations, including pain (5959; 96.1%) and edema (5134; 82.8%), which predominantly occurred in accidents involving Bothrops spp. Most local complications occurred in victims of Bothrops spp. accidents and consisted of secondary infections (148; 54.8%), extensive necrosis (80; 29.6%), compartmental syndrome (12; 4.4%), functional deficits (52; 19.3%), and amputation (7; 2.6%). Neuroparalytic symptoms such as eyelid drooping and visual disturbances were the most frequent systemic manifestations, primarily observed in victims of *Crotalus* bites (409; 79.1%). Acute kidney injury (AKI; 104; 73.2%) and respiratory failure (45; 31.6%) were the predominant systemic complications. AKI (43; 87.8%) was the main systemic complication recorded in Crotalus bites.

In accidents involving *Bothrops* spp., 98.3% of the victims were adequately treated with antibotropic serum (SABr); however, there were also cases where anticrotalic serum (SACr; 47; 0.9%) and antielapid serum (SAEla; 5; 0.1%) antivenoms were used. For *Crotalus* envenomation, 87.4% of the victims received SACr; however, SABr (6.0%), antibotropic-laquetic serum (SABL; 0.2%), and SAEla (0.1%) antivenoms were also administered in some cases. Among *Micrurus* spp. accidents, most cases (85.2%) were treated with SAELa, although a small percentage received SABr (11.1%) or SACr (3.7%).

For LPHS, the most common local manifestations were pain and edema, reported in 1027 (89.6%) and 507 (44.2%) cases, respectively (Table 2). The most frequent systemic manifestations included neuroparalytic and vagal symptoms (vomiting and diarrhea), which were observed in 20 (28.2%) and 25 cases (35.2%), respectively. In 33 accidents (2.4%), coagulation tests revealed abnormalities. The most frequent local complication was secondary infection (12 cases; 92.3%), whereas systemic complications occurred in only three cases (2.1%), comprising two cases of AKI (66.7%) and one case of respiratory failure (33.3%). The SABr, SACr, or antibotropic-crotalic serum (SABC) antivenoms were used to treat 36 patients (2.5%).

Factors related to clinical outcomes

Age, educational level, time to treatment, and snake identity were selected for logistic regression analysis to study the factors associated with clinical outcomes such as death, local complications, and systemic complications. Owing to missing data in some cases, setting the OR was not possible; however, we performed Fisher's exact test to assess significant associations. The results of our univariate analysis are presented in Table 3.

The odds of death were higher for those aged >65 years (p<0.001, OR=5.5, 95% CI=2.6-11.5), were illiterate (p=0.005, OR=5.9, 95% CI=1.7-20.4), who had access to treatment >6 h (p=0.002, OR=3.6, 95% CI=1.6-8.0), had local complications (p<0.001, OR=15.8, 95% CI=7.4–33.2), and had systemic complications (p<0.001). Access to treatment >6 h also had higher associated odds of being associated with local complications (p < 0.001, OR=2.4, 95% CI=1.8-3.2). Furthermore, the odds of developing systemic complications were higher in those aged >65 years (p<0.026, OR=1.8, 95% CI=1.1–3.0), who had access to treatment >6 h (p<0.001, OR=3.0, 95% CI=1.9-4.5), and were bitten by Crotalus snakes (vs Bothrops spp.; p<0.001, OR=2.8, 95% CI=1.9-3.9). The data are shown in Table 3, on the next page.

	Death				Local complications				Systemic complications			
Variable	Yes n (%)	No n (%)	Log Reg ^(f) p-value	OR (95% CI)	Yes n (%)	No n (%)	Log Reg ^(f) p-value	OR (95% CI)	Yes n (%)	No n (%)	Log Reg ^(f) p-value	OR (95% CI)
Age ^(a)			< 0.001	5.5 (2.6–11.5)			0.843	0.96 (0.61–1.5)			0.026	1.8 (1.1–3.0)
<65 years	24 (0.3)	8,055 (99.7)			285 (3.5)	7923 (96.5)			125 (1.5)	8003 (98.5)		
≥65 years	10 (1.6)	612 (98.4)			21 (3.3)	611 (96.7)			17 (2.7)	608 (97.3)		
Education ^(b)			0.005	5.9 (1.7-20.4)			0.347	1.4 (0.70–2.7)			0.616	0.70 (0.20-2.90)
Illiterate	3 (1.4)	206 (99.6)			9 (4.3)	199 (95.7)			2 (1.0)	207 (99.0)		
Literate	16 (0.3)	6467 (99.7)			207 (3.2)	6348 (96.8)			89 (1.4)	6423 (98.4)		
Time elapsed ^(c)			0.002	3.6 (1.6-8.0)			< 0.001	2.4 (1.8–3.2)			< 0.001	3.0 (1.9-4.5)
<6 h	24 (0.3)	7744 (99.7)			247 (3.1)	7633 (96.9)			104 (1.3)	7711 (98.7)		
≥6 h	8 (1.1)	717 (98.9)			53 (7.2)	686 (92.8)			28 (3.9)	698 (96.1)		
Snake*; (g)											< 0.001	
Bothrops spp	22 (0.4)	5985 (99.6)			270 (4.4)	5835 (95.6)			88 (1.5)	5952 (98.5)		
Crotalus	12 (1.0)	1215 (99.0)			23 (1.8)	1240 (98.2)			49 (3.9)	1197 (96.1)	< 0.001	2.8 (1.9–3.9)
Micrurus spp	0 (0)	49 (100)			0 (0)	51 (100)			2 (3.8)	50 (96.2)	0.172	2.7 (0.6–11.3)
Non-venomous	1435 (100)	0 (0)			13 (0.9)	1424 (99.1)			3 (0.2)	1427 (99.8)	< 0.001	0.14 (0.05–0.5)
Local complications ^(d)			< 0.001	15.8 (7.4–33.2)								
Yes	11 (3.9)	269 (96.1)										
No	21 (0.3)	8135 (99.7)										
Systemic complications ^(e) Yes	26 (20.0)	104 (80.0)	< 0.001									
No	6 (0.1)	8250 (99.9)										

 Table 3 - Factors associated with outcomes of death, local complication, and systemic complication in snakebite accidents occurred in the state of Paraná between 2010 and 2021.

Caption: (a) Age: ≥ 65 years compared to < 65 years; (b) Education: illiterate compared to literate; (c) Time elapsed: >6 hours compared to < 6 hours; (d, e) Local and systemic complications: yes, compared to no; (f) Logistic Regression Model; *Fisher exact test, p< 0.05; (g) Snake: compared to genus *Bothrops*. **Source**: the authors.

Discussion

This study explored the fundamental aspects of the epidemiology of snakebites in Paraná, Brazil. Most accidents were caused by Bothrops snakes, followed by Crotalus and Micrurus, and were more common among rural workers aged 16-45 years. A correlation between illiteracy and mortality was also observed. Additionally, a higher incidence of snakebites caused by LPHS snakes was found in Paraná compared to other Brazilian regions such as Amazonas, Rio Grande do Norte, and Mato Grosso do Sul.^(19, 20) The lethality rate of 0.33% observed in this study was similar to that of previous reports; notably, snakebites accounted for the second-highest number of deaths and lethality in Paraná compared to other venomous animal accidents.⁽²¹⁾ A significant drop in accidents was observed from 2017 onward, which was even more pronounced between 2020 and 2021. Although the causes of this decline were not investigated in this study, it is likely related to the coronavirus disease 2019 (COVID-19) pandemic, during which there was fewer people circulating.

Delays in treatment (>6 hours) allow venom toxins to intensify local and systemic effects, thereby compromising antivenom efficacy. Delays were identified as an independent risk factor for poor outcomes in the present analysis, which is consistent with other studies.⁽²²⁻²⁴⁾ Similarly, advanced age (>65 years) increases susceptibility to venom-related effects. Older individuals can be more vulnerable to venom-related effects due to several factors, such as a generally weakened immune system, the presence of comorbidities such as diabetes or hypertension, and a slower rate of metabolic detoxification. Additionally, age-related physiological changes can affect how the body responds to and recovers from envenomation.⁽²⁵⁻²⁷⁾

The identification of accidents caused by LPHS relies heavily on direct evidence. Along with laboratory tests, bite marks and abrasions are crucial for accurate diagnosis, otherwise, they can be mistaken for venomous snakebites, leading to improper use of antivenom.⁽²⁸⁾ Moreover, the literature on envenomation and systemic effects caused by LPHS accidents is limited.^(29, 30) Despite their known aggression, *Philodryas* spp. were involved in relatively few cases in this study, with one case of AKI in a 10-year-old child. Conversely, accidents with the non-aggressive *Dipsas* spp. had a high incidence (16.43%). *Helicops*, once thought prominent, accounted for 6.34% of cases. These discrepancies highlight the need to investigate ecological changes, behavioral adaptations, and environmental influences affecting LPHS snake envenomation incidents.

Among the identified incidence hot spots, Guaraqueçaba had the highest incidence involving PHS snakes. It is one of the most significant continuous remnants of the Atlantic rainforest on the coastal plain near the Serra do Mar, with 98% of its 2,011,357 km² area comprising conservation units and a population density of 3.69 inhabitants/km². LPHS snake accidents occurred most frequently in Marquinho, which has an area of 503,585 km² and a population density of 8.95 inhabitants/km², and is located on the Third Plateau of Paraná with mixed ombrophilous forests and grasslands.⁽⁹⁾ While this study successfully highlights critical areas with a high incidence of snakebites, future research should aim to elucidate the specific socioeconomic and environmental determinants that contribute to these hot spots, such as temperature, rainfall, humidity, vegetation loss, urbanization level, income per capita, and type of agricultural activity.^(6, 31-33)

This study had some noteworthy limitations. Incorrect data entry may occur, including all the variables analyzed in this work. Furthermore, SINAN is limited to record the occurrence or absence of complications and is unable to define their severity. Despite these limitations, by highlighting the associations between snake species, characteristics seen in victims, and clinical manifestations, our findings contribute to a broader understanding of envenomation patterns. These findings also provide a basis for further studies that improve the understanding of the reality of snakebite accidents in Paraná and can serve as a source of data for targeted preventive measures and improved clinical management.

Conclusion

In Paraná, the majority of snakebite accidents occurred during the warmer seasons. Snakes of the *Bothrops* genus were the main cause of accidents in the state. The *Crotalus* genus caused a higher proportion of systemic manifestations, a higher mortality rate, and a higher risk of developing systemic complications compared to that by *Bothrops*. Among the LPHS snakes, *Thamnodynastes* was the most significant genus of snake that caused accidents. One case of a child treated 24 h after an accident involving *Pseudablabes patagoniensis* resulted in AKI. These data reinforce the notion that LPHS snakebite accidents cannot be considered a minor problem in the overall context of snakebites.

This study highlights a critical public health problem that affects Paraná. The State Venomous and Venomous Animal Surveillance Program can be expanded and improved through education, with prevention strategies, highlighting the importance of using protective equipment, such as boots, leg protectors and gloves, especially for the most vulnerable populations, such as those who live and work in rural areas. Furthermore, the program could offer this equipment to the population.

Abbreviations

AKI: Acute Kidney Injury; CI: Confidence Interval; COVID-19: Coronavirus Disease 2019; IBGE: Brazilian Institute of Geography and Statistics; LabTax: Animal Taxonomy Laboratory; LPHS: Low Public Health Significance Snake; OR: Odds Ratio; PHS: Public Health Significance Snake; SABC: Antibotropic-Crotalic Serum; SABL: Antibotropic-Laquetic Serum; SABr: Antibotropic Serum; SACr: Anticrotalic Serum; SAEla: Antielapid Serum; SINAN: Notifiable Diseases Information System; SINAP: Venomous Animals Notification System; SPSS: Statistical Package for the Social Sciences.

Authors' declarations

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific external funding.

Acknowledgments

We thank the Zoonosis and Poisoning Surveillance Division of SESA/PR staff for helping access SINAN data and the LabTax team for identifying animals in the SINAP database.

References

- 1 Gutierrez JM. Global Availability of Antivenoms: The Relevance of Public Manufacturing Laboratories. Toxins (Basel). 2018;11(1).
- 2 Gutierrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA. Snakebite envenoming. Nat Rev Dis Primers. 2017;3:17079.
- 3 Johnston CI, Ryan NM, Page CB, Buckley NA, Brown SG, O'Leary MA, Isbister GK. The Australian Snakebite Project, 2005-2015 (ASP-20). Med J Aust. 2017;207(3):119-25. DOI: 10.5694/ mja17.00094.
- 4 Chippaux JP. Snakebite envenomation turns again into a neglected tropical disease! J Venom Anim Toxins Incl Trop Dis. 2017;23:38.

- 5 Brasil. Boletim Epidemiológico nº 36, 2021 [Web]. Brasília: Secretaria de Vigilância em Saúde; 2022 [updated 09/23/2023. 36: Boletim Epidemiológico]. Available from: https:// www.gov.br/saude/pt-br/centrais-de-conteudo/ publicacoes/boletins/epidemiologicos/edicoes/2022/boletim-epidemiologico-vol-53-no36/ view.
- 6 Schneider MC, Min KD, Hamrick PN, Montebello LR, Ranieri TM, Mardini L, *et al.* Overview of snakebite in Brazil: Possible drivers and a tool for risk mapping. PLoS Negl Trop Dis. 2021;15(1):e0009044.
- 7 SESA. Nota técnica nº 14/2021 CIATOX-PR/DVVZI/CVIA/DAV/SESA. Secretaria de Estado de Saúde do Paraná; 2021. Available from: https://www.saude.pr.gov.br/sites/default/ arquivos_restritos/files/documento/2021-11/ Nota%20t%C3%A9cnica%20n%C2%BA%20 14-2021%20CIATOX-PR-DVVZI-CVIA-DAV-SESA%20Acidentes%20of%C3%ADdicos.pdf
- 8 Miranda SC, Bustamante M, Palace M, Hagen S, Keller M, Ferreira LG. Regional variations in biomass distribution in Brazilian Savanna Woodland. Biotropica. 2014;46(2):125-38.
- 9 Duarte LS, Bergamin RS, Marcilio-Silva V, Seger GD, Marques MC. Phylobetadiversity among forest types in the Brazilian Atlantic Forest complex. PLoS One. 2014;9(8):e105043.
- 10 IPARDES. Estimativas do Paraná, PNAD -Covid-19, novembro de 2020 2021. Available from: https://www.ipardes.pr.gov.br/Pagina/ PNAD-COVID-19-Estado-do-Parana.
- 11 Trevine VC, Grazziotin FG, Giraudo A, Sallaberry-Pincheira N, Vianna JA, Zaher H. The systematics of Tachymenini (Serpentes, Dipsadidae): An updated classification based on molecular and morphological evidence. Zool Scr. 2022;51(6):643-63.
- 12 Melo-Sampaio PR, Passos P, Martins AR, Jennings WB, Moura-Leite JC, Morato SAA, *et al.* A phantom on the trees: Integrative taxonomy supports a reappraisal of rear-fanged snakes classification (Dipsadidae: Philodryadini). Zool Anz. 2021;290:19-39.

- 13 NCI. Joinpoint Trend Analysis Software. *In*: Institute NC, editor. Statical Methodology and Applications Branch. 4.9.1.0 ed. Bethesda: National Cancer Institute; 2022. p. Surveillance Research Program.
- 14 Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000; 19(3):335-51.
- 15 ESRI. How Hot Spot Analysis works 2022 Available from: https://pro.arcgis.com/en/proapp/latest/tool-reference/spatial-statistics/hhow-hot-spot-analysis-getis-ord-gi-spatialstati.htm.
- 16 ESRI. ArcGis 10.2. *In*: Institute ESR, editor. 10.2 ed. Redlands: Environmental Systems Research Institute; 2013. p. Cloud-based mapping and analysis.
- 17 IBM. Statistical Package for the Social Sciences software (SPSS version 28). *In*: IBM, editor. Statical software plataform2022.
- 18 Dotmatics. Prism Graph Pad Boston, Massachusetts2023. Available from: https://www. graphpad.com/.
- 19 Silva TB, Aly J, Figueira M, Araújo CMdG, Sousa IKFd, Tonin AA, Fernandes LG, Sousa RS. Epidemiological aspects of snakebite in the state of Amazon, Brazil, from 2007 to 2017. J Trop Pathol. 2021;50(4):315-26. DOI: https://doi.org/10.5216/rpt.v50i4.67841.
- 20 Ceron K, Vieira C, Carvalho PS, Carrillo JFC, Alonso J, Santana DJ. Epidemiology of snake envenomation from Mato Grosso do Sul, Brazil. PLoS Negl Trop Dis. 2021;15(9):e0009737.
- 21 Navarro JG, Uchida DT, Machinski Jr M. Accidents by Venomous Animals in the State of Paraná, Brazil. Rev S Publ Paraná. 2022;5(4): 1-15.
- 22 Mahendra M, Mohammed M, Mohan CN, Ramaiah M. Study of Delayed Treatment Perspective of Snake Bites and their Long-Term Effects in a Tertiary Care Hospital in Balgalkot District of Karnataka. J Intern Med. 2021;9(3): 153-8.

- 23 Mise YF, Lira-da-Silva RM, Carvalho FM. Time to treatment and severity of snake envenoming in Brazil. Rev Panam Salud Publica. 2018;42:e52.
- 24 Schneider MC, Vuckovic M, Montebello L, Sarpy C, Huang Q, Galan DI, *et al.* Snakebites in Rural Areas of Brazil by Race: Indigenous the Most Exposed Group. Int J Environ Res Public Health. 2021;18(17).
- 25 Câmara OF, da Silva DD, de Holanda MN, Bernarde PS, da Silva AM, Monteiro WM, *et al*. Ophidian envenomings in a region of Brazilian western Amazon. J Hum Growth Dev. 2020;30(1):120-8.
- 26 Feitosa EL, Sampaio VS, Salinas JL, Queiroz AM, da Silva IM, Gomes AA, et al. Older Age and Time to Medical Assistance Are Associated with Severity and Mortality of Snakebites in the Brazilian Amazon: A Case-Control Study. PLoS One. 2015;10(7):e0132237.
- 27 Ribeiro LA, Gadia R, Jorge MT. Comparison between the epidemiology of accidents and the clinical features of envenoming by snakes of the genus *Bothrops*, among elderly and nonelderly adults. Rev Soc Bras Med Trop. 2008; 41(1):46-9.
- 28 Silveira PVP, Nishioka SdA. Non-venomous snake bite and snake bite without envenoming in a Brazilian teaching hospital. Analysis of 91 cases. Rev Inst Med Trop São Paulo. 1992;34 (6):499-503.
- 29 Weinstein SA, Warrell DA, White J, Keyler DE. Venomous Bites from non-venomous snakes – A critical analysis of risk and management of "colubrid" snake bite. 1 ed. Amsterdam: Elsevier; 2011. 364 p.
- 30 Guedes JJM, de Assis CL, da Silva DH, Feio RN. New records and notes on defensive behavior of *Thamnodynastes rutilus* (Prado 1942). Neotrop Biol Conserv. 2017;12(2):154-8.
- 31 Bravo-Vega CA, Cordovez JM, Renjifo-Ibáñez C, Santos-Vega M, Sasa M. Estimating snakebite incidence from mathematical models: A test in Costa Rica. PLoS neglected tropical diseases. 2019;13:e0007914, pmid = 31790407.

- 32 Ferreira AA, Reis VPD, Boeno CN, Evangelista JR, Santana HM, Serrath SN, *et al.* Increase in the risk of snakebites incidence due to changes in humidity levels: A time series study in four municipalities of the state of Rondônia. Revista da Sociedade Brasileira de Medicina Tropical. 2020;53:1-7.
- 33 Mise YF, Lira-da-Silva RM, Carvalho FM. Agriculture and snakebite in Bahia, Brazil – An ecological study. Annals of Agricultural and Environmental Medicine. 2016;23:416-9, pmid = 27660860, publisher = Institute of Agricultural Medicine.

Received on: Oct. 14, 2024 Accepted on: Nov. 14, 2024