

Evaluation of the use of antivenom sera in the emergency service of a regional public hospital in Vitória da Conquista (BA), Brazil

Caroline Rocha Santana (<https://orcid.org/0000-0002-4460-2412>)¹

Márcio Galvão Oliveira (<https://orcid.org/0000-0001-5281-7889>)¹

Abstract *This study aims to characterize the epidemiological profile of victims of scorpion and snakebite envenomations and to evaluate the adequacy of antivenom sera prescriptions. This is a cross-sectional study whose data sources were the envenomation notification information sheets of the Notifiable Diseases Information System in the city of Vitória da Conquista (BA), Brazil. We included information on scorpion or snakebite envenomations attended in the municipality in the period between July 2016 and June 2017. The data obtained and the variables of interest were analyzed according to the questions of this study. In the observed period, 293 victims of envenomations were treated. Of these, 149 (50.9%) were men, and 114 (38.9%) were 20-59 years old. In total, 235 (80.9%) cases of scorpionism and 58 (19.1%) of ophidism were reported. Of these, 203 (69.3%) were classified as mild, and in 200 (68.5%) cases, serum therapy was prescribed for the patients. Regarding the adequacy of the prescriptions, 172 (59.7%) were considered inadequate, and of these, the use of some vials above than indicated was the most frequent. The inappropriate prescription of antivenom sera occurred in approximately 60% of the evaluated cases. Despite this, most accidents were classified as mild – in young men.*

Key words *Ophidic envenomation, Scorpion bites, Inappropriate use*

¹ Instituto Multidisciplinar em Saúde, Universidade Federal da Bahia. R. Hormindo Barros 58, Candeias. 45029-094 Vitória da Conquista BA Brasil. carolinerochaufba@gmail.com

Introduction

Scorpionism and ophidism are the main envenomations, and these events are considered neglected diseases by the World Health Organization¹, especially in tropical and subtropical countries or developing economies²⁻⁶.

Scorpionism stands out with more than 1 million cases reported per year. The Middle East, South America, India, Africa and Mexico are endemic areas of scorpions that are dangerous to human health^{6,7}. In Brazil (with 90,922 cases reported in 2016)⁸, species *Tityus stigmurus*, *Tityus serrulatus*, *Tityus bahiensis* and *Tityus cambridgei* are the primary cause of envenomations by scorpions⁷. In turn, ophidism has a high prevalence in Central and South America and Brazil. In 2016, more than 26,000 cases have been reported^{2,4,8,9}. Most Brazilian ophidic envenomations are due to snakebites of the genus *Bothrops* (approximately 90% of cases reported) and *Crotalus*¹⁰.

Ophidism and scorpionism can lead to severe clinical complications, including death^{2,11-16}. Local manifestations are the most common, especially pain, erythema and edema at the bite's site. However, high venom amounts from these animals can lead to severe systemic manifestations such as respiratory, renal, vascular, cardiac or neurological dysfunction^{4,7,11,17-20}, and children are the most susceptible to post-poisoning complications²¹⁻²³.

Patients who are scorpionism or ophidism victims are managed with the essential support of vital conditions, associated with symptomatic treatment and specific serum therapy, when necessary. Antiscorpionic serum therapy is only indicated in cases of "moderate" classification in children younger than ten years and all cases classified as severe²⁴. Antiarachnidic serum (which includes antibodies against *Tityus* venom)²⁵ may be used in the absence of antiscorpionic serum. In ophidism, treatment varies according to the snake's genus, and the following sera are available in Brazil: bothropic (for envenomations with snakes of the genus *Bothrops*, such as jararaca), crotalic (for *Crotalus* bites) and elapid (for snakebites of the genus *Micrurus*, popularly known as coral snakes). Some associated sera (bothropic-laquetic and bothropic-crotalic) are used for situations in which the snake's type is unknown, and the bothropic-laquetic serum is used mainly in envenomations where the snake involved is suspected to be of the genus *Lachesis* (more commonly known as surucucu)²⁵⁻²⁷.

In 2016, the Brazilian Ministry of Health issued a note with guidelines on the need to adjust

antivenom doses indicated for treatment due to jararacas and scorpion bites in an attempt to reduce waste, without prejudice to envenomation victims²⁸. However, several studies have shown low adherence of health professionals to the recommendations of clinical guidelines in several areas^{29,30}. This study aims to characterize the epidemiological profile of users who are victims of scorpion and snakebite accidents and to evaluate the suitability of antivenom sera prescriptions in the emergency service of a regional hospital.

Methods

This a cross-sectional study where secondary data on envenomations were analyzed through the Notifiable Diseases Information System (SINAN) in the city of Vitória da Conquista, Bahia, Brazil.

The General Hospital of Vitória da Conquista (HGVC) is a reference service for envenomations to the city of Vitória da Conquista and surrounding region (regions of scorpions of the genus *Tityus* and snakes of the genus *Bothrops* and *Crotalus*), attending daily victims of scorpionism and ophidism. Only the HGVC receives the sera in Vitória da Conquista, and when the patients use other services in the city, they are transferred to the HGVC or the sera are dispensed and transported to these services through a disease notification.

Data were collected from the envenomation notification reports released by the HGVC's Epidemiological Surveillance in the SINAN. All notifications of scorpion or snake bites accidents were included in the period between July 2016 and June 2017. For the analysis of the adequacy of the requirements of the antivenom sera, we excluded notifications in which the type of envenomation had not been described (lack of identification of the poisonous animal causing the accident in the notification form), severity classification, presence or absence of serum therapy.

The criteria for adequate use of sera were built according to the severity classification of these accidents as per Brazilian serum therapy protocols in the Manual of Diagnosis and Treatment of Envenomations (2001)²⁶ and in the Health Surveillance Guide (2014)²⁵, updated by the Informative Note of the Ministry of the General Coordination of Communicable Diseases (2016)²⁸. Data on the type of event, severity classification, presence or absence of serum therapy, number of vials prescribed and type(s) of serum(sera) used

were compared with the adequacy criteria. Thus, the described therapeutics were classified as adequate or inadequate. The observed inadequacies were classified as: “use of vials above than recommended”, “use of vial below than recommended” and “inappropriate serum type use”.

Data were tabulated in Microsoft® Office Excel 2010 database and analyzed using IBM SPSS Statistics® 20.0 software. Measurements of central tendency, dispersion and frequencies associated with the relevant variables were calculated, such as individual data (gender, age, municipality of residence, ethnicity/skin color, schooling), epidemiological data (area of occurrence, place of event, time elapsed between bite and treatment), clinical data (verifying whether or not local and systemic manifestations are present, as well as those evidenced in case of presence and classification of event severity) and data on the treatment adopted (presence or absence of serum therapy, number of vials prescribed and type(s) of serum(sera) used). The associations between categorical variables were verified through the Chi-square test, and we considered a statistically significant difference when the probability was < 0.05 ($p < 0.05$).

The Human Research Ethics Committee of the Multidisciplinary Health Institute of the Federal University of Bahia approved this research project.

Results

In total, 293 envenomation victims were treated during the study period. Of these, 149 (50.9%) were men. The age ranged from 3 months to 86 years at the time of the accident. Also, the adult age group (20-59 years of age) corresponded to 114 (38.9%) events. Regarding skin color, 127 (43.3%) self-referred as browns.

The results related to social characteristics show that 165 (56.3%) of these patients lived in urban or peri-urban areas. Regarding the schooling of victims, we could observe that 50 (17%) stated that they had three full study years or less (Table 1).

Concerning the venomous animal involved in the reported events, 235 (80.9%) were caused by scorpions and 58 (19.1%) by snakes. Of the ophidic accidents, the most frequent were bothropic, with 41 (70.6%) cases, and crotalic, with 12 (20.8%) (Table 2).

Figure 1 shows the description of the number of events occurred in each month of the obser-

vation period. The period from December 2016 to March 2017 was the one with the highest incidence in cases of scorpionism and ophidism, and January 2017 was the month with the highest number of events reported for these two conditions (37 and 16 cases, respectively).

Regarding the place of occurrence, envenomations occurred in 20 different municipalities in the southwest region of Bahia, and 249 (85%) were in the city of Vitória da Conquista (Table 2). Regarding the area of occurrence, it was possible to observe that 55 (94.8%) ophidic accidents occurred in rural areas, while 154 (65.5%) scorpionic accidents occurred in urban or peri-urban areas. There was a significant difference in the distribution of the area of occurrence concerning the type of accident ($p < 0.05$).

In 110 (37.5%) of the reported cases, treatment occurred more than one hour and up to 3 hours after the accident with the animal. Foot/

Table 1. Sociodemographic characteristics of the victims of envenomations treated in the municipality of Vitória da Conquista (BA), Brazil, from July 2016 to June 2017.

Characteristics	N	%
Gender		
Male	149	50.9
Female	144	49.1
Age group (years)		
Child (0 to 10)	91	31
Adolescent (11 to 19)	40	13.7
Adult (20 to 59)	114	38.9
Elderly (>60)	48	16.4
Skin color		
White	33	11.3
Yellow	1	0.3
Brown	127	43.3
Black	31	10.6
Undefined/not declared	101	34.5
Dwelling region		
Urban or periurban region	165	56.3
Rural region	124	42.3
Undefined/not declared	4	1.4
Schooling (full study years)		
0 to 3	50	17
4 to 7	20	6.9
8 to 10	10	3.4
> 11	12	4.1
Not applicable*	61	20.8
Unknown/not informed	140	47.8

*Children < 6 years of age.

Table 2. Epidemiological characteristics of envenomations treated in the municipality of Vitória da Conquista (BA), Brazil, from July 2016 to June 2017 (N = 293).

Variables	N	%
Type of accident		
Ophidism	58	19.9
Scorpionism	235	80.1
Type of ophidic accident		
Bothropic	41	70.6
Crotalic	12	20.8
Laquetic	1	1.7
Elapid	1	1.7
By non-venomous snake	1	1.7
Unidentified snake	2	3.5
Location of occurrence		
Vitória da Conquista	249	85
Surrounding cities	44	15
Area of occurrence by type of accident		
Ophidism		
Urban or periurban region	3	5.2
Rural region	55	94.8
Scorpionism		
Urban or periurban region	154	65.5
Rural region	72	30.7
Undefined/not declared	9	3.8
Time elapsed between the bite and the attendance (hours)		
0 to 1h	81	27.6
>1h to 3h	110	37.5
> 3h to 6h	51	17.4
> 6h to 12h	21	7.2
> 12h to 24h	8	2.7
> 24h	7	2.4
Unknown	15	5.2
Bite site		
Head	7	2.4
Arm/Forearm	20	6.8
Hand/finger	96	32.8
Torso	12	4.1
Thigh/leg	32	10.9
Foot/toe	120	41.0
Unknown/not reported	6	2

toe (120 cases, 41%) and hand/fingers (96 cases, 32.8%) were the most common bite sites (Table 2).

Regarding the clinical signs and symptoms, 270 (92.2%) patients evidenced local manifesta-

tions, and of these, 268 (99.2%) presented local pain. Patients had systemic manifestations in 54 (18.4%) of the total cases. Regarding the severity of accidents, 203 (69.3%) were classified as mild, 72 (24.6%) as moderate and 13 (4.4%) as severe (Table 3). Accident severity was associated with a shorter time elapsed between the accident and treatment ($p = 0.01$). Concerning treatment, in 200 (68.5%) of the cases, serum therapy was prescribed for these patients. As for outcomes, 239 (81.6%) of the cases developed to cure (Table 3).

The prescribed serum therapies were found to be inadequate in 172 (59.7%) of the attendances. Of the total number of inadequate treatments, the number of vials above than indicated was more frequent (124; 72.1%), totaling 323 vials prescribed more than recommended in the protocols (Table 4). There was a significant difference in the distribution of the type of inadequacy concerning the type of accident ($p < 0.01$). Ophidic accidents inadequacies were of the kind “below than recommended use of vials”, whereas serum therapy inadequacies in scorpionic events are associated with above than the recommended use of vials in protocols.

Discussion

The results presented showed that the inappropriate prescription of antivenom sera occurred in most of the users attended (59.7%). Both the prescribed sub-dose and overdoses are more likely to cause adverse events. Rational use of medicines should include the establishment of the actual product use need, as well as adequate forms, dosages, and duration of treatment³¹.

Despite the wide dissemination of clinical guidelines, some studies point to problems with little or no adherence to treatment protocols in the most diverse areas^{29,30}. Other studies show that it is necessary to know the factors underlying the decision-making of these professionals³²⁻³⁴ to understand the varying prescriptions among prescribers. The high turnover of physicians at the facility, the incipient consultation materials, possible failures in the dissemination of protocols and the lack of regular training on the diagnosis and treatment of envenomations can be cited as factors that may influence these prescriptions in the study hospital. Also, the Ministry of Health's briefing note on the approach to treatment in cases of accidents involving snakes of the genus *Bothrops* and scorpions²⁸, in the event of a shortage of antivenom, was published in a period

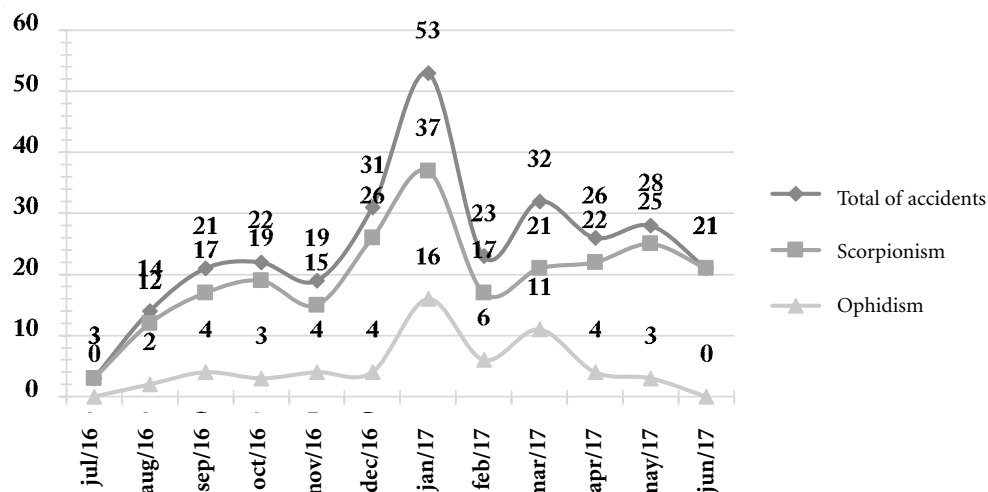


Figure 1. Distribution of the number of envenomations treated in the municipality of Vitória da Conquista (BA), Brazil, from July 2016 to June 2017.

very close to the observation period of the study.

It must be remembered that medical prescription is a complex document that guides the treatment plan for each patient. In the medication process, responsibilities must be shared and decision-making supported by other health areas³⁴. The effective insertion of a multidisciplinary urgent/emergency care team in the treatment of envenomation victims could be a measure to reduce the inadequacies pointed out in our data since several studies show that professionals such as pharmacists and nurses can act collaboratively with prescribers³⁵⁻³⁷.

A study conducted in Australia that evaluated the impact of clinical pharmacists on the emergency unit of a mid-sized hospital showed that these professionals contributed to a review of medical prescriptions, drug interventions, and staff guidelines on medications, which could decrease prescription and the inadequate administration of anti-venom sera and other therapies used in the unit³⁷. A systematic review of the performance of these professionals also evidenced these advantages and also concluded that there was a reduction of costs and hospital wastes associated with this performance³⁶.

We observed that among the inadequacies found in this present study, the most frequent was vial use above than recommended by the national protocols (72.1% of the inadequacies were

classified as overdose). Drug overdosing may expose patients to the adverse reactions resulting from the use of these sera anaphylactic or anaphylactoid, and early or late reactions, such as Serum Disease³⁸. Furthermore, there were records of recurrent crises in the supply of antivenom sera alerted by the Ministry of Health, whether due to the adequacy and refurbishment of the laboratories that produce them or to a decreased production or shortage of the raw material²⁸. Thus, the waste of anti-ophidic and anti-scorpionic sera (observed in the sum of 325 vials prescribed in excess) may contribute to the shortage of these drugs.

In contrast, in this study, we found that serum therapy used for ophidism is significantly associated with the inadequacy type of “use of vials below than recommended”. It is worth emphasizing that the fact that there are periods of shortage of anti-ophidic sera at the time of observation in the institution may have collaborated with the prescriptions of some vials below than indicated in the guidelines. However, it is noted that the sub-dose is one of the problems related to medications that may interfere with the effectiveness of the therapy and, consequently, the clinical outcome of these patients³⁹.

The sociodemographic characteristics of the studied population are similar to those of an earlier study, conducted in São Paulo, which showed

Table 3. Clinical characteristics of envenomations treated in the city of Vitória da Conquista (BA), Brazil, from July 2016 to June 2017 (N = 293).

Variables	N	%
Showed local signs and symptoms **	270	92.2
Pain	268	99.2
Edema	109	40.3
Ecchymosis	12	4.4
Necrosis	1	0.3
Showed systemic signs and symptoms **	54	18.4
Neuroparalytic (palpebral ptosis, visual turbidity)	19	35.5
Hemorrhagic (gingivorrhagia, other bleeding)	0	-
Vagus (vomiting, diarrhea)	32	59.2
Myolytic / hemolytic (myalgia, anemia, dark urine)	4	7.4
Renal (oliguria / anuria)	2	3.7
Coagulation time***		
Altered	8	2.7
Unchanged	6	2.0
Unknown/not reported	283	95.3
Classification of severity*		
Mild	203	69.3
Moderate	72	24.6
Severe	13	4.4
Unknown	5	1.7
Serum therapy use*		
Yes	200	68.5
No	92	31.5
Development		
Healed	239	81.6
Death due to accidents caused by venomous animals	3	1.0
Death by other causes	0	-
Unknown/not specified	51	17.4

*Variables with missing data. ** Had patients who reported more than one symptom. ***Variable "coagulation time" is not investigated for all cases.

a higher frequency of ophidism victims among men, adults of active working age, low educational level and residents in rural areas¹⁰. Other studies carried out in Goiás⁴⁰, Rio Grande do Norte⁴¹, Santa Catarina⁴², Minas Gerais⁴³, and Amazonas⁴⁴ also obtained profiles of envenomation victims, indicating the similarity of these characteristics in the different Brazilian regions.

Our results show high user age variability and that all age groups are susceptible to these acci-

Table 4. Analysis of serum therapy adequacy prescribed in envenomations treated in Vitória da Conquista (BA), Brazil, from July 2016 to June 2017 (N = 288).

Characteristics	N	%
Serum therapy		
Adequate	116	40.3
Inadequate	172	59.7
Type of inadequacy		
Use of vials above than indicated	124	72.1
Use of vials below than indicated	44	25.6
Inadequate type of serum	4	2.3
Total vials prescribed above than indicated in protocols	323	-
Total vials prescribed below than indicated in protocols	91	-

dents. Other studies that analyze the sociodemographic profile of victims of these accidents also showed that most of them were in the adult age group^{16,25,26}. This data can be justified by the fact that this age group contains active workers, especially rural workers, who are more likely to find venomous animals during their work routine²⁶.

The seasonality of envenomation accidents in the summer months has been evidenced in the data shown here. This period of higher accident incidence coincides with wetter months, especially summer months, a result similar to that found in several studies^{16,25,40,42,45-48}. In a systematic review of the clinical and epidemiological characteristics of scorpionism, a correlation was recorded between scorpion-related accidents by and rainfall values above 30 mm/month⁷. This phenomenon can be explained by the fact that once the rain floods the shelters of scorpions, it forces them to look for new refuges and cross the environments we share^{7,49}. Similarly, in the warmer and wetter months, the increased activity of rural workers exposes them to contact with snakes^{25,26}. Also, higher temperatures favor the mating and reproduction of scorpions, snakes, and spiders^{3,44,47,50}.

It was also possible to observe that most envenomations are scorpionic and, among the ophidic accidents, the bothropic (caused by jararacas) was the most prevalent (70.6%). These frequencies are similar to other epidemiological studies since snakes of the genus *Bothrops* have a

wide geographic distribution in Brazil, are common in several ecosystems and tend to react aggressively when they feel threatened^{9,45,46}.

There was a statistically significant difference in the area of occurrence between ophidism and scorpionism, and the former is more prevalent in the rural area and the latter in the urban/periurban zone. The rural area was the area with the highest occurrence of ophidic accidents (94.8%) since rural and hunting activities expose workers to contact with snakes^{43,51}. In turn, scorpionic accidents occurred mostly in the urban/periurban area (65.5%), as has already been shown in other studies^{3,52}, and is because the urban environment provides favorable conditions for shelter and proliferation of scorpions (higher temperatures, humidity, and presence of litter)⁷.

Regarding the areas of occurrence of the incidents, it was possible to notice that, during the observed period, the study hospital received patients from 21 different cities, in addition to Vitória da

Conquista. The diverse nature of inhabitants is justified by the fact that this institution is the reference unit in the care of envenomation victims since the city of Vitória da Conquista is a health region and reference of the macro-region of 74 neighboring cities⁵³ (Table 5).

Most accidents recorded during the period were mild (69.3%), as described in other studies^{3,43,46}. This may be associated with the short intervals between the bite and care received. In this study, most of the victims were treated within 3 hours after the bite and, as already reported in the literature, the speed of care is directly related to the accident's development^{16,26}.

On the other hand, despite the predominance of mild accidents, in most cases (68.3%), serum therapy was prescribed and 19.6% of the users developed with systemic manifestations (of greater severity than the local ones). Mortality of envenomation victims was 1%. However, we cannot infer a possible relationship between in-

Table 5. Place of occurrence of envenomations treated in the city of Vitória da Conquista (BA), Brazil, from July 2016 to June 2017 (N = 293).

Variables	Distance (km)* between the city and Vitória da Conquista	Number of snake envenomations	Number of scorpion envenomations
Vitória da Conquista	-	29	219
Surrounding cities			
Anagé	67.3	5	3
Barra da Estiva	203	2	-
Barra do Choça	45.4	1	2
Bom Jesus da Serra	116	2	-
Brumado	153	1	-
Caetanos	93	3	2
Caraíbas	96.7	1	1
Condeúba	155	1	1
Encruzilhada	92.5	1	-
Igaporã	297	1	-
Iguaí	130	-	1
Itambé	50.4	-	1
Itororó	124	1	-
Ituaçu	184	3	-
Maetinga	115	1	1
Mirante	160	2	-
Piripá	115	-	2
Planalto	68	1	-
Poções	89.3	1	1
Ribeirão do Largo	94.3	1	1
Tanhaçu	128	1	-
Total	-	58	235

* Lowest distance (km) between cities considered by Google Maps data (2018).

adequate treatment and death due to the lack of data on comorbidities.

We can point out that the possible failures in filling out the notification sheets and the unavailability of variables in these records that contained possible additional antivenom sera prescriptions as limitations of this study.

We should stress that these data show the relevance of this cause of morbimortality of the population of Vitória da Conquista and region and the need to build public policies aimed at reducing adverse outcomes from these accidents. Also, due to results with a high frequency of in-

adequate sera prescriptions presented and discussed herein, it is evident that the institution must develop strategies to subsidize measures that ensure the rational use of this supply and control of its waste.

The insertion of the multidisciplinary health team, in particular, the clinical pharmacist, in the urgent and emergency care unit can act in the review of the medical prescriptions, interventions related to the antivenom sera and guidance of the team on the use of these medicines – measures that can contribute significantly to reducing these inadequacies.

Collaborations

CR Santana and MG Oliveira participated in the conception, design, analysis and interpretation of data, writing of the article and approval of the version to be published.

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