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A retrospective study of clinical and epidemiological characteristics of snakebite in Napo Province, Ecuadorian Amazon

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Background: Snakebite envenoming remains a relevant public health problem in tropical and subtropical countries. In Ecuador, this is particularly true in an area of great diversity like the Amazon region. Nevertheless, there is scarce information about epidemiological and clinical characteristics of these accidents in this area.

Methods: This was a descriptive and retrospective study of snakebite cases treated at a tertiary hospital in the Napo Province, Ecuadorian Amazon, from 2015 to 2019. We collected sociodemographic and snakebite-related information, clinical aspects and the use of antivenom and antibiotics from medical records.

Results: Information from 133 snakebite accidents was reviewed in this time period. Reports of snakebite envenoming decreased over the years. In total, 67% of those bitten were from nearby indigenous communities, which were the most affected groups. When a species was identified, *Bothrops atrox* was responsible for the highest number of cases registered. Local clinical manifestations were more frequent than systemic signs, in keeping with the typical effects produced by bothropic venoms. Additionally, data showed that more antivenom vials were given than those suggested by the protocol of the Ecuadorian Ministry of Health, in proportion to the grade of severity. Finally, we identified a low incidence of adverse reactions with antivenom administration, as well as a frequent use of antibiotics.

Conclusions: The profile of snakebite accidents in the Napo Province is very similar to that described for other localities in the Amazon region of Ecuador and neighboring countries, with its challenges and limitations. Such aspects underlie the importance of establishing a robust and science-based public health program to respond to this frequent, but neglected, tropical disease.

Keywords: *Bothrops*, epidemiology, Ecuador, snakebite envenoming

Introduction

Snakebite envenoming, a potentially life-threatening event, is currently included in the WHO neglected tropical diseases portfolio as a Category A neglected tropical disease.[1] It remains a frequent medical challenge in communities living in a contrasting environment, rich in biodiversity but with limited access to adequate health facilities and low income. Official estimates indicate that 1.8 to 2.7 million accidents occur worldwide, causing 81 000–138 000 deaths per year.[1–3] Furthermore, 400 000 victims live with physical and psychological effects such as disability, amputation and post-traumatic disorders.[4] Usually, the number of reported cases represents only a partial assessment of the real impact of this condition, caused by limitations in the collection of comprehensive epidemiological data and incomplete central public health databases.[1] Mainly for these reasons, snakebite statistics are commonly calculated as extrapolations from data available in medical centers, population surveys and mathematical modeling.[5]

Most snakebite envenoming cases occur in South and Southeast Asia, sub-Saharan Africa and Latin America.[6] Within South America, Ecuador is characterized by a high diversity of front-fanged venomous snakes (19 species in the family Elapidae and 17 in Viperidae), as well as an important number of snakebite accidents.[7,8] From 1998 to 2007, the Ministry of Health of Ecuador registered 14 720 ophidian accidents nationwide,[9] while during 2014–2019 the average was 1506 cases per year.[10] Pitviper snakes in the *Bothrops* genus are associated with 70–80% snakebites reported in the country.[11] The Amazon region is the area with the highest snakebite events and mortality in relation to the number of inhabitants in Ecuador.[10] The most medically significant venomous species in the Ecuadorian Amazon are *Bothrops atrox*, *Bothrops bilineatus*, *Bothrops taeniatus* and *Lachesis muta*.[12] The main clinical signs and symptoms observed in hospitalized patients affected by these species are local edema, hemorrhage, myonecrosis (necrosis of muscular tissue) and systemic compromise such as acute kidney injury and coagulation disorders, as described previously.[6]

Currently, despite being the standard therapy, there are no snakebite antivenoms produced locally in Ecuador. Most public and private healthcare facilities use a lyophilized polyvalent antivenom produced at Instituto Clodomiro Picado (ICP), Costa Rica.[13] The antivenom neutralization efficacy was evaluated and confirmed by the Instituto de Investigación en Salud Pública,[14] which plays a central role as a reference laboratory for services focused on public health in Ecuador. Furthermore, previous studies have shown that immunoglobulins in this product are capable of neutralizing the toxicological effects caused by the venom of several species of snakes from Central and South America.[15] However, studies have also evidenced that effective doses may vary between each region, due to factors such as plasticity in venom composition.[16]

Despite the medical relevance, data about epidemiology and common effects of envenoming in patients from the Amazonian region of Ecuador have not been extensively reviewed.[10,12,17] In particular, no previous works address such issues in Napo province. In light of this, we analyzed the clinical aspects and epidemiology of snakebite accidents treated at the main hospital of Napo, located in the northern Ecuadorian Amazon, reviewing medical records from patients admitted for urgent care.

Methods

We carried out a hospital-based, retrospective descriptive study of snakebite envenoming cases reported at José María Velasco Ibarra Hospital in the province of Napo, Ecuador. This health facility is the reference center to treat snakebite accidents in this Amazonian province. Prior to the start of the study, institutional approval and consent was obtained for the confidential and anonymous handling of hospital records in accordance with national legislation. All records available at the hospital for 5 y (January 2015 to December 2019) were rigorously reviewed. We collected demographic data and information about different aspects of the accidents (age, gender, residence, ethnicity, activity, time/date of accident). Identification of the snake species involved was carried out according to details described in the records, therefore this was not performed by an expert. We include only cases where bite and envenoming were evidenced at the time of admission.

The classification of envenoming severity (included in hospital records) was made in line with the current guidelines of the Ministry of Health of Ecuador following a score that includes clinical, laboratory and pharmacological parameters.[11,18] We collected information about the main signs and symptoms (local and systemic manifestations) observed during admission and treatment. To obtain information on coagulation parameters, especially clotting time at admission and its evolution, we also reviewed available laboratory tests. We also retrieved information regarding the number of antivenom vials used per patient, the frequency of adverse reactions after its administration and whether antibiotic treatment was implemented. For the statistical analyses, the χ^2 (likelihood ratio χ^2) and one-way ANOVA were used, followed by the Tukey test. The level of significance was set at $p<0.05$. Analyses were performed in R Statistical Software (v4.1.2; R Core Team 2021).

Results

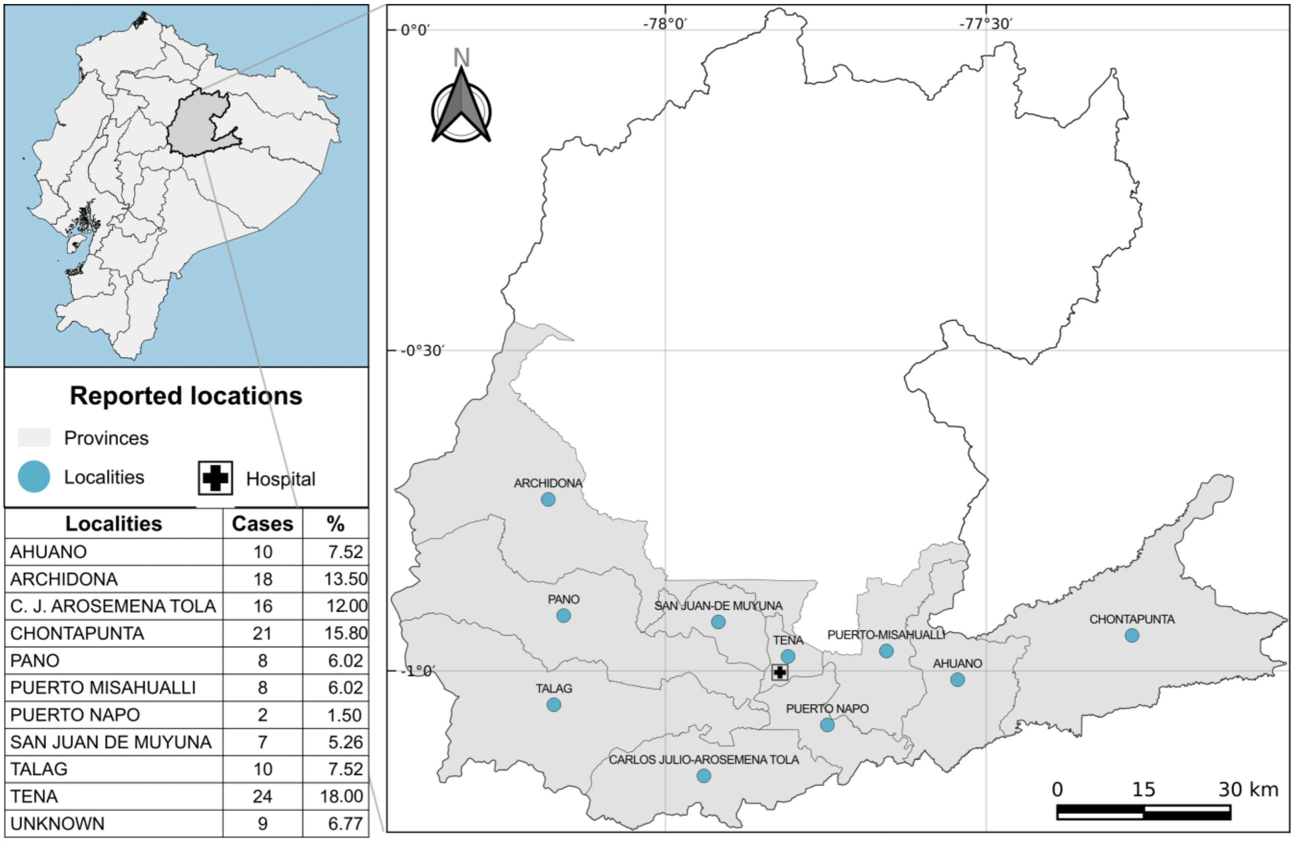
Data from 133 cases registered during 2015–2019 were available for analysis. No snakebite-related fatalities were reported during this interval of time (5 y). Patients were transferred from different localities in the province that are under the coverage of the hospital located in Tena (province's capital) (Figure 1).

Statistical analysis of the data shows that the number of cases per trimester varies from one year to another. For this reason, a clear temporal pattern related to seasonal trends and weather conditions was not identified (Table 1). The number of snakebite accidents treated at the hospital gradually decreased over time, with 35.34% of cases occurring in 2015 and 9.02% in 2019 (Table 1). The largest number of cases belonged to patients aged 16–45 y (43.61%), predominantly males (60.90%). Records showed that snakebites were more frequent in indigenous people (67.67%) and in those living in rural locations (72.93%). Furthermore, most envenoming cases occurred while carrying out agricultural activities (45.86%) or walking on roads with overgrown vegetation (24.06%). Patients were bitten between 09:00 and 16:00 h in 42.86% of incidents, while 22.56% of events took place between 17:00 and 23:00 h.

Most patients described snake species mainly by their common names, with *B. atrox* (equis, pitalala) being responsible for 56.39% of incidents (Figure 2), while *B. bilineatus* (oro palito, orito machacui) and *B. taeniatus* (orito palo), whose common names are similar, were reported in 12.03% of events (Figure 2). In 31.58% of records, the patient did not describe the snake or the recorded data were insufficient to classify the species.

Additionally, snakebites were more frequent in lower (59.39%) and upper extremities (38.37%), with head (1.47%) and chest (0.77%) injuries being much less common (Figure 3A). Likewise, information contained in emergency reports indicate that out of the 133 patients, the use of alternative treatments such as tourniquets, alternative medicine (medicinal plants and/or shamanism) and attempted venom suction were all used in 5 individuals (3.75%), while in 19 victims (14.28%) at least two of these interventions took place (Figure 3B).

As per the current severity of envenoming classification,[10,17] 53.38% of cases were diagnosed as moderate, 28.57% categorized as severe and 18.05% identified as mild. Different levels of edema and pain were identified regardless of patient envenoming severity (Table 2). From 133 records analyzed, local erythema



Localities	Cases	%
AHUANO	10	7.52
ARCHIDONA	18	13.50
C. J. AROSEMENA TOLA	16	12.00
CHONTAPUNTA	21	15.80
PANO	8	6.02
PUERTO MISAHUALLI	8	6.02
PUERTO NAPO	2	1.50
SAN JUAN DE MUYUNA	7	5.26
TALAG	10	7.52
TENA	24	18.00
UNKNOWN	9	6.77

Figure 1. Reported locations for snakebite accidents in Napo province. Data collected at José María Velasco Ibarra Hospital, Tena, 2015–2019.

(redness) (47.37%), ecchymosis (23.31%), myonecrosis (3.76%), lymphadenitis (0.75%) and adenopathy (0.75%) were described as medical signs.

Abscess formation (12.78%) and cellulitis (8.27%) were reported as infectious complications (Table 2), and systemic signs such as hemorrhage (14.29%), headaches (13.53%), gingival hemorrhage (9.77%), fever (9.02%) and vomiting (8.27%) were also present in the three envenoming severity categories. Hypertension (5.26%) and compartment syndrome (3.01%) were evidenced only in moderate and severe envenoming, while bradycardia (1.50%), hematuria (1.50%), thrombocytopenia (0.75%) and hypokalemia (0.75%) were infrequently observed (Table 2). One patient with compartment syndrome was submitted to fasciotomy after being treated with antivenom. In the remaining three cases, antivenom doses were increased to treat this complication. For all compartment syndrome patients, a disturbance in coagulation was described.

Eight patients returned to the hospital days after medical discharge due to some complication. Two individuals developed myonecrosis and were readmitted (one of them underwent surgery, losing the toe affected by being bitten). In two others, soft tissue infection was initially diagnosed and treated then recurred a few days later. One person with previously reported cellulitis on the affected limb required surgical drainage of an abscess. Two cases, without previous signs of infection, required medical care due to soft tissue infection.

More than half of the patients by category of envenoming were admitted for treatment within the first 4 h after the accident (mild=62.5%, moderate=56.34%, severe=52.63%) (Table 3). Coagulation tests performed upon admission evidenced that a delay in clotting times (>20 min) was evidenced in more than half of the patients for each severity grade category (mild=58.33%, moderate=76.46%, severe=86.84%). In most of the cases analyzed, the coagulation restoration time was 0–24 h after the first administration of antivenom (mild=95.83%, moderate=92.96%, severe=68.41%). These tests are performed regularly on patients treated for snakebite envenoming to monitor their evolution.[10]

Regarding treatment with antivenom (Table 3), measured by the total number of vials used, most of mild envenoming patients required up to 16 vials to treat toxicological effects. Additionally, for one mild case (4.17%), 21–24 doses were administered. For victims with a diagnosis of moderate envenomation, 94.36% were treated with up to 20 vials, while for severe cases, 34.22% required very high doses in comparison with the other patients (20–44 vials to neutralize toxicological effects).

We also identified that from the total number of records analyzed (133), only 12 patients (9.02%) had a complication that derived from treatment with antivenom (Table 3). Generalized rash was observed in 11 cases, and in one patient with fever (37.9°C without chills and shivering), urticaria and hemolysis was reported. Only one case of anaphylactic shock was described, where it was necessary to use adrenaline for its treatment. In all

Table 1. General characteristics of patients affected by snakebite and treated at José María Velasco Ibarra Hospital, Tena, Ecuador, 2015–2019; n_{total}=133

	Year					
Variables	2015 n=47	2016 n=31	2017 n=27	2018 n=16	2019 n=12	Totaln=133
Trimester						
First	18 (38.30)	8 (25.81)	6 (22.22)	6 (37.50)	5 (41.67)	43 (32.33)
Second	8 (17.02)	13 (41.93)	5 (18.52)	4 (25.00)	5 (41.67)	35 (26.32)
Third	13 (27.66)	6 (19.35)	11 (40.74)	2 (12.50)	1 (8.33)	33 (24.81)
Fourth	8 (17.02)	4 (12.90)	5 (18.52)	4 (25.00)	1 (8.33)	22 (16.54)
Ethnicity						
Indigenous	36 (76.60)	22 (70.97)	21 (77.78)	3 (18.75)	8 (66.67)	90 (67.67)$^{\$}$
Mestizo	11 (23.40)	8 (25.81)	5 (18.52)	1 (6.25)	1 (8.33)	26 (19.55)
Not specified	0	1 (3.23)	1 (3.70)	12(75.00)	3 (25.00)	17 (12.78)
Gender						
Male	27 (57.45)	19 (61.29)	20 (74.07)	11 (68.75)	4 (33.33)	81 (60.90)
Female	20 (42.55)	12 (38.71)	7 (25.93)	5 (31.25)	8 (66.67)	52 (39.10)
Age, y						
0–15	21 (44.68)	6 (19.35)	7 (25.93)	5 (31.25)	4 (33.33)	43 (32.33)
16–30	13 (27.66)	5 (16.13)	7 (25.93)	3 (18.75)	4 (33.33)	32 (24.06)
31–45	9 (19.15)	8 (25.81)	5 (18.52)	4 (25.00)	0	26 (19.55)
46–60	3 (6.38)	6 (19.35)	5 (18.52)	2 (12.50)	3 (25.00)	19 (14.29)
+60	1 (2.13)	6 (19.35)	3 (11.11)	2 (12.50)	1 (8.33)	13 (9.77)
Snakebite site						
Urban	6 (12.77)	6 (19.35)	6 (22.22)	4 (25.00)	2 (16.67)	24 (18.05)
Rural	39 (82.98)	20 (64.52)	17 (62.96)	11 (68.75)	10 (83.33)	97 (72.93)$^{\$\$}$
Not specified	2 (4.26)	5 (16.13)	4 (14.81)	1 (6.25)	0	12 (9.02)
Activity/location during the accident						
Agriculture	15 (31.91)	13 (41.94)	17 (62.96)	12 (75.00)	4 (33.33)	61 (45.86)$^{\$}$
Walking around riverine areas	2 (4.26)	3 (9.68)	1 (3.70)	0	1 (8.33)	6 (4.51)
Walking on trails	20 (42.55)	3 (9.68)	8 (29.63)	2 (12.50)	1 (8.33)	32 (24.06)
At home	4 (8.51)	3 (9.68)	1 (3.70)	2 (12.50)	1 (8.33)	13 (9.77)
Not specified	6 (12.77)	9 (29.03)	0	0	5 (41.67)	21 (15.79)
Time of accident, h						
00:00–08:00	10 (21.28)	13 (41.94)	6 (22.22)	0	1 (8.33)	30 (22.56)
09:00–16:00	24 (51.06)	10 (32.26)	15 (55.56)	0	8 (66.67)	57 (42.86)
17:00–23:00	13 (27.66)	8 (25.81)	6 (22.22)	0	3 (25.00)	30 (22.56)
Not specified	0	0	0	16	0	16 (12.03)

Statistically significant differences are highlighted: $^{\$}p<0.05$ and $^{\$\$}p<0.01$ (Tukey's test).

cases, antivenom administration was discontinued when symptoms and signs were observed and patients were treated with antihistamines. Adverse reactions to antivenom were noticed within the first 6 h of administration. Finally, a high frequency of antibiotic use was observed, mainly in moderate (81.69%) and severe (86.84%) envenoming. According to clinical records, crystalline penicillin, ceftriaxone and clindamycin were the antibiotics used for treatment, either alone or in combination.

Discussion

In the present study, we seek to characterize the epidemiological and clinical profile of snakebite accidents in a province located in the Ecuadorian Amazon through analysis of cases registered and treated in a tertiary public hospital. We found that snakebite incident reports at this reference center have decreased over the years in the time interval studied, similar to the trend identified by Ochoa-Avilés et al.[10] for the Ecuadorian Amazon. This reduction has also been observed in some places of the Brazilian Amazon and might have possible explanations.[19,20] Underreporting remains one of the main factors that would cause the drastic drop in cases. Maciel Salazar et al.[21] recently identified a high rate of underreporting (50%) in indigenous communities from the Brazilian Amazon. Some authors ascribe such a reduction to the growing urbanization of the area,[22] which is unlikely in the period covered by this study. Another probable scenario might be the decentralization of healthcare, with availability of antivenom treatment in secondary and even primary level health

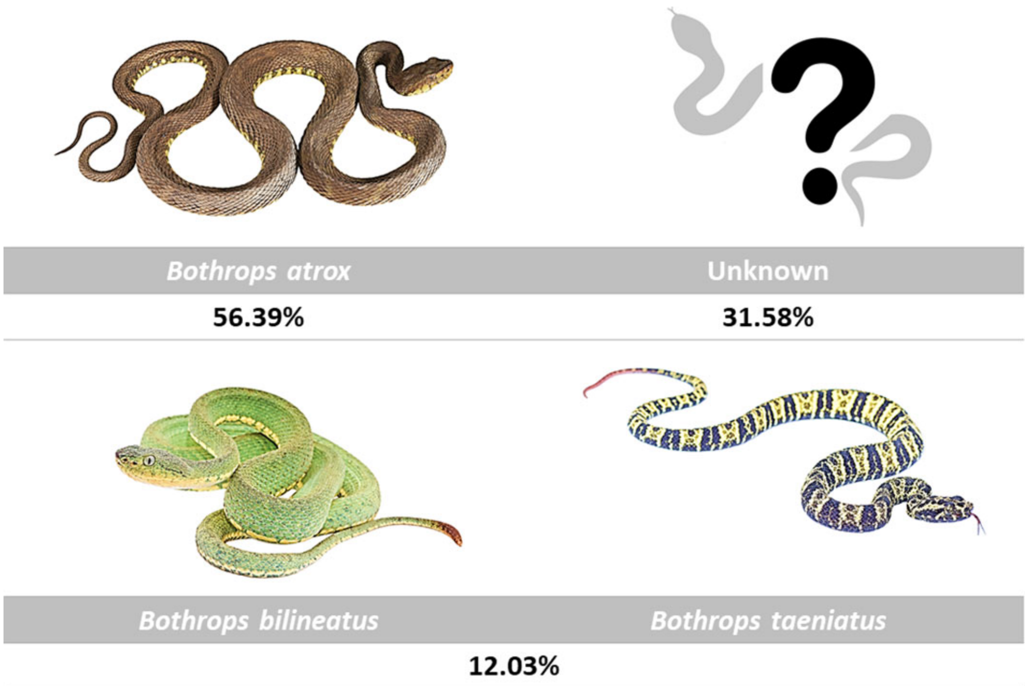


Figure 2. Species described as responsible for snakebite envenoming in Tena, Napo hospital records during 2015–2019. Photographs by Fernanda Gordón, Sebastián Valverde and Diego Quirola.

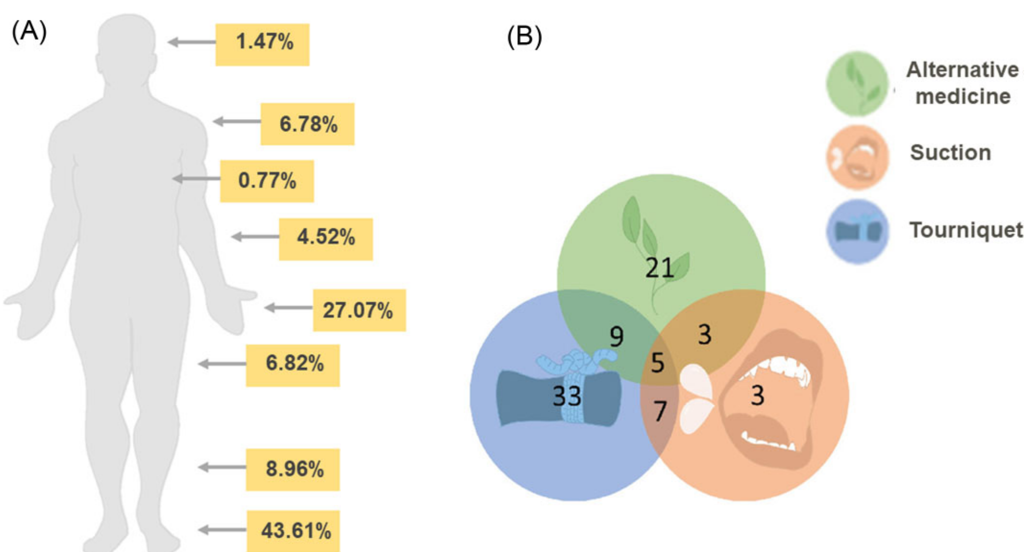


Figure 3. (A) Reported anatomic location of snakebite and (B) procedures employed before clinical treatment at José María Velasco Ibarra Hospital, Tena, Ecuador from 2015 to 2019.

facilities resulting in fewer patients being transferred to reference centers.[23]

There were no fatalities registered in this period. Such an absence of deaths (and reduction of cases) might be related to some improvements in the healthcare system at the time of the study. One example is the publication of National Clinical Practice Guidelines for the diagnosis and treatment of snakebite accidents and the provision of free-of-charge antivenom within the public healthcare system.[24] However, the possibility of a reduction in cases due to underreporting cannot be completely ruled

Table 2. Clinical manifestations of 133 snakebite patients treated at José María Velasco Ibarra Hospital, Tena, Ecuador, during 2015–2019, according to envenoming classification

Variable	Mild envenoming n=24	Moderate envenoming n=71	Severe envenoming n=38	Total n=133
Local manifestations				
Cellulitis	1 (4.17)	5 (7.04)	5 (13.16)	11 (8.27)
Abscess	3 (12.50)	7 (9.86)	7 (18.42)	17 (12.78)
Ecchymosis	7 (29.17)	13 (18.31)	11 (28.95)	31 (23.31)
Myonecrosis	0	1 (1.41)	4 (10.52)	5 (3.76)
Lymphadenitis	0	0	1 (2.63)	1 (0.75)
Adenopathy	1 (4.17)	0	0	1 (0.75)
Erythema	9 (37.50)	36 (50.70)	18 (47.37)	63 (47.37)
Edema (+)/mild	10 (41.67)	16 (22.54)	6 (15.79)	32 (24.06) **
Edema (++)/moderate	10 (41.67)	39 (54.93)	12 (31.58)	61 (45.86) **
Edema (+++)/intense	3 (12.50)	15 (21.13)	20 (52.63)	38 (28.57) **
Pain (mild)	7 (29.17)	8 (11.27)	0	15 (11.28) **
Pain (moderate)	4 (16.67)	18 (25.32)	9 (23.68)	31 (23.31) **
Pain (intense)	10 (41.67)	43 (60.56)	27 (71.05)	80 (60.15) **
Systemic manifestations				
Hemorrhage	4 (16.67)	10 (14.08)	5 (13.16)	19 (14.29)
Gingivorrhagia	3 (12.50)	4 (5.63)	6 (15.79)	13 (9.77)
Compartment syndrome	0	3 (4.23)	1 (2.63)	4 (3.01)
Headache	4 (16.67)	9 (12.68)	5 (13.16)	18 (13.53)
Hematuria	0	1 (1.41)	1 (2.63)	2 (1.50)
Hypokalemia	0	0	1 (2.63)	1 (0.75)
Bradycardia	1 (4.17)	0	1 (2.63)	2 (1.50)
Vomiting	2 (8.33)	7 (9.86)	2 (5.26)	11 (8.27)
Thrombocytopenia	1 (4.17)	0	0	1 (0.75)
Hypertension	0	4 (5.63)	3 (7.89)	7 (5.26)

Edema and pain were diagnosed in three levels of severity. For edema, (+): involves a segment of the affected limb, (++): involves 2 or 3 segments of the affected limb, (+++): involves more than three segments of the affected limb. **Indicates that $p<0.01$ (χ^2 test).

out. In the Western Brazilian Amazon (a similar region), the percentage of underreported deaths by snakebite envenoming was estimated to be almost 30%.

In Ecuador, the procedure for data collection (especially regarding snakebites and other neglected tropical diseases) varies widely from one administration to the next. In addition, clinical records might be incomplete as the healthcare workers responsible for their completion are usually overworked and undertrained. These conditions limit the reliability of the data and might lead to inconsistencies in the national epidemiological data, including the numbers of cases and deaths per year caused by snakebite envenoming. For instance, it has previously been reported that accidents in Ecuador increase during the rainy season (January–April).[25] However, the information collected for the present study did not identify an association of a higher number of cases with a specific season.

Results show that 67% of victims came from indigenous communities, therefore they represent a particularly vulnerable group. Locations where these populations live and work are high-risk environments because their agricultural practices increase their risk of exposure to snakes.[26] Recent studies from the Brazilian Amazon showed that indigenous people were more likely to have an accident with venomous snakes.[26,27] However, the scarcity of studies addressing this relationship stands out, which could be influenced by factors such as the geographical location of these populations.[27,28] In addition, it should be considered that the case reports for indigenous communities are probably lower in comparison with the actual number due to several barriers including language, traditional practices (i.e. not procuring hospital-based care) and geographical distance to health centers.[29]

The use of non-scientifically validated and alternative treatments has been commonplace and was evidenced in this study. Plant extracts have historically been used by communities in rural areas, and perhaps continues due to local conceptions and socioeconomical and geographical limitations.[25] However, there is a lack of evidence regarding the efficacy and safety of these practices.[30] Additionally, application of tourniquets or an attempt to suck out the venom was observed, actions that have been proven to be harmful.[31] Wound manipulation, poor

Table 3. Clinical aspects of snakebite patients treated at José María Velasco Ibarra Hospital, Tena, Ecuador, during 2015–2019, according to envenoming classification

Variable	Mild envenoming n_{total}=24	Moderate envenoming n_{total}=71	Severe envenoming n_{total}=38	Total n_{total}=133
Time to medical care (h)		(number of patients, %)		
1–4	15 (62.50)	40 (56.34)	20 (52.63)	75 (56.39)$^{\$\$}$
5–8	4 (16.67)	12 (16.90)	8 (21.05)	24 (18.05)
9–12	1 (4.17)	4 (5.63)	2 (5.26)	7 (5.26)
13–16	1 (4.17)	3 (4.23)	0	4 (3.01)
17–20	0	1 (1.41)	0	1 (0.75)
+21	1 (4.17)	3 (4.23)	5 (13.16)	9 (6.77)
No data	2 (8.33)	8 (11.27)	3 (7.89)	13 (9.77)
Clotting time (min)		(number of patients, %)		
0–10	4 (16.67)	3 (4.23)	1 (2.63)	8 (6.02)
11–20	2 (8.33)	10 (14.08)	4 (10.53)	16 (12.03)
Incoagulable	14 (58.33)	55 (77.46)	33 (86.84)	102 (76.69)$^{\$}$
No data	4 (16.67)	3 (4.23)	0	7 (5.26)
Time to coagulation restoration (h)		(number of patients, %)		
0–8	11 (45.83)	22 (30.99)	7 (18.42)	40 (30.08) **
9–16	9 (37.50)	26 (36.62)	9 (23.68)	44 (33.08) **
17–24	3 (12.50)	18 (25.35)	10 (26.32)	31 (23.31) **
+25	0	4 (5.63)	10 (26.32)	14 (10.53) **
No data	1 (4.17)	1 (1.41)	2 (5.26)	4 (3.01)
Number of antivenom vials used (units)		(number of patients, %)		
0–4	14 (58.33)	9 (12.68)	3 (7.89)	26 (19.55) **
5–8	5 (20.83)	27 (38.02)	3 (7.89)	35 (26.32) **
9–12	2 (8.33)	17 (23.94)	18 (47.37)	37 (27.82) **
13–16	2 (8.33)	11 (15.49)	1 (2.63)	14 (10.53) **
17–20	0	3 (4.23)	0	3 (2.26) **
21–24	1 (4.17)	2 (2.82)	6 (15.80)	9 (6.77) **
25–28	0	2 (2.82)	1 (2.63)	3 (2.26) **
29–36	0	0	4 (10.53)	4 (3.01) **
37–44	0	0	2 (5.26)	2 (1.50) **
Adverse effects to antivenom		(number of patients, %)		
Yes	0	8 (11.27)	4 (10.53)	12 (9.02)
No	24 (100)	63 (88.73)	34 (89.47)	121 (90.98)
Antibiotic use		(number of patients, %)		
Yes	13 (54.17)	58 (81.69)	33 (86.84)	104 (78.20)*
No	11 (45.83)	13 (18.31)	5 (13.16)	29 (21.80)*

Statistically significant differences are highlighted: $^{\$}p<0.05$ and $^{\$\$}p<0.01$ (Tukey's test) and $^{*}p<0.05$ and $^{**}p<0.01$ (χ^2 test).

disinfection and contamination with other products such as herbal extracts could cause infection-related complications, such as the formation of abscesses.[31] We identified that tourniquets were used in three of four patients diagnosed with compartment syndrome. On the other hand, no correlation was observed between wound manipulation and clinical complications associated with infections.

Post-hospital discharge follow-up appointments were scheduled. However, high levels of patient non-attendance were registered, which hinders a better understanding of clinical evolution. This behavior was observed even in patients who underwent surgery. Different factors, such as a lack of economic resources, residences far from the urban zone and traditions, likely contribute to this pattern. For instance, there is no information available on any possible sequelae and evolution of the patient with compartment syndrome.

Bothropic envenomings can produce cardiovascular alterations due to the action of hemorrhagic and cardiotoxic toxins. However, they are rare.[32] Our analysis pointed out two cases of bradycardia. Patients were treated by administering electrolytes (potassium or calcium). The chemical imbalance of electrolytes is one of the causes of bradycardia, so this would be the origin of the clinical sign.[33]

Complications derived from *Bothrops* envenoming take several hours to manifest.[25] For this reason, adequate and prompt care is imperative to improve the clinical course and to avoid permanent sequelae.[29] According to our data, most patients were treated in a health center during the first 4 h after the snakebite. This seems compatible with a retrospective study from Brazil where authors identified that 72% of patients were treated within 0–3 h.[34]

In a clinical study carried out in Costa Rica by Brenes-Chacón et al.,[5] for patients with mild envenoming, 1–5 vials of polyvalent produced by Instituto Clodomiro Picado antivenom were administered, for moderate cases 5–10 vials and, for severe cases, 10–15 vials. Meanwhile, the protocol issued by The Ministry of Health notes that 4 vials should be used for mild envenoming, 8 for moderate cases and 12 for severe envenoming patients.[11] These modifications were adopted considering the results of the antivenom efficacy evaluation carried out in Ecuador and validation by experts.[11,14] If the envenoming continues after 12 h of treatment, the severity needs to be reassessed. In addition, if the coagulation alteration persists, new doses should be administered following the indications of the established protocol.[11] On the other hand, if vials are available at a primary medical center, these are used to treat the patient before being transferred to hospital. This may be a source of underdose, as in some cases evaluation upon admission to hospital has shown that no further doses are necessary. In all victims the administration of the antivenom started after verifying clinical manifestations, mainly the alteration of blood coagulation.[11]

The data analyzed showed that nearly 45% of the patients received more doses than those suggested, which could represent an issue for the country. In 2012, the (already limited) production of antivenom ceased in Ecuador and, since then, it has been imported mainly from Costa Rica.[13] Patients can access treatment free of charge in public hospitals. The state is the main buyer of the product through the Ministry of Health, which in turn distributes it to the public health network.[8,35] However, the treatment is usually found in tertiary hospitals, located at great distances from indigenous communities. The number of vials to acquire is determined by considering the epidemiological figures of the previous years, which is another reason why proper data management is crucial. Antivenoms can also be purchased through private organizations at an approximately price of US$71 per vial, an unaffordable cost for the population most affected by snakebites.[8]

It is a risk for the country to depend on a foreign producer, because if the latter is affected, it could compromise the importation of the medicament.[8] For instance, the current COVID-19 pandemic has caused reductions in personnel, in the purchase of consumables and in the budget designated for the production of antivenom in various laboratories in Latin America.[36] During the study period, no shortage of vials of immunoglobulins was specifically reported. However, the general shortage of lifesaving medicines in hospitals is a common situation in the country.[37] This is something that can affect the availability of antivenoms considering that all medicines (including those used to treat envenoming) are purchased through the public health system.

In addition, there are factors such as intraspecific and interspecific variation in snake venom, which can cause an increase in effective doses to treat a patient.[13,16] In recent years, it has been proposed to resume antivenom production in Ecuador, thus increasing its availability, and it could be distributed in primary care centers.[8] This, together with the training of medical personnel and community education campaigns, could reduce the impact of the disease in remote areas.

An increase in the number of antivenom vials applied in turn increases the risk of adverse reactions.[38] However, in the case of the ICP-produced antivenom, the frequency of adverse reactions seems to be low, as previously verified in Costa Rica.[5] The therapy in adverse reactions, when detected, was primarily based on antihistamines. At the same time, the antivenom administration was stopped. Treatment was restarted when signs of anaphylaxis were controlled. A case of fever (37.9°C) was reported, a clinical manifestation that could be the result of a pyrogenic reaction, which is also characterized by symptoms such as headache, nausea, chills and shivering. In this occurrence the fever was accompanied by rash and urticaria, which are hallmarks of anaphylactic reactions.[39]

We also observed a frequent use of antibiotics, even in mild and moderate envenoming cases. Several authors have suggested avoiding widespread empirical use of antibiotics because of the important issue of bacterial resistance.[40] Furthermore, recent evidence shows that antibiotics can potentiate the activity of venom proteases on in vitro assays.[41] Rational use of antibiotics should not be promoted, reserving these drugs for patients with documented infections, or in severe envenoming cases with a high index of suspicion for infection. In fact, the clinical protocol does not recommend the prophylactic use of antibiotics and suggests a combination of these drugs to be used mainly in severe envenoming cases.[11] The prophylactic use of antibiotics may be justified to avoid consequences associated with secondary infections.[42] During the study period, there was an intermittency of availability of operating rooms, which limited treating patients with secondary infections and the frequency of alternative practices and wound manipulation.

Here, we have presented descriptive research based on a retrospective analysis of medical records in a tertiary hospital that manages most snakebite envenoming cases in the Napo Province. Data were collected from non-standardized medical reports that have not been digitized, which involves different limitations for the study. In summary, this is a first look at the situation of a single medical center, therefore cannot be generalized. For this reason, the standardization and control of clinical records with support from academia is crucial, to improve data and avoid omitting relevant information for public policies. This type of investigation should be expanded to different provinces. The availability of laboratory results was also another limitation that mainly hindered the analysis and correlation of clinical data. On the other hand, identification of the snake species from patient descriptions is unreliable. This in turn precludes associating clinical manifestations with a particular species for research and public health purposes. Nevertheless, epidemiological and clinical characteristics findings, although general, contribute to elucidating the disease dynamics in the region, especially considering the few scientific and robust reports on this topic in Ecuador.

Conclusions

Bothropic envenoming is prevalent in Napo province, with typical clinical manifestations characterized by the frequent prevalence of local effects. No deaths were registered; however, this could be associated with underreporting, a common limitation in the region. Clearly, new studies are needed to better understand the impact of envenomation in the communities from the region, especially in vulnerable groups like farmers and indigenous communities.

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