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REVIEW

Snakebites in the Americas: a Neglected Problem in Public Health

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Abstract

Purpose of Review We explored the current priority given to snakebites in 26 countries of the Americas. To describe the epidemiological characteristics of the snakebites in the Americas and the Caribbean, we looked at information collected from epidemiological sources, publications, and available from PubMed, SciELO, and LILACS. In the case of Honduras, some gray literature (theses and conference abstracts) was obtained through local networks. We also aimed at obtaining any reference made in those reports with regard to the most common snake species in the region and their toxin and the physical and mental disability in snakebite victims.

Recent Findings Many countries do not keep official reports of the snakebite incidents. In a few countries, growing knowledge of venom toxicology is leading to research and development of new antivenoms. Additionally, interest is increasing in the identification of natural treatment for symptoms caused by snake venoms, especially inflammation, pain, and blood loss. There are opportunities to undertake rigorous examination of traditional treatments, which could be incorporated to the standard of care.

Summary Snakebite surveillance needs improvement in several countries, and access to prompt treatment needs to be facilitated. With a few exceptions, scientific research is scarce in most Latin American countries. For prevention and management initiatives, it is important to highlight that the typical profile of the snakebite victim is a young male farmer with low literacy.

Keywords Snakebites · Neglected tropical diseases · Americas · Epidemiology · Disabilities · Antivenom treatment

Introduction

Poisoning and death from venomous snakebites are a serious public health problem worldwide. Snakebite envenoming usually requires hospitalization and results in significant morbidity and mortality. In many cases, snakebites lead to temporary or permanent disability [1].

In general, humans are not part of the food chain of snakes—venomous or not. Their encounters occur by accident; that is, snakes react to the potential threat of humans entering their territory. Biting is a natural snake defense mechanism, and the fangs have been adapted to inoculate venom in the body of potential victims. Snake venom is a product of an evolutionary process containing modified saliva including toxins with necrolytic, hemolytic, and nerve-acting effects. These compounds differ in proportion by snake species and geographical location [2•].

Human victims of venomous snakebites can suffer local damage and/or more generalized effects depending on factors such as the exposure to a specific type of venom, the dose inoculated, age of the person (children get more severe effects because of their smaller body mass), and the time it takes for the person to receive medical attention (every additional hour of delay implies more time for the metabolic effect of the venom) [3]. Clinical statistics, when available, give information of the number of cases and the acute outcome (survival or mortality). One important aspect that seems overlooked in passive surveillance reports is the number of victims who survive but are left with temporary or permanent disabilities. Disabilities caused by venomous snakebite can include psychological trauma, sensorial/perceptive damage, and the loss of tissue such as the muscle, bone, connective tissue, body parts, or amputations (because of necrosis and hemorrhages) [4].

The severity of the damage is related to the time elapsing between the time of the bite and the moment the victim

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reaches a health care center adequately equipped to treat the specific snakebite. Often, health care facilities lack antivenom serum, which represents an additional delay and a source of additional complications given the progression of the effects especially in the tissular necrolysis if the management does not start promptly [5].

Despite their global importance, snakebites were not included in the World Health Organization (WHO) list of priority neglected tropical diseases (NTD) until 2017. This inclusion has promoted more international visibility and should prompt countries to prioritize their importance as a public health problem.

Implementing this prioritization could start with strengthening surveillance and making snakebite events officially notifiable. Through these actions, better knowledge of its magnitude and impact would be generated [5, 6•, 7].

In the Americas, 17 countries require snakebite obligatory report [1, 8]. According to the reviewed literature, no official report is required in Belize, French Guiana, Guyana, Martinique, St. Lucia, Surinam, and Trinidad.

Mandatory reporting, however, is plagued with limitations. For instance, it is well known that many victims lack access to health services and therefore their cases go unreported. On the other hand, in some countries, there is a widespread use of natural medicine with cases, and their outcomes never reaching the national reporting system [6•, 8].

Snake Venom's Structure and Natural Purpose

Snake venoms have a natural purpose for the reptile, with a main function to immobilize or kill prey, aid in the digestion of snakes, and act as a defense mechanism against predators. Snake venom is composed of a mixture of biologically active proteins and polypeptides (representing about 90–95% of the venom volume) and other non-protein components such as carbohydrates, lipids, amines, and inorganic salts. Proteins and polypeptides are mostly enzymes including phospholipase A2 (PLA2), snake venom metalloproteases (SVMP), snake venom serine proteases, and L-amino acid oxidase (LAAO). Non-enzymatic substances include three-finger toxin (3FTx), Kunitz peptide (KUN), and disintegrin (DIS) [2•, 9].

The composition of snake venom depends on several factors, including the snake family, genus and species, geographical location, typical prey species, age, and size of the snake [8]. For example, 3FTx and PLA2 are generally predominant in elapid snakes, whereas PLA2, SVMP, and SSPA are the most abundant in vipers; 3FTx is essentially absent in vipers [9]. Venomous snakes are found in most parts of the world (including many oceans), except for some islands, icy environments, and highlands [6•].

Mechanism of Action of Snake Venoms

Through systemic snake venom administration to humans, the injected venom is absorbed and enters the systemic circulation, producing different clinical effects depending on the individual snake and the venom component [10]. Snake venom's mechanism of action is basically neurologic. Coral snake venom gains systemic access through the lymphatic veins to cause neurotoxicity and respiratory muscle weakness using competitive inhibition of the nicotinic acetylcholine receptors at the neuromuscular junction. Respiratory and cardiovascular effects occur because of the venom with presynaptic and postsynaptic sites [11•].

Additionally, phospholipase A2 may cause myotoxicity and rhabdomyolysis (dissolution of the muscle tissue) with an effect on the kidney [12]. Observation done on eastern coral snake *Micrurus fulvius* venom found that in animal models' toxicity is mainly determined by neurotoxic phospholipases A2, but also it can influence muscles (myotoxicity) and cause additional dissolution of damaged or injured skeletal muscle [11•, 13•].

Production of Antitoxins

As part of the WHO policies, the provision of pharmacotherapy for snakebites has a fundamental role. Currently, the basic therapy is antivenom, which is a compound of immunoglobulins or fragments of these obtained from the purification of the serum of horses immunized for the venoms. Latin American countries have developed experience in antitoxin production since the beginning of the twentieth century [14, 15•, 16•, 17, 18, 19•].

In the Americas, the production of antivenom is based in a few countries, namely Argentina, Brazil, Peru, Bolivia, Ecuador, Colombia, Venezuela, Costa Rica, and México. Most of the manufacturing takes place in publicly funded institutions, with susceptibility to some species to be underfunded and under-supported. As well, these institutions require keeping updated in the new innovations and the new knowledges on proteomics. Clearly, there is need to secure more investment to keep them functional for these countries, as well as for those neighboring nations lacking this technology and specialized institutions [13•, 14].

Current Situation of Snakebites in the World

According to WHO, in 2019, snakebites affected 1.8–2.7 million people each year, claiming 81,000–138,000 lives and causing 400,000 cases of permanent disability. Most snakebite events occur in Africa, Asia, and South America, but its real magnitude has been discussed in the last decades,

and its inclusion as a neglected tropical disease since 2017 by WHO has raised awareness of the need to learn more about it and get action to reduce its effect especially in those populations with limited resources to report it and access health services [6•].

The overall objective of the current review was to assess the epidemiological situation of snakebites in the American continent. Secondary objectives included describing the most common snake species in the region and their toxin and describing access to antivenoms and alternative treatments to snakebite. We also aimed at obtaining any reference made in those reports with regard to the physical and mental disability in snakebite victims.

Methodology

Epidemiological information was searched for countries in North America, Central America, South America, and the Caribbean, for a total of 26 countries.

Literature Search Methodology

Literature was searched in PubMed, SciELO, and LILAC, identifying the documents with the keywords "snakebites" and "Americas" or the name of each country in the region (e.g., snakebite AND Brazil). Language settings were English, Spanish, or Portuguese and the time period from 2000 to 2023.

In the case of Honduras, some gray literature (theses and conference abstracts) was obtained through local networks. In total, 34 publications were included in the review.

Findings

Most Common Types of Snakes and Their Classification in the Americas and by Region

Venomous snakes belong to the Viperidae family, and two of its subfamilies are the most important and abundant in the region (Americas): coral and pit vipers (Crotalinae).

Coral snakes include two genera of snakes: *Micrurus* and *Micruroid*es that are found from the Southeastern USA to Central Argentina, with a capacity to live in a variety of habitats from extremely dry areas to forests and savannas. *Micrurus* has been reported only in Central America (Table 1) [9, 13•].

About 120 species and subspecies have been identified in the Americas from both genus [9].

Morbidity and Mortality of Snakebites in the Americas

Snakebites occur frequently in the Americas, especially in rural areas and wilderness/sylvatic areas where human and snakes overlap their habitats. True to their designation as neglected tropical disease snakebites are under-reported [1, 11, 19, 20]. Brazil, Costa Rica, the USA, and Colombia have a more abundant literature than other countries in the region. However, most countries produce sporadic publications of clinical cases, case series, and in some cases, the use of traditional treatment. Most of the time, these publications, unfortunately, do not make it to the countries' official reports. However, in all countries, snakebites are a serious medical concern [1, 14].

Snakebites—or ophidic accidents as they are frequently called in the Americas—are a health event occurring periodically especially in rural areas where human dwellings and snake habitats overlap. Most reports agree that the most important barriers to prompt treatment are geographical distance to a health care center as well as cultural beliefs [1, 11•]. Empirical observation generations have led local population to use as first resource plant products without a scientific validation. Studies done in Central America showed that farmers because of their work practices expose themselves to bites and tend to underestimate the severity of snakebites and start treating them with products available in their locality: plants and ointments from animal tissues, and only when the condition of the victim worsen, they try to reach a health clinic; all the process delays an effective treatment with access to antivenom and increases the risk of mortality [8, 14, 20].

Annually, there are approximately 57,500 snakebites (annual incidence 6.2 per 100,000 population) in the region, with around 370 deaths (0.04 per 100,000 population) [1]. Due to the issues mentioned above, these figures do not reflect the true occurrence of snakebites. Table 2 shows the overall number of cases for the Americas.

As mentioned earlier, Brazil reports most cases in the Americas, outnumbering, due to its population size and geography, the number of cases reported by the rest of the American and Caribbean countries [1, 21–23]. Despite its greater number of cases, it is important to highlight that the reported snakebite case fatality rate (CFR) was lower for Brazil.

According to data published by Chippaux [1], the countries with higher incidence of snakebites per 100,000 inhabitants were Panama, Guyana, French Guiana, Venezuela, Costa Rica, Nicaragua, and Brazil. French Guiana and Guyana had the highest mortality, and the case fatality rate was higher in Bolivia (4%) and French Guiana (3%).

For Central America, publications were obtained for six out of the seven countries with Belize being the exception.

Table 1 Frequent snake species causing envenomation in the Americas

Snake species	Main toxins	Mode of action	Geographic area
Rattlesnake	Crotoxin, phospholipase A2 1 in *C. durissus*	Neurological effect 1. Presynaptic block 2. Postsynaptic effect by desensitization of nAChR	South America
Crotalus spp.	Mojave toxin, phospholipase A2 Species*: C. scutulatus*	Presynaptic ion channel blocker	Found in the deserts of the Southwestern USA and central Mexico
Bothrops atrox	Thrombin-like enzymes (SVTLEs) (batroxobin, reptilase)	Hemorrhagic 1. Deactivate factor XIII and the clots produced can easily be broken down. 2. Local damage, such as edema, hemorrhage, and necrosis, apart from systemic effects, including blood coagulation disorders	Found in the tropical lowlands of northern South America east of the Andes, as well as the Caribbean island of Trinidad
Viperid and crotalid venoms	PLA2s (phospholipase A2)	Myotoxic Cause rapid necrosis of skeletal muscle fibers, referred to as myotoxic PLA2	Found throughout the continental USA and Canada
Brazilian viper (Bothrops jararaca)	Angiotensin converting enzyme (ACE) inhibitor	Hypo tensor Causes sudden, massive drop in blood pressure	Endemic to South America in southern Brazil, Paraguay, and Northern Argentina
Agkistrodon spp. *(American copperheads)*	Metalloproteins Phospholipases A2 Serine proteases (SVSPs)	Coagulopathy and hemorrhage	North America, ranging from the Southern USA to northern Costa Rica
Bothrops spp. includes *Bothriechis*, *Cerrophidion (pit vipers)*	Metalloproteins Phospholipases	Coagulopathy and hemorrhage	Southern Mexico and Guatemala
Bothrops lanceolatus (Martinique viper)	Metalloproteins Phospholipases	Coagulopathy, thrombosis with DVT and pulmonary embolus	Endemic to the Caribbean Island of Martinique
Crotalus spp. Common name: North American rattlesnakes	Phospholipase A2 (PLA2), snake venom metalloproteinases PIII (SVMP P-III), L-amino-oxidases (LAAO), cysteine-rich secretory proteins (CRISP), C-type lectins (CTL)	Coagulopathy and hemorrhage	Found only in the Americas from southern Canada to Northern Argentina
Lachesis spp. (known as Bushmaster)	Snake venom metalloproteinases PI (SVMP P-I), bradykinin-potentiating peptides (BPP), hyaluronidase (Hya), phosphodiesterase (PDE) Bradykinin-potentiating peptides (BPPs), serine proteinases (SVSP) Metalloproteinases (SVMP) Phospholipases A2 (PLA2)	Coagulopathy and hemorrhage	Found in South America, and in the island of Trinidad in the Caribbean
Micrurus (coral snakes) *M. nigrocinctus*	Postsynaptic α-neurotoxins	Neurologic effects: Pain, nausea, paresthesia, cranial nerve involvement, altered mental status, and respiratory failure	Found only in the Americas from southern Canada to Northern Argentina

Sources: Adapted from White (2005) "Snake venoms and coagulopathy" and Ranawaka (2013) "Neurotoxicity in snakebite—the limits of our knowledge"

Table 2 Snakebites in the Americas with epidemiological indicators for 2017

Region/country	# snakebites/ year	Deaths/ year	Incidence/ 100,000	Mortality/ 100,000	CFR
North America					
Canada	100	0	0.28	0	0
USA	5000	7	1.56	0.002	0.14
Mexico	4000	50	3.34	0.042	1.25
	9100	57	1.9	0.012	0.62
North America (NA) totals					
Americas (excluding Brazil and NA)	20,795	170	8.2	0.067	0.81
Brazil	27,200	115	13.39	0.057	0.42

Adapted from Chippaux JP. Incidence and mortality due to snakebite in the Americas. PLoS Negl Trop Dis. 2017

CFR case fatality rate

No gray literature was found for Belize either. In Central America, only three countries Panama, Costa Rica, and Panama reported mortality. The CFR was lower in Panama (0.79) than in the other two reporting countries (Costa Rica and Nicaragua) with 1.0 AND 1.08, respectively [1].

Epidemiology and Clinical Manifestation of Snakebites in Different Countries

Different studies were reviewed from the America countries. Most studies reported cases from specific regions or ecological areas in these countries, and they may not represent the different ecosystems or human settled areas of the whole country.

The following is a brief account of the epidemiological situation of snakebites in selected countries.

El Salvador. A study in El Salvador from 2014 to 2019 identified five deaths and found that snakebite incidents increased in the rainy season affecting people of ages between 10 and 30 years and with a male:female ratio of 1.5:1.0; this study showed a higher occurrence of snakebites in males, due to greater occupational exposure [24]. These findings are consistent with Brazilian reports and explicitly confirm this characterization [23, 25]. They also stress the importance of climate factors and increased human activity in the fieldwork (agriculture) affecting mostly agriculture population. Increased population of both humans and snakes is also important drivers of snakebite incidents [25].

USA. Warpinski [26] in the USA identified that patients suffering bites by crotaline snakes suffer local tissue damages, coagulopathies, circulatory collapse, and anaphylactic reactions. On the other hand, the other common envenomation in the USA is caused by coral snakes, which produce neurotoxicity but with low incidence [27, 28] and its occurrence identify snakebites as an occupational risk associated with landscaping and direct work with snakes. Envenomation in the upper extremities was the most frequent in this study and resulted from unintentional interactions.

Greene [28] studied the snakebites of members of the family *Micrurus* (coral snakes) in Texas and the management of neurological effects, pain, and inflammation. Severe manifestations such as respiratory dysfunction or skeletal paralysis were not identified. No antivenom was necessary but it was available.

Baumgartner [29] identified the copperhead *(Agkistrodon contortrix*) as another important snake as cause of envenomation in the Midwest state of MO. In this case, the treatment was given with antivenom; patients required 17–28 days for total recovery. Adverse reactions to the antivenom such as pruritus and hypersensitivity were also documented.

Honduras. Studies done in three different Honduran hospitals were found. Altogether, they report 120 cases in recent years and showed that the age range for those affected by snakebites was quite broad, from 1 to 75 years (average 26). More than half (55%) of patients were male, 86% were of rural residence, and most had only attended primary school. The patient occupations included farmers, students, and housewives. The average hospital stay for this case series was 2.5 days. An additional report from a tertiary hospital included 1120 cases with similar demographic information [30–32]. The snake responsible in these incidents was mainly *Bothrops atrox* (locally called Barba amarilla), although many victims were not able to identify the type of snake attacking them [30–32].

An additional Honduran study was done for a thesis project by Ponce Arellana [33] in a pediatric population from 3 to 17 years ($n = 24$) identifying symptoms like pain, edema, and reddening of affected area, a period of 3 h between the bite and the access to medical care of 4 h which is a critical time for the initial symptoms. This study included information on alteration in the gastrointestinal tract and hematological changes. Children were left with areas of disfiguration in legs and arms, which affect the functionality of the limbs as children grow up.

Another Honduran publication by Urbina from a study involving 28 hospitals and 1120 patients indicated that the most common clinical manifestations were compartmental

syndromes (in 53% cases) and acute renal failure (7.7% cases) [34]. Other symptoms included neurological changes (motricity or sensibility) in 50% of cases. Local inflammation and edema were also observed in 86% patients around venom inoculation in [34].

A paper written in 2011 by Aleman [35] used key informants in Western Honduras, and through the interviews, he identified the presence of snakes in areas of agricultural activity with the occurrence of snakebites to humans and cattle, resulting in mortality of three farmers according to the informants. This paper described the activity of *Crotalus durissus* in the study area as well as of *Bothrops atrox.*

Venezuela. Two reports published in local university journals identified the period of June to December as the most active time for snakebites, mostly caused by *Bothrops* species, *Crotalus*, and *Lachesis*. They also documented the time elapse from snakebite to medical attention was 6 h or more [36, 37].

Mexico. Mexican authors have described the events of snakebites and the time of stay in the hospital as 10 days [38,39].

Colombia. With regard to Colombia, we identified three publications that added blisters and tissue necrosis to the symptoms caused by *Bothrops* snakes: Most snakebite victims reported in these studies in Colombia were people of African ancestry. The peak of event occurrence was during the rainy season and in the periods of agricultural products harvest [40–42].

Costa Rica. Costa Rican publications by Avila Aguero [43] and Lomonte [44] described that for the snakebite victims, the media of hospital stay was around 12.8 days and the time to get access to medical care and antivenoms was less than a day. Three young patients died of hemodynamic disorders, and secondary infections were reported as complications. Accessibility was described as a problem delaying the arrival of patients to health care and increasing the risk of complications.

Brazil. Brazil was the country with most publications in either University or Research Foundation journals. They described the mean time to reach medical care as 4 h and administration of antivenoms in 6 h. Vieira Tavares [25] analyzed 3019 cases occurring between 22007 and 2014 and found as the mean time to reach medical facilities was 3 or more hours. This author reports 13 deaths in that cohort [21–23].

Martinique and French Guyana. Ressiere et al. [45] did a study in Martinique and French Guyana and reported the role of *Bothrops lanceolatus* in the snakebites and mentioned as the most important manifestations: thrombotic effects and local tissue damage.

Ecuador. Praba Egge [46] did a study in Ecuador and reported that her sample of 142 patients had as a mean of stay in the hospital 4.3 days, 90% of they recovered, 8% suffer of abscessed post-treatment, and a mortality of 2.9% occurred because of complications such as renal failure, respiratory failure, and disseminated intravascular coagulation.

Panama. Pecchio [47] studied the clinical files of 390 patients in Panama who suffered snakebites caused by *Bothrops asper* and went for medical treatment with 25% of them arriving 6 or more hours after the event. Fifty-five percent received therapy with antivenom and 67% a dose of tetanus toxoid.

Uruguay. This country reports only cases of envenoming with *Bothrops* snakes, but they have also papers documenting written about envenoming with a *Micrurus*. One case was documented by Juanena in 2018 [48] which is relevant for the neurological manifestations.

The different studies included in our review mention the aspect of access as a barrier to appropriate and opportune treatment. An area to study is the mechanisms to increase accessibility to antivenoms in the different countries to reduce morbidity and mortality. An open question is the frequency and results of the natural treatments; some studies have been done without a final conclusive result but stating the need to explore these area [49•, 50•].

Conclusion

One of the barriers to get prompt medical care is geographical distance between the location of the snakebite incident and the health care unit with resources to treat it. Antivenoms are highly effective, but delays in their administration can have serious consequences leading to death or disability as well as the mental health disturbances of the patient. Moreover, due to its cost and cold-chain requirements, many countries do not have enough antivenom for their at-risk population. Preventive measures (e.g., protection of rural workers, agricultural students) and increased awareness of snakebites in the community can have a positive impact in decreasing incidents.

Reporting snakebite incidence is crucial for countries to assess their challenges and take proper action. Especially, more attention is needed when reporting snakebites as most publications fall short when providing patients' follow up and the impact of snakebite on mortality and disability.

Finally, the inclusion of snakebites in WHO's priority NTD list has increased the visibility of this neglected global health problem. Eliminating poverty is a lofty sustainable development goal, but while efforts are in place for its attainment, national and international mechanisms need to be in place to reduce the impact of snakebite envenomation.

Author Contribution E.F. conceptualized the review and wrote the first draft of the manuscript. P.Y. contributed with literature research

and elaborated the tables. Both authors read and approved the final manuscript.

Data Availability The information is freely available following the reference lists and links.

Compliance with Ethical Standards

Ethical Approval The sources for the manuscripts were documents online freely available. No animal specimens or human volunteers were involved in this study. No Ethical Committees or Internal Review Boards approval was required.

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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