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ORIGINAL ARTICLE

Clinical Presentations, Treatments, and Outcomes of Non-native Snake Envenomations in the United States Reported in the North American Snakebite Registry

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Abstract

Background Non-native snake envenomations in the United States are uncommon with much unknown about a patient's presenting signs and symptoms. Antivenoms for non-native snake envenomations are not typically available in hospital pharmacies which may limit their administration. What are the clinical presentations, treatments, and outcomes of non-native snake envenomation cases reported to the North American Snakebite Registry (NASBR) of the Toxicology Investigators Consortium (ToxIC)?

Methods This is a descriptive review of all non-native envenomations reported to the NASBR from 2013 to March 2022. Data abstracted included snake species, patient history, clinical signs, diagnostics, treatment (including antivenom usage), follow-up, and final outcome.

Results We identified 19 non-native snake envenomations resulting from encounters with eleven different species, eight of which belonged to the *Viperidae* family. The most common presenting symptoms were edema (18 patients), ecchymosis (seven patients), and necrosis (six patients). Systemic effects and hematologic abnormalities were less common. The most common treatments were extremity elevation and analgesia, with two patients receiving mechanical ventilation. Ten patients received antivenom. No patients died. Three patients had loss of mobility in a digit at the last follow-up visit. One patient had permanent tissue loss of a small area on a finger.

Conclusions The results of this study suggest that non-native snake envenomations in the United States frequently cause local soft tissue effects and less frequently cause systemic or hematologic effects. Most patients received antivenom, although several patients envenomated by snakes for which a specific antivenom exists did not receive any. Sequelae at the last follow-up of such encounters consisted of local mobility deficits.

Keywords Snakes · Envenomations · Non-native · Antivenom

Introduction

United States (US) poison centers recorded over 6,000 snake envenomations in 2018.[1] The vast majority of these envenomations involved native snakes including pit vipers (*Crotalinae*) and coral snakes (*Elapidae*), both of which are

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familiar to emergency physicians and medical toxicologists [1]. Medical toxicologists are generally experienced in caring for these patients, including administering antivenom.

Non-native envenomations in the US are uncommon and may be challenging to manage [2, 3]. US poison centers recorded 41 confirmed bites from venomous non-native snakes in 2018, although this is likely an underestimation of the true incidence [1]. The rarity of non-native snake envenomations is likely due to the comparatively small number of these snakes in the US, as well as underreporting due to various reasons. While most native envenomations result from encounters with pit vipers, non-native encounters result from a much more diverse array of species [3]. Challenges in managing non-native snake bites include physicians' unfamiliarity with their unique effects and difficulty in obtaining specific antivenoms [4, 5]. Even most North American medical toxicologists rarely care for patients following non-native envenomations and are likely not experienced in administering antivenom to these patients.

Given the scarcity of non-native envenomations and the diversity of encountered species, data on the clinical presentation and management of such envenomations are much more limited than for most native snakes. Thus, we aimed to describe the various clinical presentations, management, and outcomes of non-native snake envenomation cases reported to the North American Snakebite Registry (NASBR), a sub-registry of the Toxicology Investigators Consortium (ToxIC). We also aimed to determine if antivenom existed or was available for these envenomations, and if the appropriate type of antivenom was administered.

Methods

ToxIC was established in 2010 to record and report de-identified patient information from all bedside consultations performed by a medical toxicologist at participating hospitals. ToxIC established the NASBR sub-registry in 2013 with the goal of creating a prospective, detailed, and centralized source on US snake envenomations [6]. Case entry into the NASBR is voluntary, but members are encouraged to enter data on all bedside evaluations performed by medical toxicologists [7]. ToxIC investigators and NASBR subinvestigators typically operate outpatient clinics in addition to practicing at hospitals.

We reviewed all cases of envenomation by non-native snakes reported to the NASBR from January 2013 to March 2022. We used the snake identification reported by the treating toxicologist in each case, as in previous studies using NASBR data, to initially classify the envenomation as non-native [6, 8]. After this initial classification, the authors reviewed all cases, and if the encounter was confirmed as a non-native species, the case was included, regardless of clinical presentation. We excluded envenomations caused by snakes native to the US. All such determinations by the authors were unanimous.

Information for the NASBR is stored in a REDCap registry, and data were exported into a Microsoft Excel® spreadsheet. Two of the authors (JB, ESS) determined a priori which data points to abstract from the Excel® spreadsheet. Data were then abstracted by a single author (JB) and reviewed by a second author (ESS). The abstracted data included snake species, patient history, clinical signs, diagnostics, treatment (including type of antivenom and antivenom use), and outcome at final follow-up. To determine the existence of specific antivenoms, we reviewed the WCH Clinical Toxinology Resource http://www.toxinology.com/ (Women's & Children's Hospital; Adelaide, Australia) for each snake species. Three authors (E. S. S., S. G., M. E. M.) determined if 1) according to the WCH Clinical Toxinology Resource an antivenom existed for the implicated snake and 2) if a patient receiving an antivenom received the appropriate antivenom. We used simple descriptive statistics to describe the data. We followed the STROBE cohort criteria where applicable (Supplemental Fig. 1). This study was approved by the Western IRB.

Results

We identified 22 patients with reported non-native snake envenomations in the NASBR from 2013 through March 2022; three were excluded. One involved a species native to the US, one involved a non-venomous snake (only described as a "python"), and one involved an unidentified snake. This left 19 cases for inclusion (Table 1). The venomous snakes included eight species from the *Viperidae* family, two from the *Elapidae* family, and one from the *Colubridae* family.

Most patients were male ($n=16$) with most bites occurring to the upper extremity ($n=17$). Six cases were occupational exposures. Six patients had prior snakebites, but we do not know if the same snake or same species of snake inflicted both bites. Aside from two patients, all patients arrived at a hospital within an hour of the envenomation. Seven patients received care in an intensive care unit (ICU) (Table 2).

Five patients developed coagulopathies including low or undetectable fibrinogen concentrations or elevation of their prothrombin time, after being envenomated by a viper. Two of the three patients envenomated by monocled cobras (*Naja kaouthia*) developed thrombocytopenia without other abnormal coagulation parameters. No bleeding or hemorrhagic complications were reported in any patients.

All patients developed local findings after the envenomation; these occurred following bites from all three families of snakes. Six patients developed tissue necrosis at

Table 1 Demographics, symptoms, and laboratory information

Patient number	Sex/age (range)	Bite Location	Snake species	Type of interaction	Occupationally related	Previously bitten by a snake	Signs and symptoms	Lab abnormalities
	Viperidae							
1	20 s, male	Finger	*Atheris squamigera*	Bitten while feeding another snake while intoxicated	No	Yes	Swelling	None
2	50 s, female	Finger	*Bothriechis schlegelii*	Bitten while feeding her pet snake	No	No	Swelling	None
3	20 s, male	Finger	*Trimeresurus albolabris*	Intentional interaction that occurred while cleaning the snake's enclosure	No	Yes	Swelling, ecchymosis	None
4	20 s, male	Finger	*Atheris squamigera*	Bitten while trying to remove the "eye cap" from his pet snake	No	No	Swelling, ecchymosis, erythema, tachycardia, necrosis (hemorrhagic bullae)	Fibrinogen 94 mg/dL, FDP or D-Dimer elevated
5	30 s female	Hand	*Trimeresurus insularis*	Unintentional interaction but no further information was available	No	No	Swelling, erythema	None
6	20 s, male	Finger	*Trimeresurus albolabris*	Patient was the snake's caretaker	Yes	No	Swelling, tachycardia, necrosis	None
7	50 s, male	Finger	*Crotalus durissus terrificus*	Patient was a snake handler	Yes	No	Swelling, ecchymosis, necrosis, emesis, neurotoxicity (paresthesias and fasciculations)	Nadir: fibrinogen < 30 mg/dl; peak: PT 23.6 s, CPK 6499 IU/L, D-dimer or FDP
8	20 s, male	Finger	*Bothrops moojeni*	Patient works at venom lab ad was cleaning the snake enclosure	Yes	No	Swelling, ecchymosis, emesis, necrosis (hemorrhagic bullae)	Fibrinogen nadir 134 mg/dL; peak PT 15.1 s
9	40 male	Finger	*Trimeresurus albolabris*	Patient was packing the snake for a reptile show	No	Yes	Pain at bite location	None
10	20 s, female	Finger	*Atheris squamigera*	Patient was packing the snake to ship it	No	No	Swelling, ecchymosis, emesis, necrotic tissue with underlying bullae	Nadir: fibrinogen 157 mg/dL; peak: PT 17.7 s
11	40 s, male	Finger	*Bitis rhinoceros*	Patient was medicating a gravid snake	No	Yes	Swelling	None
12	Teenager, male	Finger	*Crotalus durissus terrificus*	Patient was repairing the snake enclosure	No	Yes	Swelling	None
13	Teenager, male	Finger	*Bitis nasicornis*	Patient was cleaning the cage at animal rescue shelter	Yes	No	Swelling, tachycardia	None

Table 1 (continued)

Patient number	Sex/age (range)	Bite Location	Snake species	Type of interaction	Occupationally related	Previously bitten by a snake	Signs and symptoms	Lab abnormalities
14	20 s, male	Foot	*Atheris squamigera*	Patient was preparing snake for an expos and the snake got out of the transfer device	No	No	Swelling, erythema	Nadir: fibrinogen 144 mg/dL
	Elapidae							
15	60 s, male	Groin or torso	*Naja kaouthia*	Patient is an herpetologist and snake escaped during transport	Yes	Yes	Swelling, ecchymosis, emesis, necrosis, neurotoxicity (weakness and respiratory failure), myonecrosis	Platelet nadir: 111 k/mm^3
16	40 s, male	Finger	*Naja kaouthia*	Patient was feeding a snake in an exhibit	Yes	No	Swelling, neurotoxicity (weakness and respiratory failure)	Nadir: platelets 121 k/mm^3; peak: CPK 3169
17	30 s, male	Finger	*Naja kaouthia*	Patient was transferring the snake to a container to get rid of it	No	No	Swelling, ecchymosis	None
18	20 s, male	Hand	*Dendroaspis angusticeps*	Patient was attempting to remove "shed skin" off the snake	No	No	Swelling	None
	Colubridae							
19	20 s, male	Finger	*Hydrodynastes gigas*	Patient was bitten by his pet snake	No	Unknown	Swelling	None

Table 2 Treatments and hospitalization

Patient number	Received treatment prior to the hospital	Non antivenom treatment	Time from envenomation to hospitalization	Hospital LOS	Admitted to ICU	Received a procedure for the wound	Received antivenom
	Viperidae						
1	No	Extremity elevation, opioids	0.5 h	< 24 h	No	No	No
2	No	Unknown	1 h	25–48 h	No	No	No
3	No	Extremity elevation, opioids	1 h	< 24 h	No	No	Yes
4	No	Extremity elevation, opioids, antiemetics	0.5 h	25–48 h	No	No	Yes
5	No	Extremity elevation, opioids, intravenous fluids	1 h	< 24 h	No	No	No
6	No	Intravenous fluids, extremity elevation, opioids, antihistamines	0.5 h	25–48 h	Yes	No	Yes
7	No	Immobilization, intravenous fluids, extremity elevation, antihistamine, antiemetic, opioids	0.5 h	49–72 h	Yes	No	Yes
8	No	Extremity elevation, antiemetics, opioids	1 h	< 24 h	No	No	Yes
9	No	Extremity elevation	1 h	< 24 h	No	No	No
10	Yes—tourniquet application	Extremity elevation, immobilization, antiemetics, antihistamines, opioids	1 h	49–72 h	No	Yes—debridement	Yes
11	No	Extremity elevation	0.5 h	< 24 h	No	No	No
12	No	Elevation, immobilization, antihistamines, corticosteroids, intravenous fluids	1 h	24–48 h	Yes	No	Yes
13	No	Elevation, immobilization, antihistamines, opioids, corticosteroids, intravenous fluids	0.5 h	24–48 h	Yes	No	Yes
14	No	Elevation, opioids, intravenous fluids	1 h	24–48 h	Yes	No	No
	Elapidae						
15	No	Intravenous fluids, corticosteroids, antihistamines, opioids, antiemetics, antibiotics, intubation	0.8 h	25–48 h	Yes	No	Yes
16	No	Extremity elevation, intubation	0.75 h	25–48 h	Yes	No	Yes
17	No	None	1.5 h	< 24 h	No	No	Yes
18	No	Opioids, elevation, immobilization	24 h	< 24 h	No	No	No
	Colubridae						
19	No	Extremity elevation, antibiotics, antihistamines, intravenous fluids	2.5 h	25–48 h	No	No	No

the area of the envenomation. Five of the snakes causing the necrotic injuries were *Viperidae*, while one episode of necrosis occurred following envenomation by a monocled cobra (*Naja kaouthia*), an *Elapidae*.

Neurotoxicity was reported in three patients, consisting of respiratory failure in two and perioral paresthesias and fasciculations in the third. The two patients who developed respiratory failure were envenomated by a monocled cobra

(*Naja kaouthia*); both required intubation. No other patients in the series were intubated. One patient envenomated by a South American rattlesnake (*Crotalus durissus terrificus*) developed paresthesias and fasciculations but did not require any respiratory support.

A single patient received treatment prior to arriving at the hospital (Table 2). A tourniquet was applied to a 23-year-old female envenomated by a green bush viper (*Atheris squamigera*). Seven patients received antihistamines, including patients envenomated by all three families of snakes; five received them as prophylaxis. Two patients received antibiotics. A patient envenomated by a monocled cobra (*Naja kaouthia*) received antibiotics for a wound infection, with cultures that grew *Morganella morganii*. This patient was one of three patients to receive corticosteroids, all of which were administered prophylactically. A 23-year-old envenomated by a false water cobra (*Hydrodynastes gigas*) also received prophylactic antibiotics.

Ten patients received antivenom (Table 3). All three authors were unanimous in agreeing if a specific antivenom for that snake was produced and if the antivenom that was administered was appropriate so no kappa was calculated. All three patients bitten by monocled cobras (*Naja kaouthia*) received antivenom, while seven patients bitten by vipers received antivenom. Eight patients received antivenom that was indicated for the specific species that envenomated them. A 23-year-old was envenomated by a green bush viper (*Atheris squamigera*) for which antivenom does not exist. In this case, the treating toxicologist administered South African Institute for Medical Research (SAIMR Polyvalent) antivenom (now known as South African Vaccine, Producers, Johannesburg, South Africa (SAVP)). Fifty minutes after receiving the SAVP antivenom, he developed a rash that was treated with antihistamines. The patient developed worsening coagulopathy despite SAIMR Polyvalent antivenom and was then administered SAIMR *Echis carinatus* antivenom. It was not clear if the administration of the antivenom was associated with clinical improvement. A 28-year-old male bitten by a white-lipped pit viper (*Trimeresurus albolabris*) received antivenom referred to as "other." A single case of serum sickness was reported in a 15 year old envenomated by a South American rattlesnake (*Crotalus durissus terrificus*). He received steroids (both prophylactically and to treat serum sickness) and antihistamines. No other adverse reactions to antivenom were reported.

Antivenom was available but not administered for a 35-year-old bitten by a white-lipped island pit viper (*Trimeresurus insularis*). In this case, the text on the antivenom packaging was in Chinese and did not include clear instructions for administration that were accessible to the treating physician. The language barrier in interpreting the instructions and the patient's mild symptoms both contributed to the decision to withhold antivenom.

Follow-up was obtained for 15 patients, although for nearly all, this occurred either fully or partially via telephone as opposed to in person (Table 4). At the final available follow-up encounter, persistent clinical symptoms were reported in four patients, all envenomated by vipers. A 58-year-old envenomated by a South American rattlesnake (*Crotalus durissus terrificus*) still had finger necrosis and

Table 3 Antivenom

Snake species	Time from envenomation until antivenom administration	Type of antivenom received	Number of vials
Viperidae			
Trimeresurus albolabris	1 h	Other snake antivenom	10 vials
Trimeresurus albolabris	3 h	Thai Red Cross Green Viper	3 vials
Crotalus durissus terrificus	1 h	Crotalidae-polyvalent immune fab [ovine]	12 vials
Bothrops moojeni	1.5 h	Antivipmyn TRI	10 vials
Atheris squamigera	6.5 h	SAVP polyvalent (5 vials), SAIMR *Echis carinatus* (3 vials)	8 vials
Crotalus durissus terrificus	4 h	Crotalidae-polyvalent immune fab [ovine] and Costa Rican Polyvalent	Unknown
Bitis nasicornis	12 h	SAIMR polyvalent	6 vials
Elapidae			
Naja kaouthia	1.5 h	SAIMR, MENA, Naja Kaouthia	SAIMR 4 vials, MENA 2 vials, Naja kaouthia cobra 10 vials
Naja Kaouthia	4 h	Thai Red Cross Cobra	5 vials
Naja Kaouthia	2 h	Thai Red Cross Cobra	5 vials
Colubridae			
None received antivenom			

Table 4 Follow-up

Patient number	Number of follow-ups	Time of last follow-up (days from initial envenomation or last antivenom)	Deficit at last follow-up	Method of follow-up
	Viperidae			
1	2	14	None	Phone call
2	0	N/A	N/A	N/A
3	3	16	None	In person and phone
4	3	20	Yes	In person and phone
5	0	N/A	N/A	N/A
6	3	11	None	In person and phone
7	8	41	Yes	In person and phone
8	0	N/A	N/A	N/A
9	2	31	None	Phone
10	63	78	Yes	In person and phone
11	3	50	None	Phone
12	1	11	None	In person
13	1	9	Yes	In person
14	0	N/A	N/A	N/A
	Elapidae			
15	3	21	None	In person and phone
16	13	> 13 days	None	Phone
17	3	14	None	Phone
18	1	7	None	Phone
	Colubridae			
19	2	7	None	In person and phone

N/A, not applicable

fasciculations 41 days post-envenomation. A 25-year-old envenomated by a green bush viper (*Atheris squamigera*) had necrosis and persistent loss of mobility in his finger 20 days post-envenomation. A 23-year-old that was also envenomated by a green bush viper required a debridement of her finger. Her necrotic wound did heal, but at day 78 post-envenomation, impaired mobility in her finger was still present. A 16-year-old envenomated by a rhinoceros or butterfly viper (*Bitis rhinoceros*) had loss of mobility in his finger 9 days post-envenomation.

Discussion

It is impossible to estimate how many non-native snakes are kept at home as a pet in the US, but our study reveals there exists a chance for collectors to be bitten and envenomated by these pets. According to the Toxic Exposure Surveillance System (TESS, which is now the National Poison Data System (NPDS)), there were 399 non-native snake exposures reported from 1995 to 2004 or 39.9 a year [2]. Data from TESS has multiple limitations including a significant initial coding error rate, which limits its ability to determine the actual number of non-native envenomations.

Ten patients received antivenom in our study. The antivenom administered to eight patients was consistent with antivenom recommended for those envenomations and for one patient envenomated by a white-lipped pit viper (*Trimeresurus albolabris*) the type of antivenom administered was reported as "other." According to WCH Clinical Toxinology, five different types of antivenom were available for this patient. A single patient received antivenom that was outside of standard recommendations. A patient envenomated by a green bush viper (*Atheris squamigera*) received SAVP followed by SAIMR *Echis carinatus* antivenom. The WCH Toxinology website does not list any available antivenom for bites from the green bush viper. The SAVP website lists antivenoms they produce, including the SAVP [9], but does not list green bush vipers as an indication for this antivenom. The authors could not find any published reports of green bush viper envenomations being treated with SAVP. However, the green bush viper is endemic to West and Central Africa, and SAVP antivenom is indicated for treating envenomations from other African snakes. While many of these snakes are elapids, SAVP antivenom can be used to treat envenomations from the Gaboon viper (*Bitis gabonica*) and the puff adder (*Bitis arietans*), which are African vipers [9]. There is literature that describes similarities between *Atheris* and *Echis* species giving some plausibility

that the SAIMR *E. carinatus* antivenom may be efficacious in *Atheris*' envenomations, even if we are unaware of any published reports of use of this antivenom to treat *Atheris* envenomations.

There are published reports of patients envenomated by *Atheris* species treated with blood factor replacement and FAV-Afrique antivenom, although their benefit is not clear [10–12]. A 34-year-old envenomated by a green bush viper (*Atheris squamigera*) received multiple blood products over multiple days for a coagulopathy. He improved over a few days but did not receive any antivenom [10]. A 26-year old developed compartment syndrome, a coagulopathy, and massive bleeding after being envenomated by a Western bush viper (*Atheris chlorechis*). The patient received FAV-Afrique antivenom 12 h after the envenomation along with other treatment and improved [11]. FAV-Afrique antivenom is made from ten different snake species, including snakes from the *Elapidae* and *Viperidae* families [13]. Reports do describe the use of Near Middle East Antivenom in patients bitten by African bush vipers (*Atheris* species) with mixed results [14, 15]. In our patient envenomated by the green bush viper (*Atheris squamigera*), using alternative antivenoms did not appear to benefit the patient. Additionally, one of the patients envenomated by a cobra (*Naja Kaouthia*) received multiple antivenoms. Due to delays in obtaining the desired antivenom (*Naja kaouthia* antivenom), the treating toxicologists after discussing with experts first administered SAIMR and Middle East and North Africa (MENA) antivenom without improvement prior to obtaining the preferred antivenom. In general, the authors would not recommend administering alternative antivenoms without discussing this with someone with expertise. However, the authors do understand that someone with expertise may not always be available, in which case the physician should proceed with caution while doing what they believe is best for the patient.

According to the WCH Toxinology, antivenoms exist for five of the nine envenomations not treated with antivenom. In only one case was antivenom not administered due to challenges administering it (language barrier). The Association of Zoos and Aquariums in collaboration with the American Association of Poison Control Centers does maintain translated copies of package inserts for many antivenoms (https://www.aza.org/antivenom-index?locale=en). A login is required to use the website. While many may believe that obtaining antivenom is a significant barrier to treating these patients [16, 17], this was not mentioned as a reason that patients did not receive antivenom in our series. Additionally for patients where information was available, only four received antivenom more than 3 h after being envenomated and a single other patient received alternative antivenom due to delays in obtaining the desired antivenom. This appears to indicate that physicians were able to quickly obtain antivenom, indicating minimal barriers in obtaining it. While hospitals generally do not carry antivenom for non-native snakes, zoos are a source of antivenom to treat envenomations. If one exists, they should have antivenom for any venomous snake in their possession, although they are not obligated to provide it to the hospital and any antivenom they send may be expired. Additionally, package instructions may be in a foreign language leading to difficulty administering it, such as occurred in our study. Poison centers are also a potential resource to obtain antivenom for non-native snakes [5]. The Association of Zoos and Aquariums and American Association of Poison Control Centers Online Antivenom Index or Miami Dade Fire Rescue Anti-Venin Bank are other potential resources [2, 18]. As the antivenoms are not approved by the Food and Drug Administration (FDA), pharmacy or other administration may need to go through an institutional review board, obtain an investigational new drug (IND) application, and/or report the encounter to the FDA. However, none of these restrictions or any others should delay procurement or administration of the antivenom.

In our series, a 64 year old bitten by a monocled cobra (*Naja Kaouthia*) developed a wound infection from *Morganella morganii*. The other two patients bitten by monocled cobras did not develop infections. Prior literature also demonstrates wound infections from *M. morganii* following cobra envenomations, which may cause more severe infections than other snakes [19]. In a chart review of snake envenomations from Taiwan over 10 years, 26% of patients developed cellulitis, with 44% of those requiring surgical intervention due to worsening infection. More patients bitten by a cobra than any other snake required surgical intervention due to worsening infection. In the cohort, *M. morganii* was the most commonly identified infection (14/53 patients, 26%), although it is not clear how many of these patients were bitten by cobras. Another Taiwanese study investigated wound infections following cobra envenomations [20]. Over 16 years, one hundred ninety-five cases were identified. Twenty-seven percent developed wound infections with 23 developing necrotic injuries. The most common gram-negative bacteria grown in culture was *M. morganii*. *Morganella morganii* was also the most common bacteria found in cultures from the group without wound necrosis. Furthermore, a study from Vietnam investigating cobra envenomations also demonstrated that *M. morganii* and *E. faecalis* were the most common identified causes of wound infections in these patients [21].

Prior authors also investigated non-native snake envenomations. The TESS database was used to systematically characterize non-native snake exposures in the US between 1995 and 2004 [2]. Three hundred ninety-nine exposures representing 77 distinct snake species were included. Most were *Viperidae* followed by *Elapidae* with a single report of a *Colubridae*, similar to our study. Most patients were also male. Fifteen percent were under 17 years of age which is

slightly higher than our study, where only two were under 21 years of age. Similar to our study, most encounters were not occupational, and neurotoxicity was most often associated with *Elapidae* envenomations. Relatively more patients in our study were admitted to the ICU compared to their study, although our total numbers are smaller, seven verse 114, respectively.

There were some other notable differences. In the study using the TESS database, more patients envenomated by vipers than elapids received antibiotics (10.7 vs. 4.6%) while no patients envenomated by vipers received antibiotics in our study. Additionally, only 26% of patients received antivenom compared to slightly over half (10 patients) in ours.

Another study described non-native snake envenomations reported to the Pennsylvania poison control centers from 2004 to 2018 [4]. Eighteen cases were reported, and all were either *Viperidae* or *Elapidae*. Most patients were male ($n=15$) with an age range of 16–63 years. Only one patient was envenomated at work, with the rest occurring within a private residence. Neurologic effects were limited to envenomations by *Elapidae* and a single patient bitten by a South American rattlesnake (*Crotalus durissus terrificus)*. We found a higher proportion of local soft tissue effects in our study. This may be due to the more detailed reporting form required by NASBR, which includes individual areas to describe edema, ecchymosis, etc., compared to poison center results which may contain fewer details. There are also differences in how patients in this study were managed compared to ours. In this poison center study, fewer patients received antivenom ($n=7$) with a similar delay (average of four hours with a range of 3 to 9 h) between time of envenomation and receiving antivenom. The amount of antivenom administered was not reported. Additionally, two patients envenomated by cobras received cholinesterase inhibitors, pyridostigmine, and neostigmine, although the effectiveness was not reported. Antibiotic, antihistamine, and corticosteroid utilization as well as any follow-up or long-term deficits were not reported. In our study, it is possible that having a medical toxicologist at the bedside assisted in procuring antivenom sooner as well as allowed us to better obtain information regarding medication administration and post-discharge follow-up.

European studies also investigated non-native snake envenomations [22, 23]. Comparisons are limited, as snakes native to the US are considered non-native in Europe. A 15-year review was conducted on non-native envenomations in the Czech Republic from 1999 to 2013 and included 87 patients [22]. All bites occurred in male snake breeders between the ages of 20 and 53 and occurred to the upper extremities. Twenty-nine (33.3%) were considered as systemic envenomations, with 17 (19.5%) patients receiving antivenom. Twenty-nine patients were bitten by snakes that we would consider non-native to the US. Of those, twelve received antivenom. There was, however, a prolonged period between the bite and antivenom administration (range 40 min to 5 days). Nine patients received antivenom within 3 h of the envenomation. Delays in administration of antivenom to the rest of the patients were due to late presentations and not because of difficulty obtaining the antivenom, according to the authors. Although few patients received steroids or antihistamines in our study, all patients received them prophylactically in this review. While patient's demographics were similar to ours, the non-native snakes that were included and the management were different. A separate manuscript reviewed bites and stings from exotic pets reported to poison centers covering Northeastern Germany and Southeastern France [23]. While information is very limited, the review included 155 snakebites with 29 considered severe, including 19 by snakes that we would consider non-native to the US. The types of non-native snakes included multiple vipers and a species of cobra that were also included in our study. Antivenom was only administered to six of the 19 patients, less than what was observed in our patients. Little other information is available, limiting any other comparisons.

Limitations

The NASBR includes patients managed at the bedside by medical toxicologists who are trained in snakebite management. Although US medical toxicologists are not necessarily familiar with the specific management of envenomation by non-native snake species, their expertise and familiarity with snakebites in general and with antivenom use limits generalizability of this study to patients treated by other physicians and specialists. The small sample size and the limited number of snake species included also limits applicability, although the species included in this study were consistent with those reported in other studies. While the registry is very detailed, full medical decision-making (MDM) regarding why patients did or did not receive antivenom is not included. The registry is limited to upper level data and whatever comments were entered by the medical toxicologist. Since this is a retrospective examination of data in this registry, we were not able to obtain any further data from the treating or bedside providers of these patients. Had the entire MDM been available for review by our team of investigators, our opinions regarding their care and their decision to use or not use antivenom may be different. Additionally, only patients evaluated by a medical toxicologist that was a contributing partner in ToxIC were included. Patients treated at hospitals without a medical toxicologist on site or that do not participate in ToxIC would not be included, potentially leading to underreporting or a selection bias which may impact our findings. Snakes were identified by the treating medical toxicologist based on patient report and recall. There is not necessarily a consistent way that toxicologists identified

a snake, and additional confirmation is not a required part of this registry. However, many of the patients are experienced handling snakes and likely knew what type of snake bit them. While we believe it is unlikely that snakes were misidentified, if they were, this would alter our findings.

Conclusion

Victims of non-native snake encounters in the US most frequently presented with soft tissue effects. Systemic and hematologic effects were less common. Antivenom use varied, while corticosteroids and antibiotics were infrequently administered. Long-term sequelae at the final follow-up were infrequent.

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Declarations

Conflict of Interest M. R., P. W., and E. S. are all members of the Board of Directors for ACMT which receives funding from BTG® for the North American Snakebite Registry.

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