Evaluation of Risk Factors of Snake Envenomation Associated Complications Presenting to Two Emergency Departments in Oman

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Abstract

Objectives: This study aims to assess the risk factors of snake envenomation and the associated complications that patients present with, using data from two different emergency departments in Oman. The secondary outcome was to describe the common characteristics of patients presenting after snake envenomation.

Methods: This was a multicenter retrospective observational study of all patients who presented with a snake bite to the emergency department of Sultan Qaboos University Hospital from March 2016 until August 2017 and Rustaq Hospital from August 2015 till August 2017.

Results: A total of two hundred and twelve patients met the inclusion criteria. Coagulopathy was the major complication associated with snakebite, observed in 82 patients (38.7%), while 14 patients (6.6%) had acute kidney injury (AKI) and 5 patients (2.4%) had external bleeding. Of the patients who developed AKI, 85.7% ($P < 0.001$) had encountered the snake in a valley and initially presented with bleeding from the site of the bite ($P <0.001$) and vomiting ($P <0.007$). Furthermore, a prolonged time from bite to receiving the anti-snake venom (ASV) led to a significant risk in developing AKI ($P <0.006$). Of the patients who developed coagulopathy, 47.6% ($P <0.001$) had encountered the snake on a farm and 72% ($P <0.002$) received the bite to a lower limb. Similarly to those with AKI, a prolonged time from bite to ASV led to a significant risk in developing coagulopathy ($P < 0.001$).

Conclusion: This study noted that the location in which the snake was encountered affected the patient's risk for developing either AKI or coagulopathy, and that a prolonged time from bite to ASV was significantly associated with an increased risk of developing either an AKI or coagulopathy in snake bite patients.

Keywords: Risk factors, snake envenomation, Oman, emergency department

Introduction

The Sultanate of Oman has varied wildlife, with the country's topography (valley, desert and mountains) making it a suitable host to many species of snake. There are more than 20 different species of snakes in Oman, with 9 of those species being venomous.[1] Of the 9 venomous snakes, 90% of envenomation is caused by the saw-scaled viper (*Echis carinatus*) from *Viperidae* family, which can be found throughout Oman, especially in rocky areas. Around 9% of bites are caused by a related species, Burton's carpet viper (*Echis coloratus*) found in hilly regions, or the horned viper (*Cerastes gasperetti*) which inhabits the deserts.[2]

Snake bites are common cases in the emergency department, with an estimated 421,000 envenomation cases and 20,000 deaths due to snakebites occurring each year worldwide.[3] Currently, the incidence of snakebites is not well known in Oman due to a lack of reporting. The clinical presentations range from mild, with only local manifestations, to severe envenomation, with systemic manifestations. Antivenom is indicated when there are significant local signs of bite, systemic signs, circulatory collapse or systemic bleeding. [4] Snakebite envenomation can cause considerable morbidity and mortality, therefore early management is essential to avoid significant complications, such as venom-induced consumption coagulopathy, renal toxicity, cardiac toxicity and even death. It is not known which patients will develop these complications and what risk factors lead to these complications. A study of the mortality in patients with poisonous snake bite in tertiary care hospitals in central India concluded that certain predictors, such as bleeding, respiratory failure and hematotoxicty, can be predictors for mortality among snakebite patients.[5] Risk factors for renal toxicity after snakebite have been described in many studies.[6-10]

To the best of our knowledge, there is no study investigating the risk factors for developing various snakebite complications in Oman. This study aims to assess the risk factors of snakebite-associated complications from cases presenting to two emergency departments in Oman.

Methods

This was a multicentre retrospective observational study, using data from two different emergency departments, namely Sultan Qaboos University Hospital (SQUH), a tertiary hospital in Muscat, Oman, and Rustaq Hospital, a secondary hospital in Al Batina governorate.

The study was approved by the Institutional Ethical Committee of both hospitals. Patient data was obtained from hospital electronic records. Patient demographics, the area where the snake was encountered, site of the bite, initial symptoms and vital signs at presentation, laboratory investigations, time from the bite to hospital presentation, time from the bite to administration of anti-snake venom (ASV), the dose of ASV used initially and total amount during hospitalization (in mg), the use of antibiotics and tetanus toxoid, duration of hospitalization (days) and complications were evaluated.

Inclusion criteria

- A definitive history of snakebite.
- Clinical picture consistent with a snake bite, the presence of fang marks or cellulitis or coagulopathy or neuroparalysis.

Exclusion Criteria

- Unknown bite and/or clinical picture is not consistent with snake bite.
- Patients with preexisting renal diseases, e.g. serum creatinine >1.5 mg/dl before snake bite.
- Missing laboratory results.
- The patient was known to have a deranged coagulation profile or known to be on anticoagulants.

Definitions

Acute kidney injury (AKI) was defined as an abrupt (within 48 hours) absolute increase in the serum creatinine concentration of ≥0.3 mg/dl from baseline, measured after admission or elsewhere after the snake bite, or an increase in the serum creatinine concentration of ≥50% above baseline, or oliguria of less than 0.5 ml/kg per hour for more than 6 hours, or serum creatinine more than 1.5 mg/dl or oliguria (urine output less than 400 mL/day).[6] Venom-induced consumption coagulopathy was defined as patients with a prolonged prothrombin time (PT) defined as >1.5 times normal, and a partial thromoplastin time (PTT) of more than 10 seconds above control value was classified severe coagulopathy.[11-12] Compartment syndrome was defined based on clinical findings in the affected limb, including presence of pallor, lack of pulse, pain, change of color and increased swelling. Swelling at the bite site was classified as mild, moderate and severe based on the physician's assessment using the national management guideline of poisoning.[4]

Statistical analysis

A t-test was used to assess continuous normally distributed variables. For the categorical data, the Chi-square test was used, with the Fischer-exact test being used for small numbers. For variables that were not normally distributed, the Wilcoxon's Mann-Whitney U-test was used. A *P* value of 0.05 or less was considered to be statistically significant. The statistical analysis was conducted using the Statistical Package for the Social Sciences, version 11.0 (IBM Corp, Armonk, NY, USA).

Results

A total of 236 snakebite patients were identified, with 24 patients being excluded for not meeting the inclusion criteria, therefore, 212 patients were included in this study. From those 212 patients, 11 patients presented at SQUH and 201 patients at Rustaq Hospital. Table 1 illustrates the baseline characteristic of the included patients. The median age was 30 years and the majority of cases were male (84%). The youngest case was a one-year-old patient, with the oldest patient being 85 years old. Most of the cases were bitten on a farm (62.3%), while 16.5% were bitten in a valley, with 20.8% were bitten at home. The monthly incidence in snakebite cases increased from March to September, peaking in August (Figure 1).

Table 1: Sociodemographic characteristics of the 212 participants included in this study

Baseline Characteristic	n (%)
Age (median, IQR)	30 (23-41)
Sex	
Male	178 (84)
Female	34 (16)
Nationality	
Omani	130 (61.3)
Non-Omani	82 (38.7)
Hospital	
SQUH	11 (5.2)
Rustaq Hospital	201 (94.8)
Area where snake encountered	
Farm	132 (62.3)
V**alley**	35 (16.5)
Home	44 (20.8)

IQR = interquartile range; SQUH = Sultan Qaboos University Hospital

Table 2 illustrates the clinical features of the patients, with the majority of patients presenting with pain (97.2%) and swelling (85.5%) as their main complaints. Bleeding from the site of the bite was present in 8.5% of patients and nausea or vomiting was noted in 9.9%. With regards to location of the bite, 124 (58.5%) patients had a bite on their lower limb and 85 (40.1%) had a bite on an upper limb, while only three patients being bitten on their torso.

Table 2: Clinical variables of the 212 participants in this study

Clinical variables	n (%)
Initial symptoms	
Pain	206 (97.2)
Swelling	182 (85.5)
Bleeding from site of bite	18 (8.5)
Nausea/vomiting	21 (9.9)

Shortness of breath	-
Site of bite	
Lower limb	124 (58.5)
Upper limb	85 (40.1)
Torse	3 (1.4)
Classification of swelling	
None	33 (15.6)
Mild	125 (59)
Moderate	51 (24.1)
Severe	3 (1.4)

Of the 212 patients included in this study, 102 patients (41%) developed a complication from the snake bite, with the major complications being observed to be coagulopathy (38.7%), AKI (6.6%), and external bleeding (2.4%), with only 1 (0.5%) child developing compartment syndrome which required a transfer from a secondary to a tertiary hospital. No deaths were recorded during the study period.

Among the variables which were included for bivariate analysis (Table 3), there was an independent association of AKI with bleeding as an initial symptom and the area where the snake was encountered. For those who developed coagulopathy, the bivariate analysis (Table 4) showed that there was an independent association between coagulopathy and bleeding, nausea and vomiting as initial symptoms, swelling at the site of the bite and also delayed presentation from the time of snake bite to the time of ASV administration.

Table 3: Association of the variables with acute kidney injury (AKI)

Variables	**With AKI (n=14) (%)**	**Without AKI (n=198) (%)**	***P* Value**
Age (median, IQR)	40 (22-56)	30 (23-40)	0.085
Sex			
Male	12 (85.7)	166 (83.8)	>0.05
Female	2 (14.3)	32 (16.2)	
Nationality			

Omani	13 (92.9)	117 (59.1)	0.011
Non-Omani	1 (7.1)	81 (40.9)	
Area where snake encountered			
Desert	-	1 (0.5)	<0.001
Farm	2 (14.3)	130 (65.7)	
Valley	12 (85.7)	23 (11.6)	
Home	-	44 (22.2)	
Site of bite			
Lower limb	10 (71.4)	114 (57.6)	0.506
Upper limb	4 (28.6)	81 (40.9)	
Torso	-	3 (1.5)	
Symptoms			
Nausea/vomiting	5 (35.7)	16 (8.1)	0.007
Bleeding	6 (42.9)	12 (6.1)	<0.001
Swelling	14 (100)	168 (84.8)	0.227
Pain	14 (100)	192 (98.0)	>0.05

Laboratory results			
Hemoglobin			
Anemia	2 (14.3)	10 (5.1)	0.464
Normal	8 (57.1)	123 (62.4)	
Polycythemia	4 (28.6)	64 (32.5)	
INR			
Normal	9 (64.3)	169 (85.4)	0.033
Mild-moderate	2 (14.3)	2 (1.0)	
Severe	3 (21.4)	27 (13.6)	
WBC			
Normal	12 (85.7)	137 (69.9)	0.360
Abnormal	2 (14.3)	59 (30.1)	
Platelets			
Low	0	9 (4.6)	
Normal	14 (100)	184 (93.4)	0.398
High	0	2 (2.0)	
Prothrombin time			
Normal	1 (7.1)	50 (25.3)	0.178
Mild-moderate	9 (64.3)	119 (60)	
Severe	4 (28.6)	29 (14.7)	
Time from bite to hospital in minutes (median, IQR)	145 (98-323)	120 (65-180)	0.157
Presentation to receiving ASV in minutes (median, IQR)	133 (88-203)	100 (22-120)	0.016
Total antivenom received in mg (± SD)	80 (40-120)	40 (40-80)	0.061

AKI = acute kidney injury; ASV = anti-snake venom; INR = international normalized ratio; IQR = interquartile range; SD = standard deviation; WBC = white blood cell count

Table 4: Association of the variables with coagulopathy

Variables	With coagulopathy (n=82)	Without coagulopathy (n=130)	*P* value
Age (median, IQR)	28.5 (18-41)	31 (24-41)	>0.05
Gender			>0.05
Male	71 (86.6)	107 (82.3)	
Female	11 (13.4)	23 (17.7)	
Nationality			
Omani	54 (66)	76 (58.5)	0.313
Non-Omani	28 (34)	54 (41.5)	
Area where snake encountered			
Desert	-	1 (0.8)	<0.001
Farm	39 (47.6)	93 (71.5)	
Valley	25 (30.5)	10 (7.7)	
Home	18 (22)	26 (20)	
Site of bite			
Lower limb	59 (72)	65 (50)	0.002
Upper limb	23 (28)	62 (47.7)	
Torso	-	3 (2.3)	
Symptoms			
Nausea/vomiting	16 (19.5)	2 (1.5)	<0.001
Bleeding	16 (19.5)	12 (6.1)	<0.001
Swelling	81 (98.8)	101 (77.7)	<0.001
Pain	82 (100)	125 (97)	0.301
Laboratory results			
Hemoglobin			
Anemia	5 (6.1)	7 (5.4)	0.903
Normal	52 (63.4)	79 (61.2)	
Polycythemia	25(30.5)	43 (33.3)	
Creatinine			
Normal	78 (95.1)	126 (97.7)	0.435

Abnormal	4 (4.9)	3 (2.3)	
WBC			
Normal	53 (64.6)	96 (75)	0.121
Abnormal	29 (35.4)	32 (25)	
Platelets			
Low	6 (7.3)	3 (2.3)	0.199
Normal	74 (90.2)	124 (96.1)	
High	2 (2.4)	2 (1.6)	
Time from bite to hospital in minutes (median, IQR)	120 (120-187)	120 (120-180)	0.052
Presentation to receiving ASV in minutes (median, IQR)	120 (120-171)	75 (75-120)	<0.001
Total antivenom received in mg (± SD)	80 (40-80)	40 (40)	<0.001

ASV = anti-snake venom; IQR = interquartile range; SD = standard deviation; WBC = white blood cell count

Discussion

The findings from this study demonstrated that snakebite victims mostly male adults, with most of the incidents occurring on a farm, a common habitat for snakes in Oman.

Most of these incidents occurred during the summer months (March to September), with the highest incident rate occurring in August. This could be explained due to snakes being more active during the summer months, as compare to the colder months when they hibernate and become inactive, a finding which was noted in another study.[13]

The most common site of the bite was the lower limb while the torso had the least number of bites. Lower limbs are more exposed while walking around farms or valleys, with no protective footwear being worn. This finding has also been described in other studies.[14,15]

Notably, those presenting with snakebites from the valleys who had bleeding from the site of bite were at higher risk of developing AKI compared to those who were bitten on a farm. This is

probably due to the venom of the saw-scaled viper (*Echis carinatus*), which is found throughout Oman, but especially in rocky areas and valleys.[2] Bites from the *Echis carinatus* have been reported to cause direct nephrotoxicity.[16-18] Their venom also causes intravascular hemolysis leading to bleeding from the site of the bite.[8,17] Other multifactorial causes leading to AKI after snake bite envenomation are hypotension and significant bleeding, these were not observed in patients who developed AKI in this study.[17]

Patients who were bitten on a farm tended to develop coagulopathy, as noted in this study, probably due to the venom of the Burton's carpet viper (*Echis coloratus*) from *Viperidae* family, which are found in hilly regions and farms.[2] These species are known to cause venom-induced consumption coagulopathy, which occurs secondary to the activation of a coagulation cascade by procoagulant toxins in the snake venom, in turn leading to a severe coagulation factor deficiency that ultimately causes hemorrhage.[19-21] The toxin in the snake venom causes these patients to present with nausea, vomiting, swelling and bleeding at the site of bite, all of which were observed in this study.

The results from this study showed that delayed presentation to the emergency department and delayed administration of ASV were risk factors for developing coagulopathy. The delay of administration of ASV was observed in the secondary hospital, as they had a protocol to only administer the antivenom in the admission ward to those in high dependency beds rather than in the emergency department. The administration of ASV requires observation for any anaphylactic reactions, a possible side effect. This observation period can be done in the emergency department, which keeps those patients under close observation and provides support in case of anaphylaxis. It is well known that the early presentation to the emergency room and early administration of ASV is closely linked to an increased efficacy of the ASV and good outcomes.[22] Therefore, we recommend that ASV administration should not be delayed and be given to the patients in the emergency department.

This study has several limitations, most notably that it is a retrospective study, therefore there was missing data and also some laboratory variables could not be studied as they were not acquired from the patients. The other limitation is that the identification of the snakes was not

carried out or reported in the patients' charts, though this is usually not feasible. Also, the sample size was small, therefore we were unable to run a multivariate analysis for some variables as predictors of complications.

Conclusion

To the best of our knowledge, this is the first study of its kind in Oman. This study noted that the place where the snake was encountered, whether it was a valley or farm, was correlated with the risk for developing either AKI or coagulopathy. Prolonged bite to ASV administration time was associated with the risk of developing of coagulopathy. Therefore, rapid administration of ASV to avoid unnecessary complications is crucial.

Disclosure

The abstract has been published in the European Journal of Emergency Medicine

Conflicts of interest

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Competing interests: None declared.

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