

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

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ABSTRACT

Objectives: 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 aim was to describe the common characteristics of the presenting patients. **Methods:** This multicenter retrospective observational study reviewed all cases presenting with symptoms of snakebite to the emergency departments of Sultan Qaboos University Hospital (tertiary) from March 2016 until August 2017 and Rustaq Hospital (secondary) from August 2015 to August 2017. **Results:** A total of 212 cases met the inclusion criteria. Coagulopathy was observed in 82 (38.7%) patients, while 14 (6.6%) had acute kidney injury (AKI) and 5 (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 had bleeding from the site of the bite ($p < 0.001$) and vomiting ($p < 0.007$). The delay in receiving the anti-snake venom (ASV) increased the risk of AKI ($p < 0.016$). Of the patients who developed coagulopathy, 47.6% ($p < 0.001$) had encountered the snake on a farm and 72.0% ($p < 0.002$) received the bite to a lower limb. Increased time from bite to ASV was associated with development of coagulopathy ($p < 0.001$). No patient death was recorded. **Conclusions:** The location (terrain) where the snake was encountered was associated with the patient's risk for either AKI or coagulopathy, which suggests the preference of different snake species to different types of habitat. The time elapsed between the bite and the ASV administration was associated with higher risk of development of AKI or coagulopathy.

Wildlife in Oman is as varied as the country's topography which consist of vast deserts, mountains, rocky hills, valleys, and even tropical rain forests. Among more than 20 species of snakes in Oman, nine are venomous.¹ Most of the latter belong to the *Viperidae* family, whose venom is primarily hemotoxic. Of these, 90% cases of human envenomation are caused by the saw-scaled viper (*Echis carinatus*), found throughout the country, with a preference to rocky areas. Around 9% are caused by Burton's carpet viper (*Echis coloratus*) found in hilly regions, or the horned viper (*Cerastes gasperetti*) which inhabits the deserts.²

Worldwide, an estimated 421 000 envenomation cases and 20 000 deaths occur due to snakebites each year.³ The incidence in Oman is not clear due to under-reporting from rural areas where most bites occur. Clinical presentations range from mild

and localized, to severe systemic manifestations. Antivenom is indicated when there are significant local signs of bite, systemic signs, circulatory collapse, or systemic bleeding.⁴ Early management is essential to avoid complications, such as venom-induced consumption coagulopathy, renal toxicity, cardiac toxicity, and even death. A study in tertiary care hospitals in central India concluded that certain predictors, such as bleeding, respiratory failure, and hematotoxicity, can be predictors for mortality among snakebite patients.⁵ Risk factors for renal toxicity after snakebite have been described in many studies.⁶⁻¹⁰ Despite such indicators, it is difficult to predict which individual patient might be at significant risk of developing complications.

To the best of our knowledge, no study has investigated the risk factors for developing snakebite-related complications in Oman. This study aims to narrow the research gap by assessing the risk factors of snakebite-associated complications by evaluating

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cases presenting to emergency departments of two hospitals in Oman.

METHODS

This was a multicenter retrospective observational study, using data from two different emergency departments, namely Sultan Qaboos University Hospital (SQUH), a tertiary hospital in Muscat city, and Rustaq Hospital, a secondary hospital located in a semi-rural town in South Al Batinah governorate.

The study was approved by the institutional ethical committees of both hospitals. Patient's data was obtained from the hospital electronic records. Patient demographics, the geographical location (terrain) where the snake was encountered, site of the bite, initial symptoms and vital signs at presentation, laboratory investigations, time elapsed from the bite to hospital presentation, time taken from the bite to administration of anti-snake venom (ASV), the dose of ASV used initially and total amount administered during hospitalization, the use of antibiotics and tetanus toxoid, and details of complications that arose, were obtained and evaluated.

Inclusion criteria comprised: (a) a definitive patient report of snakebite; (b) a clinical picture consistent with snakebite, such as the presence of fang marks, cellulitis, coagulopathy, or neuroparalysis; and (c) where laboratory results confirmed snake envenomation. Excluded from the study were: (a) cases of unknown bite source; (b) where the clinical picture was not consistent with snakebite; (c) patients with preexisting renal diseases (e.g. serum creatinine > 1.5 mg/dl before snake bite), with preexisting deranged coagulation profiles, or known to be on anticoagulants; and (d) where laboratory data was unavailable.

Acute kidney injury (AKI) was defined as an abrupt (< 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, an increase in the serum creatinine concentration of $\geq 50\%$ above baseline, oliguria of < 0.5 mL/kg per hour for more than 6 hours, serum creatinine of > 1.5 mg/dL, or oliguria (urine output < 400 mL/day).⁶ Venom-induced consumption coagulopathy was defined a prolonged prothrombin time (PT) of > 1.5 times normal. Partial thromboplastin time (PTT) of > 10 seconds above control value was classified severe coagulopathy.^{11,12}

Table 1: Sociodemographic characteristics of the participants (N = 212).

Baseline Characteristic	n (%)
Age (median, IQR)	30 (23–41)
Sex	
Male	178 (84.0)
Female	34 (16.0)
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)
Valley	35 (16.5)
Home	44 (20.8)

IQR: interquartile range; SQUH: Sultan Qaboos University Hospital.

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 Oman's national management guideline of poisoning.⁴

The t-test was used to assess continuous normally distributed variables. For categorical data, the Chi-square test was used, with the Fisher's exact test for small numbers. For variables that were not normally distributed, the Mann-Whitney U test was used. A *p*-value of < 0.05 was considered statistically significant. The statistical analysis was performed using the Statistical Package for the Social Sciences, version 11.0 (SPSS Inc. (1999). SPSS Base 10.0 for Windows User's Guide. SPSS Inc., Chicago IL).

RESULTS

Among a total of 236 snakebite cases identified from the hospital databases, 24 patients did not meet the inclusion criteria. Therefore, 212 cases were included in this study. Of these, 11 patients presented at SQUH and 201 patients at Rustaq Hospital. Table 1 illustrates the baseline characteristics of the included patients. The median age was 30 years and 84.0% were male. The youngest patient was one year old, and the oldest was 85 years old. Most snakebites occurred on farms (62.3%), 16.5% in valleys, while 20.8% patients were bitten at home. The monthly

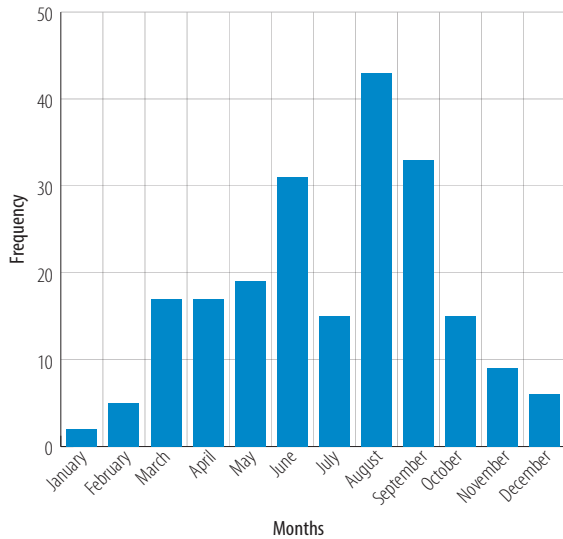


Figure 1: Frequency of snake bites by month.

incidence in cases followed a rising trend during the summer months, peaking in August [Figure 1].

Table 2 illustrates the clinical features of the patients, with the vast majority complaining of pain (97.2%) and swelling (85.8%). Bleeding from the site of the bite was present in 8.5% cases and nausea or vomiting in 9.9%. The majority of the patients (124, 58.5%) were bitten on a lower limb and 85 (40.1%) on an upper limb. Three patients were bitten on the torso.

Of the 212 patients included in this study, 102 (48.1%) developed complication from the snake bite, the major ones being coagulopathy (38.7%), AKI (6.6%), and external bleeding (2.4%). One

Table 2: Clinical variables of the participants (N = 212).

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)

Table 3: Association of the variables with acute kidney injury.

Variables	With AKI (n=14) n (%)	Without AKI (n=198) n (%)	p-value
Age (median, IQR)	40 (22–56)	30 (23–40)	0.085
Sex			
Male	12 (85.7)	166 (83.8)	> 0.050
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 (97.0)	> 0.050
Laboratory results			
<i>Hemoglobin</i>			0.464
Anemia	2 (14.3)	10 (5.1)	
Normal	8 (57.1)	123 (62.1)	
Polycythemia	4 (28.6)	64 (32.3)	
<i>INR</i>			0.033
Normal	9 (64.3)	169 (85.4)	
Mild-moderate	2 (14.3)	2 (1.0)	
Severe	3 (21.4)	27 (13.6)	
<i>WBC</i>			0.36
Normal	12 (85.7)	137 (69.2)	
Abnormal	2 (14.3)	59 (29.8)	
<i>Platelets</i>			0.398
Low	0	9 (4.5)	
Normal	14 (100)	184 (92.9)	
High	0	2 (1.0)	
<i>Prothrombin time</i>			0.178
Normal	1 (7.1)	50 (25.3)	
Mild-moderate	9 (64.3)	119 (60.1)	
Severe	4 (28.6)	29 (14.6)	
<i>Time from bite to hospital in minutes (median, IQR)</i>	145 (98–323)	120 (65–180)	0.157
<i>Presentation to receiving ASV in minutes (median, IQR)</i>	133 (88–203)	100 (22–120)	0.016
<i>Total antivenom received in mg (± SD)</i>	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 (18–41)	31 (24–41)	> 0.050
Gender			> 0.050
Male	71 (86.6)	107 (82.3)	
Female	11 (13.4)	23 (17.7)	
Nationality			0.313
Omani	54 (65.9)	76 (58.5)	
Non-Omani	28 (34.1)	54 (41.5)	
Area of snake encounter			< 0.001
Desert	-	1 (0.8)	
Farm	39 (47.6)	93 (71.5)	
Valley	25 (30.5)	10 (7.7)	
Home	18 (22.0)	26 (20.0)	
Site of bite			0.002
Lower limb	59 (72.0)	65 (50.0)	
Upper limb	23 (28.0)	62 (47.7)	
Torso	-	3 (2.3)	
Symptoms			
Nausea/vomiting	16 (19.5)	2 (1.5)	< 0.001
Bleeding	16 (19.5)	12 (9.2)	< 0.001
Swelling	81 (98.8)	101 (77.7)	< 0.001
Pain	82 (100)	125 (96.2)	0.301
Laboratory results			
Hemoglobin			0.903
Anemia	5 (6.1)	7 (5.4)	
Normal	52 (63.4)	79 (60.8)	
Polycythemia	25 (30.5)	43 (33.1)	
Creatinine			0.435
Normal	78 (95.1)	126 (96.9)	
Abnormal	4 (4.9)	3 (2.3)	
WBC			0.121
Normal	53 (64.6)	96 (73.8)	
Abnormal	29 (35.4)	32 (24.6)	
Platelets			0.199
Low	6 (7.3)	3 (2.3)	
Normal	74 (90.2)	124 (95.4)	
High	2 (2.4)	2 (1.5)	
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 (\pm SD)	80 (40–80)	40 (40)	< 0.001

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

pediatric patient developed compartment syndrome and had to be transferred to a tertiary hospital. No deaths were recorded during the study period.

Among the variables included for bivariate analysis [Table 3], there was an independent association of AKI with bleeding as an initial symptom and the geographical location (rocky valley)

where the snake was encountered. For those who developed coagulopathy, the bivariate analysis [Table 4] showed an independent association between coagulopathy and bleeding, nausea and vomiting as initial symptoms, swelling at the site of the bite, and delay between the time of snake bite till the time of presentation and ASV administration.

DISCUSSION

The snakebite victims in this study were mostly male adults, with most incidents occurring in farms, a common habitat for snakes in Oman. Most incidents occurred during the summer months (March to September), peaking in August; snakes are known to be more active during summers than in winters.¹³ The most common site of the bite was a lower limb, followed by an upper limb while bites to the torso were rare, with just three cases. Lower limbs appear to be vulnerable while walking in farms or traversing valleys without appropriate footwear. Similar trend has been described in other studies.^{14,15}

Notably, those presenting with snakebites received in the valleys and had bleeding from the site of bite were at higher risk of developing AKI than those who were bitten on a farm. This may be because in the rocky valleys of Oman there is high possibility of being bitten by saw-scaled viper (*Echis carinatus*)² whose venom is reported to trigger direct nephrotoxicity.¹⁶⁻¹⁸ The venom of this snake also causes intravascular hemolysis leading to bleeding from the site of the bite.^{8,17} Other causes mentioned in literature as leading to AKI after snake bite envenomation, namely, hypotension and significant bleeding,¹⁷ were not observed in AKI patients in this study.

Patients in this study who were bitten on a farm tended to develop coagulopathy, probably due to being bitten by another member of the *Viperidae* family, the Burton's carpet viper (*Echis coloratus*), often found in hilly regions and farms.² Its bite is 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 *Echis coloratus* victims also tend to present with nausea, vomiting, swelling, and bleeding at the site of bite, were observed in this study.

The results from this study showed that delayed presentation to the emergency department and delayed administration of ASV were the main risk factors for developing coagulopathy. The delay of administration of ASV was observed in Rustaq 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, which can be conducted in an adequately equipped emergency department. As it is well known that the early presentation to the emergency room and early administration of ASV are closely linked to an increased efficacy of the ASV and good outcomes,²² and also supported by the current study's findings, we recommend revision of the protocol in secondary hospitals in Oman so that ASV can administered and the patients monitored in the emergency department itself. As the vast majority of cases occur in rural areas and the need for urgent treatment, we also recommend that rural primary health centers situated far from secondary hospitals to be fully equipped to facilitate the administration of ASV.

The most notable limitation of this study is its retrospective nature. Certain laboratory variables could not be studied as they had not been acquired from the patients. Another limitation was that the identification of the snakes was not carried out or reported in the patient records, though this is usually not feasible. In addition, the sample size being small, multivariate analysis could not be run for some variables as predictors of complications. Finally, this study represents only the northern part of Oman. For a more representative picture, future studies need to include other parts of the country, especially the southern Dhofar governorate, which has a monsoon climate and the home to other snake species such as the Arabian cobra whose venom is predominantly neurotoxic.

CONCLUSION

To the best of our knowledge, this is the first study of its kind in Oman. This study noted that the type of the location where the snake was encountered, whether a valley or a farm, was correlated with the risk for developing either AKI or coagulopathy. Time taken from the bite till ASV administration was associated with the risk of developing of coagulopathy. Therefore, rapid administration of ASV to avoid unnecessary complications is crucial. As most snakebites occur in rural areas and the need for immediate treatment, there is a strong case for equipping rural and semi-rural secondary hospitals, and even primary health centers in Oman with sufficient facilities and expertise to manage these emergencies.

Disclosure

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