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Case study

## Snakebites in Hajjah, Yemen Republic: Epidemiology, management and the relation of the degree of acuity at presentation with outcome

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### ABSTRACT

Snakebites are a common environmental hazard in many regions of the world. The objectives were to study the epidemiology, clinical, laboratory features of snakebites, the pattern of management with its outcome, and studying the association between the presenting clinical and initial laboratory findings with the outcome.

**Method:** a retrospective, hospital-based study was conducted from March 1997–April 2001 at the Saudi Hospital in the Hajjah governorate, Yemen Republic. The demographics, clinical, laboratory, management, outcome data and selected variables were collected for detecting any association between the degree of acuity of snakebites and the outcome.

**Results:** The data of 186 patients was collected over the period of 4 years. Eighty three percent of snakebite victims were below 40 years of age and males made up 73.7% of all cases. The average incidence was 43 cases per year, with the highest number of cases recorded in July–October. Local swelling then redness was the most common clinical features and the systemic hematological manifestations were double the neurological signs. Lower limbs were involved in 55% of cases. Anemia, leukocytosis, leucopenia and thrombocytopenia were recorded in 34%, 28%, 11% and 8% of cases respectively. Abnormal coagulation was seen in 30% of patients. Admission was necessitated for one third of patients. Surgical assessment was required for 15% of patients. Antivenom was administered for 80% but only 31.7% received this within the first 8 h. Blood products were used for 42% of patients. The complications from the snakebites were recorded in 26% of all cases. There was a statistically significantly association between the rate of complications and the presence of more than three clinical and laboratory findings on arrival. The overall mortality rate was 3.7%.

**Conclusion:** Snakebites are an important public health problem with a relatively high rate of mortalities and other complications associated with delay in the administration of antivenom. Acknowledging more than three clinical and/or laboratory manifestations on arrival to hospital might help in anticipating clinically important complications.

**Keywords:** Snake bites, Epidemiology, Manifestations, Mortality, Hajjah, Yemen

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## INTRODUCTION

Snakebites are a known environmental hazard that can lead to morbidity and mortality [1–5]. Not all snakes are poisonous and not all bites from poisonous snakes are associated with significant envenomations [3,6,7] due to the variation in the amount and the severity of the poison injected [2,3,7–9]. It is thought that the age of the snake may play a role in the severity of envenomation [10]. The incidence of snakebites varies between different countries and even within the same country [11–16]. Seasonal variation is another noticeable phenomenon [17–21]. Intentional exposure represents the most common cause of snakebites [22]. The outcome depends on many factors including the positive effect of the appropriate use of first aid measures [11,23], which is documented in the minority of patients [25]. In contrast, the application of different local herbal preparations and incisions can have a negative effect [24]. The most important determinant of the outcome however is the timing of administration of an appropriate antivenom that has been manufactured based on local snake species [26]. Venom detection kits are designed to identify the type of snake venom which allow for the appropriate administration of antivenom [25,27]. There are 55 snake species in the Arabian Peninsula, and approximately 40% are venomous [28]. The poisonous species in the southern part of Saudi Arabia on the border with the Yemeni governorate where the study was conducted are [28]: *Cerastes cerastes gasperetii*, *Echis carinatus*, *Echis coloratus*, *Naja hajje arabicus*, *Atractaspis microlepiota*, *Malpolon moilensis*, *Psammophis schokari*, *Telescopus dhara*. To the best of the author's knowledge, there has been no study to date of snakebites in the Hajjah governorate, Yemen Republic. In addition, no study could be found that focuses on the identification of simple predictors for the outcome of snakebites by utilizing only the initial presenting clinical manifestations and initial laboratory assessment. The objectives of this study were twofold. The first objective was to study the epidemiology, clinical, laboratory features of snakebites and the pattern of management with its outcome. The second objective was to study the association between the clinical manifestations at presentation and the initial laboratory findings with mortality and other complications.

## METHODS

This retrospective hospital-based study was conducted over a 4-year period from March 1997–April 2001 at the Saudi Hospital in the Hajjah governorate (population approximately 1.5 million), Yemen Republic. The hospital provides secondary care services and is considered a referral center for other areas of the governorate and neighboring governorates, with approximately a thousand patients seen in the outpatient and emergency departments daily. Snakebite patient's medical files were identified from the emergency room logbook. The files were reviewed for age, sex, site of bite, the month and the year, clinical manifestations, duration of bite prior to hospital arrival, laboratory workup including complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), biochemistry including renal function (creatinine), the need for admission and surgical evaluation, the type of surgical and medical management including the need for antivenom and total amount administered, complications either from the snake bite or antivenom and the mortality rate. The laboratory values that were considered normal are as follows: WBC  $4-12 \times 10^3$  mcl, HGB (hemoglobin)  $> 11$  g/dl, PLT (platelets)  $\geq 150000$ /cmm, SCR (serum creatinine)  $< 1.3$  mg/dl ( $< 115$   $\mu$ mol/L), PT (prothrombin time) and aPTT (activated partial thromboplastin time)  $\leq 4$  s above the control based on the laboratory's normal ranges of a parameter (in line with the majority of reference ranges). INR (International Normalized Ratio) was not consistently reported in patient files and therefore was not considered in this study. The presenting clinical features and initial laboratory data were divided into different categories for patients with three or less or three or more positive findings for: pain, local signs of swelling or redness, bleeding from any site, neurological manifestations (bulbar palsy, respiratory paralysis, change in the level of consciousness), gastrointestinal manifestations (epigastric abdominal pain, vomiting), abnormal leukocyte counts (leukocytosis or leucopenia), thrombocytopenia, prolonged coagulation profile and elevated creatinine. The selection of three abnormalities to be the cutoff for patients considered in the study was that most cases of systemic manifestations were few compared to the local ones, so if two features were selected the comparison would have been between local and systemic abnormalities and if four had been selected then there would not have been enough subjects eligible for comparison, accordingly we balanced this by adding at least one systemic manifestation. The antivenom administered to patients presenting with snakebites was the Polyvalent Snake Antivenom–Equine, a product of the National Antivenom and

Vaccine Production Center, National Guard Health Affairs, Saudi Arabia, containing F(ab)2 fractions of the immunoglobulin raised against the venoms of six terrestrial Saudi snakes (*bitis arietans*, *echis coloratus*, *echis carinatus*, *naja haje*, *cerastes cerastes*, *walterinesia aegyptia*).

SPSS14.0 statistical package was used for both the descriptive statistics and the Fisher's Exact Test to determine the association of the degree of acuity at presentation with the rate of complications and mortality. A p-value of < 0.05 was considered to be statistically significant.

## RESULTS

The data of 186 patients was collected over a 4-year period. The age of patients admitted to the hospital ranged from 1–70 years, 42 (22.6%) were 15 years or below, 60.8% were between the ages 15–40 years and only 16.6% of patients were more than 40 years old. The majority of patients were found to be males (73.7%). The incidence of cases ranged from 25–51 patients per year, with an average of 43 patients being admitted per year. The highest incidence of cases was recorded from July to October in the range of 17–25 cases, with a mean of 21.8 cases. The lowest incidence recorded was in the period from November to February with a range of 8–10 cases and a mean of 8.3 (p. value of 0.006). The medium level of incidence was between March and June with a range of 13–21 cases and with a mean of 16.5 (p value 0.15). Swelling then redness were the most common clinical features on presentation (Table 1).

**Table 1. Clinical manifestations for patients with snakebites in Hajjah, Yemen.**

Feature	Number of patients	Percentage (%)
Local swelling	99	53.2
Redness	29	15.6
Bite marks	20	10.8
Bleeding (local & systemic)	13	7
Neurological manifestation	6	3.2
Vesicles	4	2.2
Signs of ischemia	2	1.1
Shock	1	0.5

Forty-four patients (23.6%) did not present with systemic manifestations nor any local physical signs and therefore their bites were considered dry bites (without envenomation) and were not included in the analysis. Local pain in 12 patients with no physical signs. Lower limbs were mostly involved (55%). The range of timing from the event of a snakebite till arrival to the hospital was 0.25–360 h, with a mean time on presentation of 37 h. It was found that only 21% and 10.7% of patients presented within the first 4 and 8 h respectively.

Hemoglobin level was known in 156 patients, 66 (42.3%) were detected with a level below 11 g/dl, the majority (82%) of the anemic group had a level more than 8 g/dl. Leukocyte count was determined for 159 patients (85.5%), 46.5% with an abnormal count, 53 patients had leukocytosis with a count more than  $12 \times 10^3/\mu\text{L}$  and 28.4% had leucopenia with a count below  $4 \times 10^3/\mu\text{L}$ . A platelet count was performed only for 40 patients (21.5%), 16 (40%) had a count below 150,000/ml, two patients had a count below 50,000/ml and one patient with a count below 20,000/ml. Coagulation parameters were measured for 178 patients (95.7%), 30% of these with an abnormal PT or PTT more than 4 s above the control value. Approximately 50% of the abnormal coagulation group had more than 20 s above the control. Serum creatinine levels were analyzed in only 12 patients, 3 of which (25%) had abnormal values (1.7 mg/dl, 5.5 mg/dl and 9.8 mg/dl).

Admission was required for 32.5% of the patients but 60% were discharged within 24 h; and the mean hospital stay was 1.7 days. Twenty-nine of patients (15.6%) were evaluated by a surgeon but only 10 of these cases required surgical intervention, mainly involving longitudinal incisions and abscess drainage.

Antivenom was used for 80% of patients but only 31.7% received this within the first 8 h, out of these 72% received this in one single occasion and it was rarely administered on more than three occasions. The administration of antivenom however ranged from 1–7 occasions. In 92% of cases the dose for antivenom was 20–40 ml (2–4 ampoules) but it ranged from 5 ml to 320 ml (32 ampoules). Urticaria developed in 3 patients (1.6%) as a result of the antivenom but pre-treatment was not given. Blood products were used for 42% of patients, mostly (80.8%) as fresh frozen plasma.

Complications due to this were recorded in 26% of patients with cellulites and DIC (Disseminated Intravascular Coagulation) being the most common problems (Table 2).

The rate of complications was found to be significantly higher for patients that had more than three positive clinical manifestations at the time of presentation. The mortality rate however did not reach a statistically significant level (Table 3).

**Table 2. Mortality rate and other complications of snakebites in Hajjah, Yemen.**

Complication	Number of patients	%
Cellulites	18	9.6
Bleeding (systemic & local)	10	5.4
Skin defect	5	2.7
Abscess	3	1.6
Acute renal failure	1	0.54
Respiratory paralysis	1	0.54
Osteomyelitis	1	0.54
Shock	1	0.54
Premature ventricular contraction	1	0.54
Total	41	22.0
Mortality rate	7	3.7
Grand Total	49	26.2

**Table 3. The association between the degree of acuity at presentation with the mortality rate and the development of other complications due to snakebites in Hajjah, Yemen.**

Variable	Category	Score		P Value
		≤3 findings N (%)	>3 findings N (%)	
Age	< or =15 Years	32(24.1)	5(55.6)	0.052
Gender	Male	99(74.4)	8(88.9)	0.300
Site of bite	Lower limb	80(66.7)	6(75)	0.478
Time till administering antivenom	< or =6 h	33(32.4)	2(25)	0.503
Admission to hospital	Admitted	50(37.6)	6(75)	0.043
Hospital stay	<2 days	105(79.5)	5(55.6)	0.107
Complications	Complications present	35(26.3)	6(66.7)	0.017
Mortality	Deaths	5(3.8)	2(22.2)	0.064

There were 7 mortalities recorded which gave an overall mortality rate of 3.7% (children 7.1% and adults 3.5%). Four patients died with a severe picture of DIC, one with respiratory failure and coma, one with hypertensive crisis and possibly with intracranial bleeding (a CT scan was not performed and therefore this cannot be confirmed), and one patient suffered a sudden cardiac arrest with no documented comments about the possible causes of death.

## DISCUSSION

The average incidence of snakebites in this study was higher than what has been reported in the south-western part of Saudi Arabia which is located on the border with the Hajjah governorate where this study was conducted [15]. The number of cases of snakebites was also found to be higher than that in other countries worldwide [29–31]. As this was a hospital-based study however, it did not reflect the actual incidence. The most active age group (15 years of age or below) formed the majority of snakebite cases [13,15,16]. The majority of cases also involved males as in several other studies [6,13,16,18–20,29,30] due to their higher level of outdoor exposure. The higher incidence in summer is explained by the fact that hibernation of snakes occurs in winter [32–36].

Local signs were present in the majority of patients [7,16,30]. Systemic hematological signs were double the signs of neurological involvement [7,16,36], reflecting the type of envenomation of snake species in this region. There was not enough data to indicate the type of first aid measures that were taken and the effects of this, nor the type of snake species that were involved. It is thought that the same species of snakes identified in the southern region of Saudi Arabia were involved in the cases recorded in Hajjah, due to the similarities in the geography, weather and clinical manifestations, as well as the potent effect of the antivenom manufactured and imported from Saudi Arabia [37,38]. Lower limbs were predominantly affected as in other studies [13,32–34]. Similar rates of

envenomation have been reported in studies conducted in parts of Africa and India [16,19]. The mean time to hospital arrival was longer than that recorded in other studies [8,39,32]. The high rate of complications could be explained by the delayed presentation particularly as a result of poor hygiene and the absence of primary health care services in the rural areas. Snakebites has also been reported to be one of the causes of renal failure in Yemen [40].

Similar to a previous study, antivenom was found to be given unnecessarily to 23% of patients without clinical manifestations of envenomation i.e. dry bites [6]. The adverse effects of antivenom were rare and mild [41] but in this study the underestimation of the possible side effects could have been due to their low rate of documentation however, no mortalities were documented as a result of administering the antivenom. Pre-treatment was not used [42]. It was found that most patients presenting at the Saudi Hospital with snakebites were given a dose lower than the recommended in many previous studies [1,43,44]. Most probably the majority of antibiotics used were not indicated [45]. Several other studies showed a lower mortality rate (MR) compared to the overall MR recorded in this study [3,8,12,13,19,27,35]. Due to the limited number of cases and consequently the small number of fatalities, in order to get an accurate statistical measurement we were obligated to divide the patients into only two groups for the detection of any association between the degree of acuity at presentation and the outcome. This selection of three positive findings that it includes the minimum systemic manifestations in addition to the local findings. There was a statically significant association of patients presenting with more than three positive findings and a higher complication rate but not with cases of fatality and other factors such as younger age and high rate of admission. However owing to the relatively small number of deaths recorded in this study, further significant associations with fatality cannot be excluded. Few studies of mortality have been conducted, but in most cases a more specific measure was investigated e.g. collecting data during the whole period for hospitalization for predicting mortality [46] or assessing the severity of snakebites in relation to a specific species [47–49]. In this study the investigation of snakebite severity was thought to be more practical as in most cases the species of snake was not always known to the physicians.

It is important to acknowledge a number of limitations of the study. Firstly, as this was a retrospective study a number of data was missing at the time of analysis and the existence of any laboratory procedural abnormalities could not be excluded. Secondly, as this study was hospital-based a number of milder cases where medical advice was not sought could have been missed, including more severe cases where individuals might have died at home or on the way to the hospital. Thirdly, as the prognostic significance may vary between patients presenting with the same clinical manifestations, the associations need to be validated.

## CONCLUSION

The study has identified that snakebites in the Hajjah governorate of Yemen is an important public health problem that requires further consideration. It was found that in most cases there was a delay in snakebite victims seeking medical advice. The use of the antivenom was either not received within the most effective time and/or was given inappropriately. Acknowledging the presence of more than three clinical signs or laboratory abnormalities on arrival to the hospital could help in anticipating clinically important complications. The development of a detailed protocol for appropriate utilization of antivenom, including increased awareness about the importance of early administration of antivenom is recommended. Prospective cohort studies are required for identifying the possible validated prognostic factors at the time of presentation and species identification.

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