

# Clinical course and outcome of snake envenomation at a hospital in Karachi

Mahmood K, Naqvi I H, Talib A, Salkeen S, Abbasi B, Akhter T, Iftikhar N, Ali A

## ABSTRACT

**Introduction:** Snake envenomation is a frequently reported medical emergency at the Civil Hospital Karachi, Pakistan, thus obviating the need to assess the patterns of the clinical course and outcome of snake envenomation cases.

**Methods:** The demographic characteristics, clinical signs and symptoms, laboratory findings, treatment and outcome of 80 victims of snake bite were recorded. These patients were admitted to the Civil Hospital Karachi between January 2006 and September 2007. The data of all the cases was analysed statistically using the Statistical Package for the Social Sciences version 11.0.

**Results:** The majority of the 80 victims of snake bite were male (80 percent) and 20 percent were female. The mean age of the patients was 33.3 years. The main type of envenomation was vasculotoxic (92.5 percent), and none were neurotoxic or myotoxic. Both local and systemic clinical features of envenomation were present. Bleeding was reported in 43.8 percent of the patients. 71.3 percent of the patients showed coagulopathy of defibrination and the anti-coagulant type. All patients received anti-snake venom. Five (6.3 percent) patients in the study died.

**Conclusion:** The most common type of snake envenomation in this part of the province of Sindh is vasculotoxic due to the high inhabitancy of Viperidae. High morbidity and mortality rates can be reduced significantly through patient education on the precautions that need to be taken by farmers and field workers against snake bite. Early referral to a well-equipped health facility is necessary, as the mortality rate was high among those patients who arrived late.

**Keywords:** activated partial thromboplastin time, anti-snake venom, envenomation, prothrombin time

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## INTRODUCTION

Snake bites are a major cause of injury-related deaths, with an estimated worldwide mortality rate of 30,000 to 110,000 per year.<sup>(1)</sup> There are 3,000 species of snakes in the world and only 300 are venomous. Almost 300,000 to 400,000 venomous bites occur every year.<sup>(2)</sup> In Asia alone, it has been estimated that four million snake bites occur each year, with 50% envenomation resulting in 100,000 deaths annually.<sup>(3)</sup> Snake bites occur all over Pakistan. There are 72 species of snakes that can be found in different parts of the country.<sup>(4)</sup> Every year, 8,000 cases of snake bites occur in the province of Sindh alone, with most of the cases being reported from the Thar district.<sup>(5,6)</sup>

Snake envenomation produces a diverse range of clinical effects, from minimal envenomation such as pain, itching, puncture wounds and mild oedema to highly fatal symptoms such as bleeding, renal failure, hypotension and shock, particularly with viper bites, and sudden flaccid paralysis and respiratory failure in neurotoxic bites.<sup>(7)</sup> Patterns of envenomation depend on the species of snake, which can be broadly categorised into four different families, namely, Colubridae, Elapidae, Viperidae and Hydrophidae, which can cause minimal envenomation, neurotoxicity, vasculotoxicity and myotoxicity, respectively.<sup>(8)</sup> The severity of envenomation is classified as mild (local effects such as swelling, pain, tenderness or confined to the immediate bitten part, no systemic effects, no clinical or laboratory coagulation abnormality), moderate (local effects such as swelling, pain, tenderness/echymoses extending beyond the immediate bitten part, systemic effects like nausea, vomiting, fasciculation, mild hypotension with evidence of coagulopathy but without clinical bleeding), or severe (local effects extending and involving the entire limb along with systemic effects like shock, severe bradycardia, tachypnoea or respiratory failure and marked coagulation abnormalities with bleeding manifestations).<sup>(9)</sup>

The outcomes of envenomation are dependent on many factors, such as the amount of time taken to arrive at a health care facility, the severity of envenomation, the availability of anti-snake venom (ASV) at rural health care centres, as well as impending complications like coagulopathy, disseminated intravascular coagulation

Department of  
Medicine,  
Civil Hospital Karachi  
and Dow University  
of Health Sciences,  
Baba-e-Urdu Road,  
Karachi 7400,  
Sindh,  
Pakistan

Mahmood K, MBBS,  
FCPS, FRCP  
Professor and  
Chairperson

### Medical Unit III

Naqvi IH, MBBS,  
FCPS  
Assistant Professor

Talib A, MBBS,  
FCPS  
Associate Professor

Salkeen S, MBBS,  
FCPS  
Assistant Professor

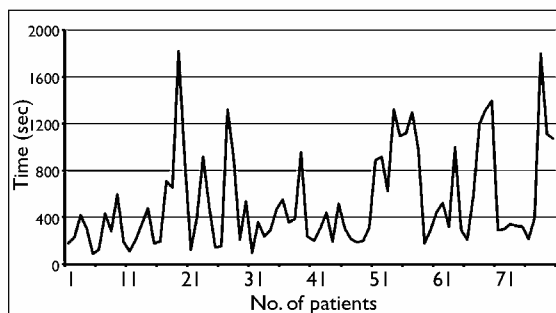
Abbasi B, MBBS,  
FCPS  
Assistant Professor

Akhter T, MBBS,  
FCPS  
Senior Registrar

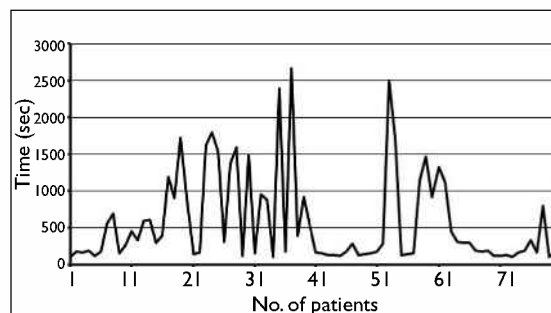
Iftikhar N, MBBS  
House Officer

Ali A, MBBS, MD  
Senior Physician

**Correspondence to:**  
Dr Iftikhar Haider  
Naqvi  
Tel: (92) 21 664 7077  
Fax: (92) 21 664 7077  
Email: driftikharhaider  
@hotmail.com



**Fig. 1** Graphical presentation of prolonged bleeding time in the study.



**Fig. 2** Graphical presentation of prolonged clotting time in the study.

and sepsis. The outcomes of envenomation also depend on the number of doses of ASV administered at the tertiary care centre, the use of blood or blood products such as fresh frozen plasma and surgical intervention, if required.

This study was conducted so as to observe the clinical presentations and outcomes of snake bite cases from different parts of the provinces of Sindh and Baluchistan.

## METHODS

An observational study was conducted by collecting cases of snake bite seen at the Civil Hospital Karachi between January 2006 and September 2007. The Civil Hospital Karachi is a tertiary care, 2,000-bed hospital with 15 units per ward for various medical and other specialties. Approximately 2,000 walk-in and referred patients attend the emergency and outpatient department services, with 10,000 patients admitted into the general medical wards per month. The hospital caters not only to patients from Karachi but also to those from other areas of the province of Sindh and those in the adjoining areas of the province of Baluchistan.

All snake bite patients (irrespective of toxicity) aged 12–60 years who had not received ASV were included in the study. The definition of snake bite and its toxicities for each case were applied using the reference book of toxicology.<sup>(10)</sup> Vasculotoxicity (or a vasculotoxic bite) was defined as severe local symptoms along with a marked vasculotoxic effect, which includes intense local pain, swelling, echymoses, blisters, severe oozing, nausea, vomiting, vasculotoxic effects such as petechial haemorrhage, epistaxis, haematemesis, melena and eventual shock. Neurotoxicity (or a neurotoxic bite) was defined as the existence of mild local symptoms, marked neurotoxic manifestations, including a slight burning pain at the bitten site with triple response, nausea, vomiting, giddiness, lethargy, muscular weakness, spreading paralysis (within 15 minutes to 2 hours), dysphasia, dysphagia, ptosis, external ophthalmoplegia,

slow laboured breathing and respiratory arrest with or without convulsion. Myotoxicity (or a myotoxic bite) was defined as a sharp initial prick (painless later), generalised muscular pain, stiffness (starting in the neck and limb girdle), myoglobinuria as characterised by the brown discolouration of urine and eventual respiratory failure.<sup>(10)</sup>

This study excluded those who had been administered with ASV before arriving at the emergency department of our hospital. This was to ensure that the entire clinical course of envenomation of even the mildest degree was recorded, which would have been missed otherwise. After obtaining informed consent, a detailed history was taken and an examination was performed for each patient. Patients were advised and followed up for two weeks after being discharged. The data was collected through a detailed pro forma which was designed to gather all demographic, clinical and management details about envenomation. The Statistical Package for the Social Sciences version 11.0 (SPSS Inc, Chicago, IL, USA) was utilised for statistical analysis, where standard deviation (SD) was applied for the continuous variables and proportions were applied for the categorical variables.

## RESULTS

In total, there were 80 victims of snake bite reported during the study period. Most of the patients were male (80%), with a 4:1 ratio of male and female. Most of the victims were either farmers or field workers. The mean age of presentation was 33.3 (SD  $\pm$  13.8) years. 38 out of 80 (47.5%) patients, arrived at the hospital within 12 hours of being bitten, whereas 28 (35.0%) patients arrived between 12 and 24 hours later and only 14 (17.5%) patients arrived later than 24 hours after being bitten. The main type of envenomation encountered in this study was vasculotoxic (74 out of 80), while none was myotoxic or neurotoxic, and six were cases of minimal envenomation. The local signs included oedema or swelling (96.3%), pain (100%), a wound with ragged margins (7.5%) and oozing or wound bleeding (7.5%). Haemorrhagic signs at

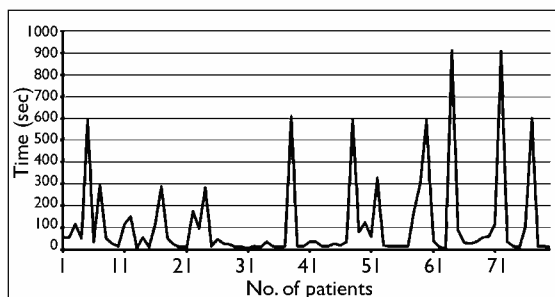


Fig. 3 Graphical presentation of prolonged prothrombin time in the study.

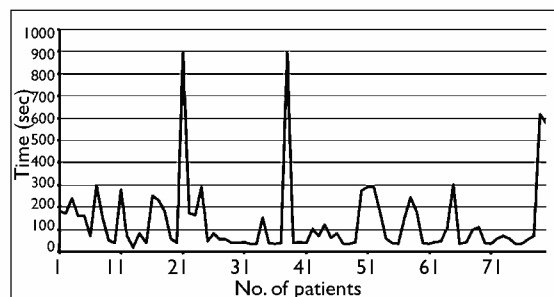


Fig. 4 Graphical presentation of prolonged activated partial thromboplastin time in the study.

the bitten part (ecchymoses, purpura and haemorrhagic bullae) were seen in 13 (16.3%) patients. The general symptoms were anxiety (63.2%), malaise (28.8%), fever (12.5%) and lethargy (15.0%). Among the gastrointestinal symptoms encountered, nausea was the most common (62.5%), followed by vomiting (37.5%) and diarrhoea (5.0%). Bleeding was reported in 35 (43.8%) patients, while 45 (56.3%) patients did not bleed.

The bleeding patterns included gum bleeding (17.5%), haematemesis and melena (12.5%), haematuria (7.5%) and vaginal bleeding (7.5%). Among the coagulation parameters, bleeding time (BT) was prolonged in 23 (28.8%) patients (Fig. 1), with a mean of 534.6 (SD  $\pm$  410.9) seconds. The clotting time (CT) was prolonged in 47 (58.8%) patients (Fig. 2), with a mean of 586.4 (SD  $\pm$  621.4) seconds. The prothrombin time (PT) was increased in 56 (70.0%) patients (Fig. 3), with a mean of 117.9 (SD  $\pm$  195.4) seconds. The activated partial thromboplastin time (APTT) was deranged in 57 (71.3%) patients (Fig. 4), with a mean of 133.5 (SD  $\pm$  167.2) seconds. Platelets were low in 21 (26.3%) patients. 71.3% of the patients showed coagulopathy, with 33.3% having the defibrination type and 66.7% having the anti-coagulation type. The complications observed were acute renal failure (61.3%) which was mostly multifactorial, septicaemia (3.8%), gangrene (2.5%) and compartment syndrome (1.3%).

Polyvalent ASV was administered to all the patients. 23 (28.8%) patients required 50 ml, 30 (37.5%) patients required 100 ml, 19 (23.8%) patients required 200–300 ml and only eight (10.0%) patients received more than 300 ml. Fresh frozen plasma was provided to 44 (55.0%) patients, blood transfusion to two (2.5%), dialysis was performed in two (2.5%) patients and surgical intervention was required for three (3.8%) patients. Five patients died in the study, yielding a death rate of 6.3%, likely due to delayed presentation.

## DISCUSSION

Snake envenomation is a common problem in Pakistan and in the province of Sindh. In this study, there were

more male victims than female ones. As men tend to work in the fields, most bites occur during the day time. The mean age of the patients was 33.3 years. A large number of the patients reported to the hospital after 12–24 hours of the snake bite, and this affected the severity of the outcome of the envenomation. Akbar et al studied 100 victims of snake bite and found that most of their patients with severe toxicity were in the delayed presentation group who arrived at the hospital after 12 hours.<sup>(11)</sup> The delay in arrival at the hospital of more than 12 hours in over 50% of the patients in this study was due to long distances between the rural areas and the hospital (about 60–300 km) in addition to inadequate transport facilities. The general health-seeking behaviour of the public is also riddled with delay tactics as a result of multiple factors including a lack of education, poverty which renders patients unable to afford medical treatment, and a lack of health facilities at their doorstep. The practice of alternative medicine is rampant, especially in small towns and villages, and this is yet another reason for the lengthy delays in arrival at a hospital. All the above factors contributed to delayed arrival in this study.

The main type of envenomation encountered in this study was vasculotoxic (74 out of 80 patients). None of the patients exhibited myotoxic or neurotoxic features, while a few (6 out of 80 patients) showed minimal envenomation. A study by Madaki et al found that 96% of their patients had vasculotoxic bites.<sup>(12)</sup> Another study by Bux et al in southern Sindh (Pirpatho, Mirpur Khas and Nawabshah) found 95% of their patients in the vasculotoxic category and 5% in the neurotoxic category, thus increasing the possibility of the presence of Cobra snakes in that particular terrain (desert).<sup>(13)</sup> Almost exclusive vasculotoxic bites in our study endorse the prevalence of the pit viper (Korali) in our area of study.<sup>(14)</sup> There are other species from the Viperidae family, such as chain vipers (*Daboia russelii*) and saw scaled vipers (*Echis carinatus*), which are found in Sindh as well as in the adjacent parts of India and Iran.<sup>(15)</sup> A recent Iranian study on the same species showed vasculotoxicity in the

**Table I. Characteristics of the deceased patients.**

	Patient no.; time of arrival after snake bite				
	1; 14 hrs	2; 15.5 hrs	3; 27 hrs	4; 9.3 hrs	5; 22 hrs
Pulse (b/m)	118	110	120	110	118
Blood pressure (mm Hg)	70/40	90/70	60/40	110/70	80/50
Temperature (°F)	99	100	101	99.1	100
Respiratory rate (b/m)	28	24	30	22	28
Clinical severity	Severe	Moderate	Severe	Moderate–Severe	Severe
Renal indices					
Urea (mg/dL)	110	93	169	65 (initial), 102 (later)	130
Creatinine (mg/dL)	4.3	2.1	7.1	1.9 (initial), 4.7 (later)	6.9
Coagulation parameters					
Bleeding time (sec)	1,400	1,322	1,823	1,200	1,800
Clotting time (sec)	2,400	1,805	2,673	1,719	2,509
Prothrombin time (sec)	604	591	908	303	612
Activated partial thromboplastin time (sec)	620	303	900	290	580
Platelets (mCL)	20,000	23,000	18,000	21,000	19,000
Complications					
Sepsis	Yes	Yes	Yes	Yes	Yes
Bleeding	Yes	Yes	Yes	Yes	Yes
Acute renal failure	Yes	Yes	Yes	Yes	Yes
Compartment syndrome	No	No	Yes	No	No
Total dose of anti-snake venom (ml)	270	250	300	260	290
Fresh frozen plasma (units)	23	17	26	19	25

form of high coagulopathy and bleeding.<sup>(16)</sup> An earlier Indian study had shown that the Russell viper was the main culprit of mortality.<sup>(17)</sup> Despite the fact that these areas are inhabited by the same species of snake, there is a stark difference in clinical presentations, which suggests geographical variations in the venom composition.<sup>(17)</sup>

Among the clinical features at the bitten extremity, this study showed pain in 100% of the patients, swelling/oedema in 96.3%, a wound with rugged margins in 7.5%, oozing/bleeding from the bitten site in 7.5%, while haemorrhagic signs at the bitten part (echymoses, purpura and haemorrhagic bullae) were observed in 16.3% of patients. The clinical features at the bitten extremity studied by Frangides et al showed oedema in 98.6% of patients, echymoses in 60.5% and pain in 100% of their patients. A high percentage of oedema was observed in the majority of cases in their study as well.<sup>(18)</sup>

The most common general symptom found was anxiety in 31.3% of patients, followed by malaise, fever and lethargy. Among the gastrointestinal symptoms encountered, nausea was the commonest complaint, with 62.5% of patients reporting it, followed by vomiting in 37.5% and diarrhoea in 5.0% of the patients. Frangides et al found nausea in 16%–33% and vomiting in 12%–93% of their patients.<sup>(18)</sup> In terms of bleeding due to vasculotoxicity, oral bleeding was observed to be the commonest (17.5%), followed by upper gastrointestinal,

vaginal and nasal bleeding.

In this study, the coagulation parameters were found to be the most affected, as PT was prolonged in 56 out of the 80 cases, with a mean of 117.9 (SD ± 195.4) seconds. APTT was prolonged in 57 patients, with a mean value of 133.5 (SD ± 167.2) seconds. Two types of coagulopathy were observed in vasculotoxic snake bites: the defibrination and anti-coagulant types.<sup>(19)</sup> The study showed defibrination (consumptive coagulopathy) in 19 patients, where PT and APTT were both deranged along with elevated fibrin degradation products, D-dimer, hypofibrinogenaemia and low platelets. On the other hand, the anti-coagulation type of coagulopathy was found in 38 patients, where PT and APTT were both prolonged without raised levels of fibrin degradation products, with normal or slightly low platelets. The aforementioned two types of coagulopathy are consequent to venom-induced coagulopathy. It is important to differentiate between these two types of coagulopathies due to the clinical features and management of venom induction. The hallmark of defibrination coagulopathy is bleeding, and hence fresh frozen plasma should be provided along with ASV. However, if there is no bleeding in the anti-coagulation type of coagulopathy, only repeated doses of ASV can correct the coagulopathy. Fresh frozen plasma should not be provided if there is no bleeding.<sup>(20)</sup>

Akbar et al found coagulopathy in about 80% of their

patients. However, their study did not mention the type of coagulopathy and bleeding pattern in patients with delayed versus early arrival after the snake bite.<sup>(11)</sup> Santos-Soares et al found coagulopathy in 38 patients in their study, 17 (45%) of which exhibited raised PT and APTT.<sup>(21)</sup> In another study conducted by Jayarama et al, 17 patients exhibited raised PT and APTT.<sup>(22)</sup> Akbar et al showed a mean APTT of about 117.1 (SD  $\pm$  107.6) seconds in the delayed group of snake poisoning patients.<sup>(11)</sup>

The delayed arrival of patients to health facilities and the high values of PT and APTT (clinical coagulopathy) in our study are mostly suggestive of vasculotoxic envenomation. The delayed arrival of patients is a result of the long distances between rural areas and the Civil Hospital Karachi, which can be between 60 and 300 km. The rural areas from which patients were referred to the Civil Hospital Karachi included the coastal belt of Sindh, the province of Baluchistan and the plains of Sindh. The snakes in these rural areas include the Viperidae (Pit viper, Russell viper),<sup>(14,15)</sup> which are vasculotoxic, as evidenced by the coagulation profile. The delayed arrival of patients further contributed to the severe vasculotoxicity. The BT was prolonged in 23 (out of 80) patients, with a mean of 534.6 (SD  $\pm$  410.9) seconds and the CT was prolonged in 47 (out of 80) patients, with a mean value of 586.4 seconds or 9.8 minutes (SD  $\pm$  621.4 seconds). Earlier studies have shown a prolonged CT of more than 20–30 minutes in vasculotoxic bites.<sup>(12,13)</sup> In this study, low platelets were due to defibrination coagulopathy, although venom-induced thrombocytopenia could be another possibility in snake bite emergencies.

Apart from coagulopathy, acute renal failure was among the complications observed in 49 of the 80 patients. The reasons for this were multifactorial, either due to pre-renal azotaemia (caused by vomiting, bleeding or sepsis), or by intrinsic renal failure. Intrinsic renal damage was either due to the venom itself or due to rhabdomyolysis in myotoxic bites and neurological envenomation. Acute renal failure can occur with or without coagulopathy, as shown in a study by Khan.<sup>(23)</sup> In our study, two patients with acute renal failure required dialysis. Other complications included septicaemia (three patients), compartment syndrome (one patient) and gangrene (three patients). Studies exclusively conducted on vasculotoxic bites have reported tissue necrosis, gangrene, acute renal failure, compartment syndrome and digit amputation in lower proportions, which was probably due to earlier arrival of the patients to the hospital and the prompt administration of polyvalent ASV.

Polyvalent ASV prepared by the National Institute of Health, Islamabad, was administered to all 80

victims. Patients with minimal envenomation, such as those simply experiencing pain and itching, were also administered with ASV because venom detection kits were not available locally and there have been experiences where some patients with minimal or no signs of envenomation initially appeared to be symptom-free, but later presented with severe envenomation, even after 12–24 hours. For repeated doses of ASV, the World Health Organization (WHO) criteria were applied, where in vasculotoxic envenomation, after an initial dose of ASV, the incoagulability of blood was assessed clinically by the severity of local swelling and through the CT every six hours, which would determine the next dose of ASV.<sup>(24)</sup> Maintaining the WHO criteria as a standard, 50 ml of ASV was administered to 23 patients, 100 ml to 30 patients, 200–300 ml to 19 patients, and more than 300 ml was administered to eight patients. The high doses of ASV administered in this study, i.e. more than 200 ml, suggest both moderate and severe forms of envenomation. The earlier studies from Sindh and outside the province conducted on the same species also reported the use of high doses of ASV.<sup>(13)</sup>

Four patients showed hypersensitivity reactions to the ASV and were treated with corticosteroids and antihistamines. Other studies also reported similar results.<sup>(11,13)</sup> Madaki et al reported the administration of 20–30 ml of ASV to patients,<sup>(12)</sup> which was proportionally lower than the amount administered in our study. A study by Whitehall et al reported the administration of more than 40 vials in three patients, while 119 patients received ten vials.<sup>(25)</sup>

All patients with clinical bleeding, who had biochemical coagulopathy with or without thrombocytopenia, were managed with ASV, fresh frozen plasma and blood, as per the requirements. The patient was transfused with blood if the haemoglobin was found to be  $< 7$  g/dL, according to the criterion used for blood transfusion.<sup>(2)</sup> Fresh frozen plasma was provided in defibrination coagulopathy and also in those cases in which impending consumptive coagulopathy was present, as evidenced by prolonged PT, APTT and low platelets.<sup>(2)</sup>

Patients without bleeding but had biochemical coagulopathy and thrombocytopenia were managed with repeated doses of ASV, strict monitoring of the coagulation parameters, and fresh frozen plasma only in cases in which impending consumptive coagulopathy was feared. This stable group of patients showed improvement in their coagulation profiles, including thrombocytopenia by ASV, as evidenced by the correction of the initial coagulation parameters.

In our study, fresh frozen plasma was required in 44 of the 80 patients. Blood was administered to two patients. Five patients died, resulting in a mortality rate of 6.3%. The characteristics of the patients who died due to envenomation in this study are shown in Table I. The major cause of death was severe coagulopathy with bleeding or complications such as septicaemia and compartment syndrome. Most of the patients who died arrived at the hospital late. Another factor for mortality in some cases was the late administration of ASV, as it is not effusively available at rural health centres and the storage facilities are either not available or improper.<sup>(26)</sup>

A study from central India by Kalantri et al reported a mortality rate of 10%,<sup>(27)</sup> while another study in southern Sindh reported a mortality rate of 5.1%, but that was mainly due to Cobra bite envenomation.<sup>(13)</sup> The mortality rate depends on the type of envenomation and the arrival time at a health care facility, as Akbar et al reported an 11% mortality rate in their delayed arrival group.<sup>(11)</sup>

In this part of the province of Sindh, the most common type of envenomation is vasculotoxic due to the high prevalence of the Viperidae family of snake. Education on prevention of snake bite should be imparted among farmers and field workers. They should be advised to use long boots and not to walk on their bare feet or disturb snakes in the fields. Early referral to a well-equipped health facility is necessary, as the mortality rate is high among patients who arrive late.

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