

A Study of Cardiac Profile in Patients with Snake Envenomation and Its Complications

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How to cite this paper: Ramakrishna C.D. and Kanattu, P.S. (2017) A Study of Cardiac Profile in Patients with Snake Envenomation and Its Complications. *International Journal of Clinical Medicine*, 8, 167-177.

<https://doi.org/10.4236/ijcm.2017.83017>

Received: January 17, 2017

Accepted: March 28, 2017

Published: March 31, 2017

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Abstract

Background: Snake bite is a common and frequently devastating environmental and occupational disease, especially in rural areas of tropical developing countries. The present study was undertaken to evaluate the effect on cardiac profile in patients with snake envenomation and its complications. **Methods:** A total of 200 patients with snake envenomation were enrolled in this study excluding patients having history of any cardiovascular disease, renal disease, coagulopathy, liver disease, neuromuscular disease and those cases who bitten by non-poisonous snakes. All patients underwent physical examination, laboratory, Electrocardiogram (ECG), X-ray of chest and echocardiogram investigations. **Results:** A total of 200 cases had envenomation having 116 (58%) of male subjects. Most common local signs were edema 187 (93.5%), tenderness 141 (70.5%), skin necrosis 81 (40.5%) and blistering 12 (6%). Severity of local envenomation was graded into mild 66 (33%), moderate 120 (60%) and severe 14 (7%) cases. Systemic manifestations were present in 83 patients of venomous bites. It includes that majorly 53 (26.5%) cases had vomiting, 44 (22%) cases had abdominal pain and 9 (4.5%) cases of hypotension. ECG manifestation showed 27 (13.5%), 6 (3%) and 1 (0.5%) patients had sinus tachycardia, sinus bradycardia and ventricular tachycardia respectively. While, 9 (4.5%) cases had T inversion alone in precordial leads. Mortality (3%) was observed in intracranial bleed, neurotoxicity and capillary leak syndrome. However, cardiovascular involvement was not responsible for mortality in any cases. **Conclusion:** In conclusion, ventricular tachycardia is one of the manifestations of snake envenomation. Moreover, sinus tachycardia is common cardiovascular sign which may not be due to cardiac causes. Mortality results conclude that, cardiovascular involvement could not be responsible for mortality in snake envenomation.

Keywords

Snake Envenomation, Cardiac Complications, Sinus Tachycardia

1. Introduction

Snake bite is one of the major public health problems especially in tropical and subtropical countries. Snake bite is a common medical emergency encountered in the tropics and an estimated 35,000 - 50,000 people die of snake every year in India. Approximately 15% of 3000 species of snakes found worldwide are considered to be dangerous to humans. Among those species 52 poisonous species found in India, majority of bites and consequent mortality is attributable to 5 species viz. *Ophiophagus hannah* (king cobra), *Naja naja* (common cobra), *Daboia russelli* (Russell's viper), *Bungarus caeruleus* (krait) and *Echis carinatae* (saw-scaled viper). In Kerala, around 104 species are known, of which 37 are poisonous [1] [2] [3].

Snake venom is probably the oldest known poison to mankind and has been described in oldest medical books and myths. The snake venom contains many enzymes like digestive hydrolases, hyaluronidase, and activators or inactivators of physiological processes which include L-amino acid oxidase, phosphomono and diesterase, 5'-nucleotidase, DNAase, NAD-Nucleosidase, phospholipase A₂, and peptidases. Also contains non enzymatic proteins and polypeptides. Among non enzymatic proteins, hemorrhagins, neurotoxins and cardiotoxins are important. Hemorrhagins are present mainly in *Echis carinatus*. Haemorrhage, shock and acute renal failure are the main causes of death in cases of elapide bite [4] [5]. Cardiotoxicity is also seen in many cases dying of severe viper bite. This may occur in the form of sudden hypotension, cardiac arrhythmia, myocardial infarction and changes in the electrocardiogram mainly of ST segment and T wave. Many cases of myocardial infarction following snake bite have seen reported [6] [7]. Coronary angiogram showed normal coronaries except in case where segmental contraction of coronaries was present. A case of second degree atrioventricular block has been reported [8]. In addition to this there may be pulmonary edema and alteration in enzymes like serum aspartate (SGOT) and creatine phosphokinase [5].

Mechanism of cardiotoxicity includes direct toxic effect on the myocardium, coagulation abnormalities and vasospasm induced by hemorrhagins or endothelins contained in the venom of some snakes [9]. Causes of hypotension and shock include hypovolemia, vasodilatation, and myocardial dysfunction. Moreover, bradykinin prolongs hypotensive effect by inactivating the peptidyl dipeptidase responsible both for destroying and for converting angiotensin I to angiotensin II. This observation led to the synthesis of angiotensin-converting enzyme inhibitors (ACEI). Bradykinin-potentiating and ACE-inhibiting peptides have also been found in a number of other crotaline venoms [10] [11]. So far, least work has been done in India on complications and cardiotoxicity profile

following poisonous snake bite. Therefore, present study was undertaken to find out the effect on cardiac profile and complications in the victims of snake envenomation.

2. Methods

2.1. Patient Population and Study Design

The prospective study was conducted in 200 patients of snake envenomation. Snake bite victims admitted to Government Medical College, Kottayam, Kerala, India from May 2005 to August 2006 were included in this study. Those patients had definite evidence (sign and symptoms) of snake envenomation were enrolled. While, those patients having history of any cardiovascular disease, renal disease, coagulopathy, liver disease and liver muscular disease were excluded from this study. In addition, those cases who bitten by non-poisonous snakes were also excluded. All recruitments were conducted after obtaining informed written consent who qualifies the selection criteria.

All patients underwent physical examination, routine and specific laboratory investigation pertaining to snake envenomation. Moreover, specific cardiac profile determined by 12 lead Electrocardiogram (ECG), X-ray of chest and echocardiogram in all patients. Severity of bite was classified according to criteria suggested by Ramming with some modification by Saini *et al.* (1984) [12]. The details severity based classification depicted in **Table 1**. The treatment was given as per WHO guidelines. The initial dose of polyspecific antsnake venom was given as 100 cc without any change in dose for adults or children. Secondary dose can be given with 20 to 50 cc at interval of 2 - 6 h. Patients were continuously monitored for the development of any complication and were managed accordingly.

All investigations were conducted in conformity with ethical principles of research and according to guideline of declaration of Helsinki and approved by the ethical review board of the institution.

Table 1. Scoring classification based on severity of sign and symptoms in patients of snake envenomation.

	Local	Systemic	Coagulation
Minimal	Swelling, erythema or ecchymoses confined to site of bite	No coagulation signs or symptoms	No coagulation abnormalities or other important laboratory abnormalities
Moderate	Progress of swelling, erythema or ecchymosis beyond the site of bite	Non life threatening signs and symptoms (Nausea, vomiting, perioral paraesthesia, myokymia & mild hypotension)	Mildly abnormal coagulation profile, clinically significant bleeding and mild abnormalities on other tests
Severe	Rapid swelling, erythema or ecchymosis involving the entire body part	Markedly severe signs and symptoms (hypotension-SBP < 90 mmHg, altered sensorium, tachycardia, tachypnoe and respiratory distress)	Markedly abnormal coagulation profile with evidence of bleeding or threat of spontaneous hemorrhage, (unmeasurable INR, a PTT & fibrinogen and severe thrombocytopenia < 20,000/cmm)

2.2. Statistical Analysis

Patient baseline characteristics and procedural data were presented as frequency and percentages. In case of normal distribution, data presented as mean \pm SD while non-normal distribution data were presented as median (interquartile ranges).

3. Results

3.1. Participant's Basic and Demographic Characteristics

A total of 586 patients with suspected snake bites admitted to Pariyaram Medical College, Kannur, Kerala during study period. Out of these 586 patients, 200 cases had envenomation having 58% of male subjects. The age group most affected was 31 - 50 years (52%). Majority (76.6%) of cases of snake bite came to the hospital within 24 hours of bite while 40% reported within the first 12 hours. Venomous bite occurred in 93% of subject outdoor whereas, 7% patients were victim of indoor bites. Accidental bites occurs to 98.5% patients and rest 1.5% are snake charmers (occupation bites). In addition, site of bite at lower limb (81%) is much more than upper limb (19%). Whereas, no bites were observed over face or other part of body. All baseline characteristics of envenomated patients are depicted in **Table 2**.

Table 2. Baseline characteristics of envenomated patients.

Variable	
Total number of subjects, n	200
Female, n (%)	84 (42%)
Age, median	Median 40 (4 - 60)
Location and type of Bite	
Outdoor bites, n (%)	186 (93%)
Indoor bites, n (%)	14 (7%)
Accidental bites, n (%)	197 (98.5%)
Occupational (snake charmer) bites, n (%)	3 (1.5%)
Site of Bite	
Lower limb, n (%)	162 (81%)
Upper limb, n (%)	38 (19%)
Rest of Body, n (%)	0 (0%)
Type of snakes	
Viper, n (%)	65 (32.5%)
Cobra, n (%)	3 (1.5%)
Krait, n (%)	1 (0.5%)
Unknown, n (%)	131 (65.5%)

3.2. Clinical Manifestations

Local envenomation: signs and severity

Fang mark was present in 107 cases which constituted about 53.5% of venomous bites and 93 patients had no definite fang mark. Most common local sign was edema (93.5%), tenderness (70.5%), skin necrosis (40.5%) and blistering (6%). Severity of local envenomation was assessed by presence and extends of local edema which graded into mild (33%), moderate (60%) and severe (7%) cases.

Systemic manifestation:

Systemic manifestations were present in 83 patients of venomous bites. It includes majorly 53 cases had vomiting, 44 cases had abdominal pain and 9 cases of hypotension. Moreover, one patient suffered with cardiac arrhythmia. The patient presented with a sustained monomorphic ventricular tachycardia (VT) at the rate of 180/minute but did not have hypotension treated with i.v. amiodarone and not require cardioversion. Echocardiogram was normal with left ventricular function. It may be incidental cardiac arrhythmia or complication of snake envenomation but seen only in 0.5% of patients. Details systemic manifestation is depicted in **Table 3**.

Table 3. Clinical course of envenomated patients.

Variable	
Local Signs	
Definite fang mark, n (%)	107 (53.5%)
Undefinite fang mark, n (%)	93 (46.5%)
Edema, n (%)	187 (93.5%)
Tenderness, n (%)	141 (70.5%)
Skin necrosis, n (%)	81 (40.5%)
Blistering, n (%)	12 (6%)
Severity of Envenomation	
Mild, n (%)	66 (33%)
Moderate, n (%)	120 (60%)
Severe, n (%)	14 (7%)
Systemic manifestation	
Vomiting, n (%)	53 (26.5%)
Abdominal Pain, n (%)	44 (22%)
Oliguria/anuria, n (%)	14 (7%)
Hypotension, n (%)	9 (4.5%)
Bleeding manifestation, n (%)	8 (4%)
Neurological symptoms, n (%)	6 (3%)
Presyncope/syncope, n (%)	4 (2%)
Cardiac arrhythmia, n (%)	1 (0.5%)

3.3. Laboratory Investigations

Basic blood investigation were done along with bedside monitoring of clotting time, coagulation parameter like prothrombin time and activated partial thromboplastin time (PTT). Results suggest that, 127 patients have clotting time above the cut off value *i.e.* 20 minutes. Moreover, 104 patients showed cut off time greater than 10 second for PTT. Regarding low platelet count, 15 patients out of 76 patients (19%) had severe thrombocytopenia (<50,000) requiring platelet transfusion. Routine and other specific laboratory investigation were depicted in **Table 4**.

3.4. Electrocardiogram Examinations

ECG manifestation showed 27 cases had sinus tachycardia, 6 patients had sinus bradycardia. While 9 cases had T inversion alone in precordial leads. Detail of changes were observed in the ECG were represented in **Figure 1**.

Table 4. Initial laboratory findings of snake envenomated patients.

Parameters	Cut of Value	Number of patients	
		Normal	Abnormal
Hemoglobin	>13.5 g/dl in males >12 g/dl in females	142	58
Total leukocyte count	<11,000/cmm	140	60
Platelet count	>100,000/cmm	124	76
Blood urea	<40 mg/dl	149	51
Serum creatinine	<1.4 mg/dl	149	51
Clotting time	>20 minutes	73	127
Prothombin time	>15 seconds	74	126
Activated PTT time	>10 seconds	96	104

PTT: Partial thromboplastin time.

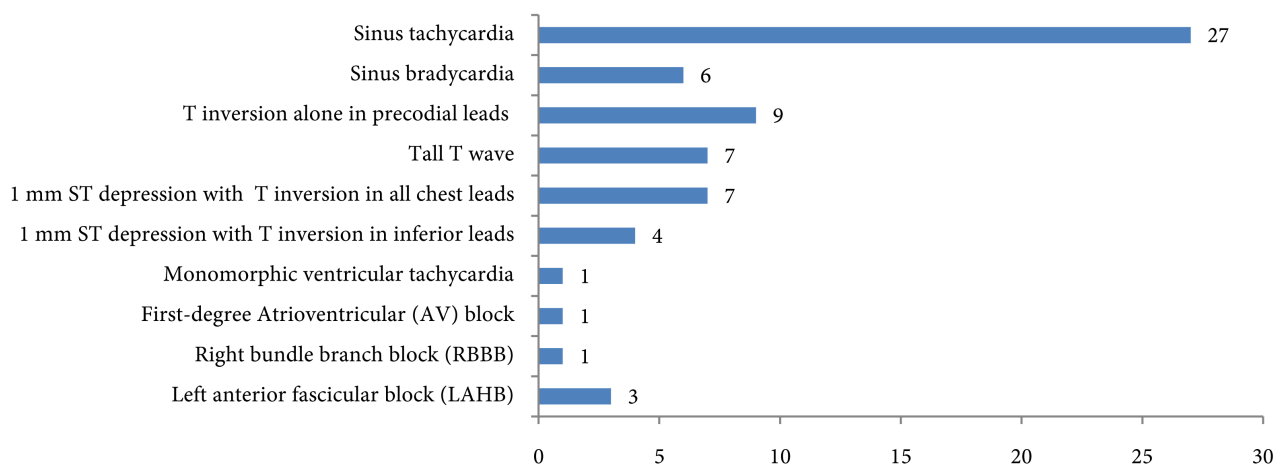


Figure 1. Changes observed during electrocardiogram examination of snake envenomated patients.

3.5. Echocardiogram Investigation

Echocardiographic findings were within normal limits in all patients except 3 patients who had asymmetrical septal hypertrophy as an incidental finding. Patients with ventricular tachycardia had good ventricular function.

3.6. Complications

A total of 79 patients had presented with at least single complication. **Table 5** represents the most common complications were acute renal failure in 51 patients and 39 cases of Intra vascular haemolysis. Compartment syndrome, secondary infection and unexplained hypotension were observed in 4 (2%), 5 (2.5%) and 8 (4%) patients. One case had ventricular tachycardia with no risk for coronary artery disease, which is reverted to normal sinus rhythm with direct current (DC) cardioversion followed by anti snake venom. This patient with ventricular tachycardia had good ventricular function.

3.7. Laboratory Investigations

Mortality

Mortality was observed in 6 cases of total venomous bites patients (**Figure 2**). Mortality was observed in intracranial bleed, neurotoxicity and capillary leak syndrome. Clinically, neurotoxicity was assessed by testing for muscle power and for adequacy of ventilatory function. However, cardiovascular involvement was not responsible for mortality in any cases.

4. Discussion

This study on the profile of cardiovascular complications due to snake bite was carried out with a view to observe the changes in cardiovascular system. A total of 200 subjects with venomous bites were studied. There were 116 males and 84 females with ratio of 1.4:1.

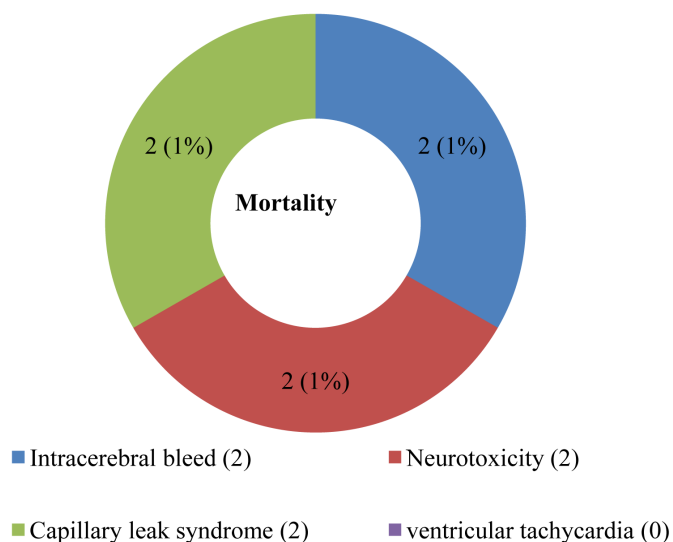


Figure 2. The effect on mortality in snake envenomated patients.

Table 5. Different complications in snake envenomated patients.

Complications	Patients
Acute renal failure	51 (25.5%)
Intra vascular haemolysis	39 (19.5%)
Unexplained hypotension	8 (4%)
Secondary infection	5 (2.5%)
Compartment syndrome	4 (2.0%)
Intra cerebral bleed	4 (2.0%)
Neurotoxicity	2 (1.0%)
Ventricular tachycardia	1 (0.5%)
Capillary leak syndrome	2 (1.0%)

Systemic manifestations were present in 83 patients (41.5% of venomous bites). Most common manifestation noted was vomiting which was present in 26.5% patients. Prolonged clotting time was the commonest manifestation of systemic toxicity in haemotoxic snake bites. In addition, Pain abdomen was present in 22% and 7% patients had renal manifestation in the form of oliguria/anuria, hypotension was noted in 4.5% of venomous bites. Moreover, 2% patients with presyncope/syncope and 4 cases presented in a coma state due to intra cerebral bleed secondary to haemotoxic envenomation. One patient presented with palpitation due to ventricular tachycardia which reverted to normal with DC shock followed by antsnake venom administration. Nayak *et al.* (1990) showed 25% of cardiotoxicity among viperine bite [3]. In our study, cardiac involvement as evidenced by electrocardiographic changes which reverted to normal was present in 31.5% of patients. Out of this only one patient had serious complication like ventricular tachycardia. Most common cardiac manifestation was sinus tachycardia which was present in 27 patients. Even though there are earlier reports of myocardial infarction [7] [13], none of our patients had ST elevation in electrocardiogram suggestive myocardial infarction. Eleven patients had ST depression in either anterior or inferior leads which might be due to coronary artery involvement or myocarditis. None of our patients had chest pain even though ECG showed changes like ST depression. Previous reported cardiotoxicity in 7% cases or elapide bite and none in viper bite case [14]. None of the patients in our study had features of pulmonary edema. Features of peripheral circulatory failure were present in 4% patients who responded to antsnake venom, volume replacement and inotropes.

In the present study, heart rate disturbance was present in 16.5 percent out of which 13.5% had tachycardia and 3% had bradycardia. This finding is almost reverse of the observation of Reid *et al.* (1975) [5]. In patients who had tachycardia without other ECG changes, heart rate returned to normal in 12 - 20 hours. Tachycardia was probably because of shock, fever or acute blood loss. However, bradycardia may occur due to direct depressant action of snake venom over sinoatrial node. Rhythm disturbance in the form of ventricular tachycardia was

seen in 1 patient of our series. Ventricular tachycardia as a presentation of snake envenomation has been reported earlier [15].

Eight patients had unexplained hypotension (4%) and none of the patient had hypertension. These observations are similar to those of previous literature. Hypertension has noted in patients with snake bite, which was probably psychogenic in origin which is a well known factor in producing hypertension. The possible mechanisms responsible for hypotension could be excessive blood loss as bleeding tendency was seen in 63% patients in our study and vasovagal syncope after snake bite or bradykinin induced vasodilation [16]. None of the patient had pulmonary edema. However, previously pulmonary edema was reported in 6.6% of snake envenomated patients by Nayak *et al.* (1990) [3].

Our results reflect, abnormality in ECG was found in 31.5% patients. Most of these appear to be due to sinus tachycardia, which may be related to the stress of illness or being hospitalized, and may make the rate of “abnormality” seem high. However, this incidence differs from the reported observations of Reid who reported an abnormal ECG in 2% cases [5]. Ischaemic changes like ST depression were seen in 5.5% cases which reverted to normal within 3 - 4 days. These ECG changes can be explained by two possibilities; one is that changes in ST-T segment because of thrombosis or sub-intimal haemorrhage in coronary vessels. Snake venom causes disseminated intravascular coagulation which can lead to thrombosis or sub-intimal haemorrhage in coronary arteries and produces ECG changes. Another possibility may be direct toxic effect of venom on heart which may likely give an explanation for sinus bradycardia, arrhythmias and atrioventricular block [17].

In addition, mortality was 3% which is varies from previous literature, as 10% and 1.96% mortality were observed by Nayak *et al.* (1990) and Bhat *et al.* (1974) [3] [18]. All those patients had severe envenomation and late hospitalization. Also, they were in shock, and some may had massive bleeding. Cardiovascular complication was not responsible for mortality in any of the cases.

5. Limitations of the Study

Being a tertiary care center, study may not be real reflection of the original magnitude of the problem in the community. Moreover, majority of the study groups were haemotoxic bites and the number of elapid bites was very small in the study group. However, there were no long term follow up of the patients who showed ECG abnormalities.

6. Conclusion

Overall analysis of results suggests that, cardiac involvement is uncommon in snake envenomation. As occurrence of sinus tachycardia in snake envenomation was most likely due to non-cardiac causes. Mortality results suggest that, cardiovascular involvement may not be responsible for mortality in snake envenomation.

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