

## ORIGINAL RESEARCH

### The study of biochemical (CPK-MB) ,ECG, and Echocardiographic changes in patients of snake bite

Dr.Roopesh Singh Kirar<sup>1</sup>, Dr.Ritesh Yadav<sup>2</sup>

<sup>1</sup>Senior Resident, Department of Medicine, NSCB Medical College, Jabalpur, MP

<sup>2</sup>Assistant Professor, Department of medicine, SRVSMC, Shivpuri, MP

Corresponding Author: DrRiteshYadav, Assistant Professor, Department of Medicine, SRVSMC, Shivpuri, MP

E-mail: Dr.RiteshYadav,[dr.ritesh\\_123@yahoo.co.in](mailto:dr.ritesh_123@yahoo.co.in)

#### ABSTRACT

**Background:**Snake bite is an occupational hazard for farmers and farm laborers in the Indian subcontinent. Every year approximately 15,000 people reportedly died due to snake venom interaction in India alone. However, unreported deaths are estimated to be many times greater than the reported cases in the subcontinent.

**Materials & Methods:**This Cross Sectional Observational Study was carried on sample size of 75 patients of snake bite admitted in Ward/ICU, Department Of Medicine, NSCB Medical College, and Jabalpur on patients of snake bite reporting from all over mahakaushal area of central India from March 2017 to August 2018.

**Results:** CPK-MB analysis shown to have highest raised values in neurotoxic group that is  $32.3\pm 0.9$  IU/L which was higher in cases where local signs were prominent,  $34.0\pm 1.1$  IU/L and in cases without local signs it was lower  $30.7\pm 1.6$  IU/L. CPK-MB values were for vasculotoxic bites was also raised  $27.3\pm 1.2$  IU/L, while for non-poisonous snake bites it was below upper limit,  $21\pm 2.1$  IU/L. A total of 39.2% (n=33) patients shown to have positive ECG findings while rest 60.7% (n=51) shown no abnormality in electrocardiogram. Analysis of 2D-ECHO findings was done for pattern of positive findings and found that most common positive finding was pericardial effusion with 9 (10.71%) patients followed by 6 (7.1%) patients showed diastolic dysfunction, and 5 (5.9%) patients each shown to have systolic dysfunction and RWMA.

**Conclusion:** CPK-MB analysis shown to have highest raised values in neurotoxic group which was higher in cases where local signs were prominent, and in cases without local signs it was lower. Abnormal ECG was significant predictor of mortality in vasculotoxic snake bites. Echocardiography was a significant predictor of mortality in neurotoxic bites.

**Key words:** Snake bite, CPK-MB, ECG, Echocardiography.

#### INTRODUCTION

Snake bite is a common medical emergency in most of the countries especially in tropics where they represent a major health problem. Throughout the world snake bites are estimated to account for 30,000 to 40,000 deaths annually<sup>1</sup>. The largest no. occur in Burma (Russell's viper) & Brazil (Bothrops species, Lance headed viper). In tropical countries where snake bite is a serious problem there are few reliable data. An estimated 15,000-20,000 people die each year from snake bite in India<sup>2</sup>.

Snake bite is an occupational hazard for farmers and farm laborers in the Indian subcontinent. Every year approximately 15,000 people reportedly died due to snake venom interaction in India alone<sup>3</sup>. However, unreported deaths are estimated to be many times greater than the reported cases in the subcontinent. Astonishingly, very little mention has been made in the medical curricula, which may be one of the contributing factors to the high number of fatalities. Statistics show that the majority of victims belong to the group of rural farmers in the productive age, so any loss of life in snake bite may severely affect the economy of victim's family<sup>4</sup>.

The common poisonous snakes found in India are *Echiscarinatus* (saw scaled viper), *Vipera Russell* (Russell's viper) both of which are predominantly haematotoxic, *Najanaja* (Indian cobra), *Bungaruscaeruleus* (Krait) which are predominantly neurotoxic.

There is 2500 to 3000 sp. of snakes prevalent worldwide, about 500 are venomous. Main species in India is king cobra, common cobra, Russell viper, krait, saw scaled viper.

The severity of envenomation following a snake bite depends up on:

- Dose of venom injected which in turn depends upon the mechanical efficiency of bite & species & size of snake.
- Composition & hence potency of venom, depends on species, geographical location, season and age of snake.
- Health, age, size, & specific immunity of human victim.
- Nature & timing of first aid & medical management<sup>2</sup>.

The pathologic effect due to venom may not be noticed until about 6 hours of the snake bite (varying between 1.5 – 72 hr), and it may remain functionally active causing persistent coagulopathy even after three weeks of the bite. Hence, duration of antigenemia is an important determinant for the extent of pathological effect. It has been unequivocally proved by studying the venom level by Enzyme linked immunosorbent assay (ELISA) that effect due to envenomation depend upon the venom hours (i.e. blood venom level  $\times$  time elapsed between bite and institution of treatment) rather than blood level of venom alone. Hence, with the same level of venom features due to envenomation may become progressively severe with passage of time.

Cardiac complications are an important cause of morbidity & mortality among these patients. So this study has been planned to deal with assessment of cardiovascular complication in patients of snake bite.

Various ECG changes have been reported in a large percentage of cases of snake bite (particularly viper and krait) from time to time. A wide variety of cardiac arrhythmia and conduction disturbances occur but their true incidence and etio-pathogenesis is still not known. Possible mechanism for development of arrhythmia is either a toxic effect of snake venom or electrolyte disturbance brought on by focal myocardial damage due cardio toxin. Reported incidence and type of rhythm disturbances have been found different in studies conducted so far, which may be due to different evaluation and management strategies that were followed. Various studies also conducted to evaluate biochemical changes with envenomation, especially cardiac markers CK-MB and troponin.

In this work, we study pattern and prevalence of CVS (CPK-MB, ECG and 2D-ECHO) Morbidity and Mortality associated with snake bite.

## **MATERIAL AND METHODS**

This Cross Sectional Observational Study was carried on sample size of 75 patients of snake bite admitted in Ward/ICU, Department Of Medicine, NSCB Medical College, and Jabalpur on

patients of snake bite reporting from all over mahakaushal area of central India from March 2017 to August 2018.

**Inclusion criteria were:**

1. Patients giving the history of snake bite (Poisonous, Non Poisonous).
2. Proved case of snake bite on clinical grounds i.e. Bite mark, local changes e.g. signs of local inflammation, appearance of bullae, Tingling & numbness over tongue, mouth scalp, purpuric rashes & necrosis as well as systemic manifestation as psychological trauma, flaccid paralysis etc.

**Exclusion criteria were:**

1. Patients giving history of bites other than snake.
2. Patients who are giving history of any illness-
  - a. Congenital heart disease.
  - b. Valvular heart disease.
  - c. Ischemic heart disease.
  - d. All cases of arrhythmias and conduction defects (ECG proved)

Cases of bite other than snake were excluded by careful history, local examination for bite mark & systemic examination.

All the routine investigations aimed to evaluate the organ damage especially cardiovascular system were done and included with Electrocardiography, Echocardiography and Cardiac enzyme (CPK-MB).

**OBSERVATION AND RESULTS**

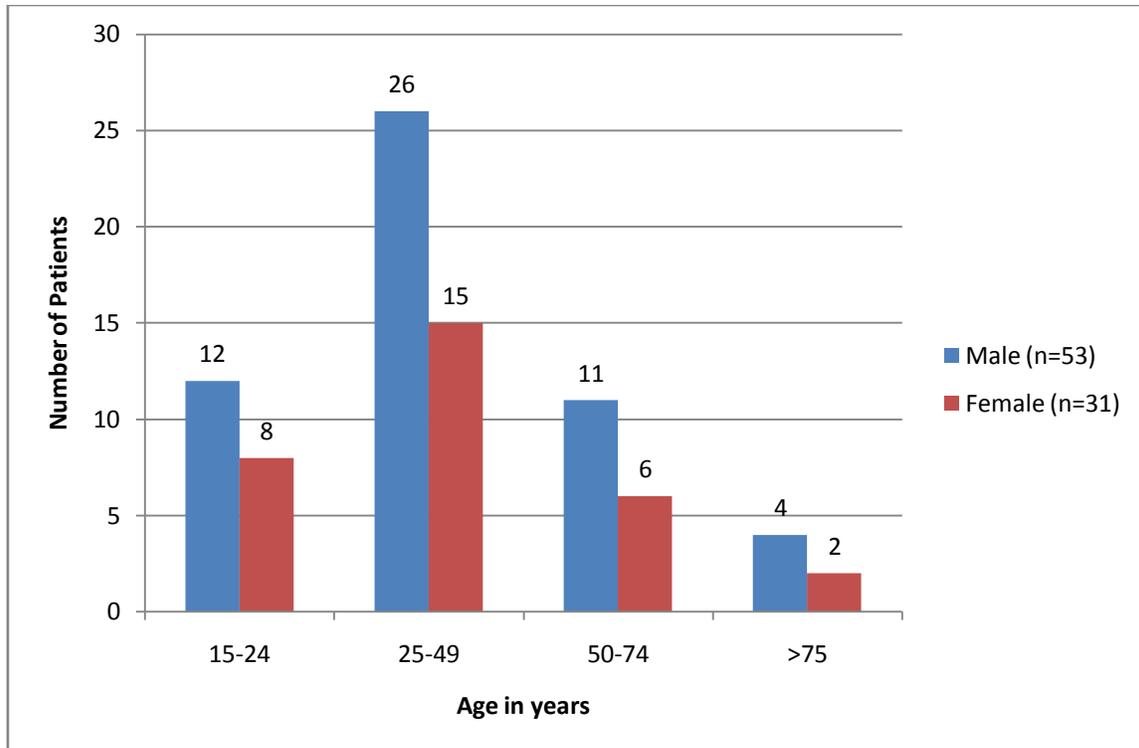
**Table 1:** Showing distribution of patients into age groups and sex.

Age Group (in years)	Male	Female
15-24	12 (14.29%)	8 (9.52%)
25-49	26 (30.95%)	15 (17.86%)
50-74	11 (13.1%)	6 (7.14%)
>75	4 (4.76%)	2 (2.38%)
<b>Total</b>	<b>53 (63.1%)</b>	<b>31 (36.9%)</b>

On demographic analysis, study population of 84 patients of snake bite was consisted of 63.1% males (n=53) and 36.9% females (n=31) with male preponderance.

Most common victims of snake bites were young adult in the age group of 25-49 years with 48.81% (n=41) patients in this age group followed by 15-24 years with 23.81% (n=20), 50-74 with 20.24% (n=17) patients and 7.14% (n=6) patients were more than 75 years of age.

Statistical analysis with Chi-square does not reveal any significant trend in distribution with  $p > 0.05$  ( $p = 0.7238$ ).



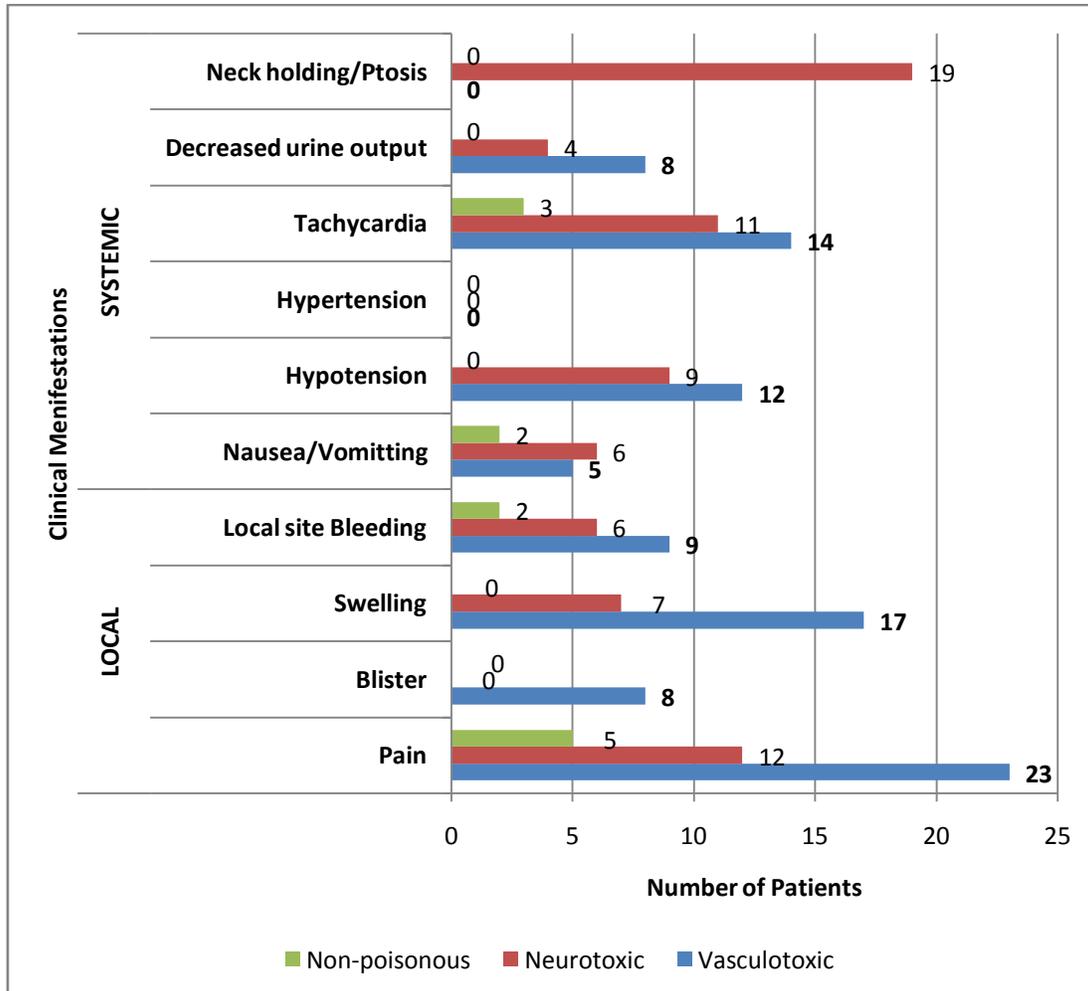
**Graph 1:** Showing distribution of patients into age groups and sex.

**Table 2:** Distribution of patients according to clinical presentation (Local and systemic signs) among different types of bites.

Clinical Feature		Vasculotoxic		Neurotoxic		Non-poisonous	
		No.	%	No.	%	No.	%
LOCAL	Pain	23	27.38	12	14.29	5	5.95
	Blister	8	9.52	0	0.00	0	0.00
	Swelling	17	20.24	7	8.33	0	0.00
	Local site Bleeding	9	10.71	6	7.14	2	2.38
SYSTEMIC	Nausea/Vomitting	5	5.95	6	7.14	2	2.38
	Hypotension	12	14.29	9	10.71	0	0.00
	Hypertension	0	0.00	0	0.00	0	0.00
	Tachycardia	14	16.67	11	13.10	3	3.57
	Decreased urine output	8	9.52	4	4.76	0	0.00
	Neck holding/Ptosis	0	0.0	19	22.62	0	0.00

Snake bites with vasculotoxic poisons shown to have much of the local symptoms. Pain was the most common symptom in all three categories, with 27.38% in vasculotoxic bites, 14.29% with neurotoxic bites while only 5.95% with non-poisonous bite. Pain was followed by swelling, local site bleeding and blister formation. The blister formation only occurred with vasculotoxic bites.

Most common systemic manifestation in a vasculotoxic bite was tachycardia (16.67%) and Hypotension (14.29%) followed by decreased urine output and nausea/vomiting. While most common systemic manifestation in neurotoxic bite was difficulty in neck holding and ptosis (22.62%).



**Graph 2:** Distribution of patients according to clinical presentation (Local and systemic signs) among different types of bites.

**Table 3:** Showing means values of CPK-MB in different types of bites.

Type of bite	CPK-MB (Mean±SEM, Normal Value 0-25 IU/l)	
Vasculotoxic	27.3±1.2	
Neurotoxic	With Local signs	34.0±1.1
	Without local signs	30.7±1.6
Non-poisonous	21±2.1	

CPK-MB analysis shown to have highest raised values in neurotoxic group that is 32.3±0.9 IU/L which was higher in cases where local signs were prominent, 34.0±1.1 IU/L and in cases without local signs it was lower 30.7±1.6 IU/L. CPK-MB values were for vasculotoxic bites was also

raised  $27.3 \pm 1.2$  IU/L, while for non-poisonous snake bites it was below upper limit,  $21 \pm 2.1$  IU/L.

There was a significant ( $p < 0.01$ ) difference in CPK-MB values on intergroup analysis for variance (ANOVA) in all three groups. In neurotoxic snake bite group CPK-MB significantly ( $p < 0.05$ ) higher in patients with local sign than without local signs

**Table 4:** Showing pattern of ECG findings and distribution of patients according to ECG pattern.

ECG changes	Number of patients	Percentage (%)
Sinus tachycardia	15	17.8
Sinus bradycardia	8	9.5
Sinus arrhythmia	2	2.3
AV block	3	3.5
ST-T changes	5	5.9
Normal	51	60.7
<b>Total</b>	<b>84</b>	<b>100</b>

A total of 39.2% (n=33) patients shown to have positive ECG findings while rest 60.7% (n=51) shown no abnormality in electrocardiogram.

The most common abnormality was sinus tachycardia, presented in 17.8% (n=15) patients followed by sinus bradycardia 9.5% (n=8), ST-T changes in 5.9% (n=5), AV block in 3.5% (n=3) and sinus arrhythmia in 2.3% (n=2).

**Table 5:** Showing pattern of 2D ECHO findings in Poisonous and Non-poisonous bites.

2D ECHO Findings	NO OF CASES	PERCENTAGE %
Systolic dysfunction (EF<40)	5	5.9
Diastolic dysfunction	6	7.1
RWMA	5	5.9
Pericardial Effusion	9	10.71
Normal	59	70.2
<b>Total</b>	<b>84</b>	<b>100</b>

Analysis of 2D-ECHO findings was done for pattern of positive findings and found that most common positive finding was pericardial effusion with **9 (10.71%)** patients followed by **6 (7.1%)** patients showed diastolic dysfunction, and **5 (5.9%)** patients each shown to have systolic dysfunction and RWMA.

## DISCUSSION

Snake bite is still a major health problem in tropical countries, which affects the most productive group of human being leading to adverse effect on working man power. Seeing the magnitude of problem of snake bite as a whole and the least and inconsistent available knowledge regarding the ECG, Echocardiographic and biochemical (CPK-MB) changes in patients of snake bite, the present study was conducted in 84 patients of snake bite to understand fully the intricacies of the cardiac profile and to render help in the management of the problem arising out of them.

In the present study, Most common victims of snake bites were young adult in the age group of 25-49 years with 48.81% (n=41) patients in this age group followed by 15-24 years with 23.81% (n=20) which makes the majority of patients (72.62%) were found in the age group of 15-50

years. Our this observation is corroborated by an incidence of nearly 80% of the victims being in 11-50 years age group admitted in Safdarjang hospital, new Delhi during 1970-74{*Banerjee,1978*}, while **Sawani et al. 1974** reported 71% of patients of this age group. The maximum incidence of snake bite was found in the fourth decade (26%); this observation is in agreement with that of **Tambe et al. 1975**<sup>6</sup>.

Out of the 84 patients taken in the study, 63.1% were males and 36.9% were females. Male predominance was also reported by other authors {**66.1% by Sawani et al 1974, 70% by Bhat 1974, 80% by Tambe et al 1974, 76% by Bhargava et al 1976 & 75% by Banerjee and Siddiqui 1976**}. The observation that largest majority of the patients are the male and in the age group of 11-50 years, suggested that bite predominantly affects the most active section of the population and during outdoor activities rather than in house hold environment<sup>7</sup>.

Fear, anxiety, fright were present in most of cases. Local pain after snake bite appeared within 5-10 minutes. In cases of Cobras bite patients were also complaining of burning sensation of the bite site. Local swelling was present in 28.57% of cases which was significantly higher in vasculotoxic bites, while 80% as reported by **Bhat 1974**. Increased vascular permeability was responsible for local swelling. After hospitalization increase in extent of swelling was also observed which was attributed to proteases, phospholipases, membrane damaging polypeptide toxins, hyaluronidase and endogenous autotoxins like histamine, 5-hydroxytryptamine and kinins released by venom of snake. Blisters developed around the bite site in 9.52% vasculotoxic cases varying from size of few millimeters to few cms in diameter<sup>8</sup>.

Hemorrhagic manifestation was the most important clinical manifestation of the viperine snake bite. These manifestations in viper bite are the results of a toxic vascular damage combined with defibrination syndrome. The predominant coagulation defect seen are hypofibrinogenemia with secondary depletion of plasma clotting factors. Pathological effect of venom may not be noticed until about 6 hrs of bite (varying between 1.5-72 hrs) {**Dutta and Vijeth 1995**}. In our study, all cases had hemorrhagic manifestation with in 72 hrs<sup>9</sup>.

In the present study 17.85% of all symptomatic cases showed hemorrhagic manifestation. **sarangi et al. 1977 and Banerjee 1978** observed the incidence to be 83.3% and 37-70% respectively. While **Bhat 1974 and Saini et al. 1984a** reported 65% and 47.8% cases of hemorrhagic manifestation among poisonous snake bite<sup>10</sup>.

Oliguria developed in 12 (14.28%) cases by the time of hospitalization. In that case, hypotension was observed which along with disseminated intravascular coagulation and a direct nephrotoxic action of venom was regarded to be the cause of acute renal failure. Acute renal failure was managed by fluid restriction, frusemide, and dopamine (2-5microgram /kg/min) perfusion drip and the patient recovered fully. Pathological finding in the kidney including acute tubular necrosis, bilateral diffuse cortical necrosis, proliferative glomerulonephritis and hemorrhagic interstitial nephritis have been reported in patients who have had acute renal failure following snake bite {**Efrati and Relf,1953; Amorim and Mello,1954; Marsden and Reid, 1961; Varaguman and Panabokke, 1970; Sant and Purandare,1972**}<sup>11</sup>.

Neurologic manifestations were present in 22.62% of cases in our study. Incidence of neuroparalytic manifestations was observed between 6 to 10.2% by **Bhat 1974, Sarangi et al. 1977, Saini et al. 1984**, while **Banerjee 1978** reported 45%. These manifestations were caused by cobras and kraits.

The symptoms and signs of neuroparalytic envenomation appeared early and nearly all the patients were hospitalized with in 12 hrs of bite. neuroparalytic envenomation was manifested by gradual progression of signs and symptoms leading to coma<sup>12</sup>.

Paralysis was first detected as ptosis and external ophthalmoplegia, as ocular muscles are most sensitive to neuromuscular blockade. Later paralysis of facial muscles, palate, jaw, tongue, vocal cords and muscles of deglutition were observed. Respiratory paralysis was observed before limb paralysis, and even in a state of generalized flaccid paralysis, slight movement of digits was possible<sup>13</sup>.

CPK-MB analysis shown to have highest raised values in neurotoxic group that is  $32.3 \pm 0.9$  IU/L which was higher in cases where local signs were prominent,  $34.0 \pm 1.1$  IU/L and+ in cases without local signs it was lower  $30.7 \pm 1.6$  IU/L. CPK-MB values were for vasculotoxic bites was also raised  $27.3 \pm 1.2$  IU/L, while for non-poisonous snake bites it was below upper limit,  $21 \pm 2.1$  IU/L. There was a significant ( $p < 0.01$ ) difference in CPK-MB values on intergroup analysis for variance (ANOVA) in all three groups. In neurotoxic snake bite group CPK-MB significantly ( $p < 0.05$ ) higher in patients with local sign than without local signs. In a case series by **Kumar et al (2012)** AST was elevated in 28% and CPK was elevated in 48% of patients. Cardiac Troponin I assay was found to be positive in high titers and CPK-MB was raised significantly by **Chakrabarti et al (2015)**. Creatinine kinase was 831 U/L several hours later with a positive MB-fraction<sup>14</sup>.

Among the 84 patients, the significant ECG abnormalities were found in 39.1%, while 65% had normal rate and rhythm. Of the 39.1%, 9.5% had Sinus Bradycardia, 17.8% had Sinus Tachycardia, Sinus arrhythmia in 2.3% and 3.5% had Heart block. T wave inversion in precordial leads was present in 5.9%. The ECG changes were transient and recovered after treatment of snake bite. Ventricular ectopics and Bundle branch blocks were not found in our study (Pahlajani and Hafeez). In study by **Nayak et al** electrocardiographic changes were sinus tachycardia, sinus arrhythmia (6.6%), sinus bradycardia (10%), tall T-wave in V2 (3.3%), nonspecific ST-T changes (16.7%) and atrioventricular block (3.3%).<sup>4</sup> In a study by **Anitha et al (2017)** sinus tachycardia was present in 38%, Sinus bradycardia in 10%, heart block in 2% Tall-T in 4% and sinus arrhythmia was not present in any of the patients<sup>15</sup>.

A total of **25 (29.7%)** patients showed positive 2D-ECHO findings, out of which **23 (27.4%)** patients were in poisonous bites while rest **02 (2.3%)** patients were in the no poisonous snake bite group. Analysis of 2D-ECHO findings was done for pattern of positive findings and found that most common positive finding was pericardial effusion with **9 (10.71%)** patients followed by **6 (7.1%)** patients showed diastolic dysfunction, and **5 (5.9%) patients each** shown to have systolic dysfunction and RWMA<sup>16</sup>.

Baseline screening 2-dimensional echocardiography performed in view of cardiogenic shock revealed normal Left Ventricular End Diastolic Dimension (LVEDD, 43 mm); increased Inter Ventricular Septal thickness in Diastole (IVSD, 13 mm); severe left ventricular global hypokinesia with LVEF of 22% using biplane modified Simpsons method and no evidence of valvular abnormalities or pulmonary hypertension. Two dimensional echocardiogram, was normal in a report by **Silva et al (2012)**<sup>17-18</sup>.

## CONCLUSIONS

The most common local clinical abnormality was pain and systemic was tachycardia and hypotension, and these findings were significantly higher in poisonous snake bite. CPK-MB analysis shown to have highest raised values in neurotoxic group which was higher in cases where local signs were prominent, and in cases without local signs it was lower. CPK-MB values were for vasculotoxic bites were also raised, while for non-poisonous snake bites it was normal. Most of the patients with poisonous snake bite had sinus tachycardia on ECG whereas

the maximum number of patients with non poisonous snake bite had normal sinus rhythm. Abnormal ECG was significant predictor of mortality in vasculotoxic snake bites. Echocardiography was normal in all patients of non poisonous snake bite while various echocardiographic changes were observed in large number of patients with poisonous snake bite. Echocardiography was a significant predictor of mortality in neurotoxic bites. Out of them maximum number of patients had pericardial effusion.

## REFERENCES

1. Sanford JP, snake bite, in Cecile text book of medicine. Vol.2, 20<sup>th</sup>edi. WB Saunders, London, 1996: 1951-1953.
2. Warrell DA, Animal toxins. In Mansons tropical disease. Ed. Cook G, 20<sup>th</sup> Ed., WB Saunders London , 1996a; 468-515.
3. Agrawal PN, Aggarwal AN et al. Management of respiratory failure in severe neuromuscular snake envenomation. *Neurol. India*, 2001, 49, 25-8.
4. Nayak KC, Jain AK, Sharda DP, Mishra SN; Profile of cardiac complication of snake bite. *Indian Heart Journal*, may- june 1990,43, 185-188.
5. Angaji S, Houshmandi A, ZareMirakabadi A. Acute Effects of the Iranian Snake (NajaNajaOxiana) Venom on Heart. *Biomacromolecular Journal*, 2016; 2(2): 97-101
6. Asad MHHB, Murtaza G, Ubaid M et al. Najanajakarachiensis Envenomation: Biochemical Parameters for Cardiac, Liver, and Renal Damage along with Their Neutralization by Medicinal Plants. *BioMed Research International Biomed Res Int*. 2014; 2014:970540.
7. World Health Organization: Regional Office for South-East Asia. Management of snake bites in South East Asia. The Clinical Management of Snake Bites in the Southeast Region Asia. 2010, [Cited on 27.07.2018]
8. Banerjee RN, Siddiqui ZA. Therapeutic advance in the treatment of snake venom poisoning. *Proc. 5th international symposium on Animal plant and Microbial Toxins, Toxicology*; 1976.
9. Saini RK, Sharma S, Singh S, Pathania NS. Snake bite poisoning: A preliminary report. *JAPI* 1984; 32:195-197.
10. Sarangi A, Janal I, Sahoo H, Dass JP. A profile of snake bite in references to hematological, renal , neurological and electrocardiographic abnormalities. *JAPI* 1977;25:555-60
11. Efrati P and Reid L. Clinical and pathological observation on 65 cases of viper bite in Israel. *Am. J. Trop. Med. Hyg* .1953; 2:1085-1108.
12. Amorim MF, Mello RF. Intermediate nephron nephrosis from snake poisoning in man; histopathologic study. *Am. J. Pathol*. 1954; 30:479–499.
13. Marsden ATH, Reid HA. Pathology of Sea-snake Poisoning. *Br Med J*. 1961 May 6; 1(5235): 1290–1293.
14. Varagunam T, Panabokke RG. Bilateral cortical necrosis of the kidneys following snakebite. *Postgrad Med J*. 1970 Jul; 46(537): 449–451.
15. Sant SM, Purandare NM. Autopsy study of cases of snake bite with special reference to the renal lesions. *J Postgrad Med*. 1972 Oct; 18(4):181-8.
16. Sokolovsky M, Structure- function relationship of endothelins, sarafotoxins and their receptor subtype. *J. Neurochem* 1992; 59:809-21.

17. Reid HA: Venomous bite and sting. FLBS and Bailliers Tindal Publication, London. 18th Edi. 1982: 546.
18. Wu WG. Cobra cardiotoxin and phospholipase A2 as GAG binding toxins: on the path from structure to cardiotoxicity and inflammation. Trends Cardiovasc Med 1998; 8:270-8.