"CLINICAL AND COAGULATION PROFILE IN PATIENTS WITH SNAKE BITES IN A TERTIARY CARE HOSPITAL"

By

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Dr. SAGAR S. BIRADAR

LIST OF ABBREVIATIONS

ADR .....Adverse drug reaction

ARF.....Acute renal failure

ASV.....Antisnake venom

AV block.....Atrioventricular block

BT .....Bleeding time

CBC.....Complete blood count

CPK.....Creatinine phosphokinase

CPM .....Chlorpheniramine maleate

CSF .....Cerebrospinal fluid

CSL .....Common Wealth Serum Laboratories

CT .....Clotting time

DIC.....Disseminated intravascular coagulation

DLC.....Differential leucocyte count

ECG.....Electrocardiograph

ELISA .....Enzyme linked immunosrobent assay

F .....Female

H.....Haemotoxic

Hb.....Hemoglobin

HC .....Hydrocortisone

I/O .....Indoor / Outdoor

ICH.....Intracranial hemorrhage

L .....Lower

LFT .....Liver function test

M .....Male

Mdl.....Middle

Mi.....Mild

Mo .....Moderate

N.....Normal

Neu.....Neurotoxic

NV.....Non-venomous

PT.....Prothrombin time

S .....Severe

SES.....Socioeconomic status

SR.....Skin rash

TH .....Treatment from traditional healers

TLC .....Total leucocyte count

U.....Upper

V.....Venomous

ABSTRACT

CLINICAL AND COAGULATION PROFILE IN PATIENTS WITH SNAKE BITES IN A TERTIARY CARE HOSPITAL

OBJECTIVE OF THE STUDY: To study the different clinical manifestations profile and coagulation following snakebite.

MATERIALS AND METHOD

1. SOURCE OF DATA:

The information for the study was collected from snake bite patients admitted to BLDEU'S Shri B.M Patil Medical college Hospital and Research Centre, Vijayapur between December 2014 to March 2016.

Results: Totally 36 cases of snakebite admitted in BLDEU'S Shri B.M Patil Medical college Hospital and Research Centre, Vijayapur between December 2014 to March 2016 were studied. Males 23 (63.9%) were affected more than females 13 (36.1%) in the ratio of approximately 2:1. Most common age group is 20-39 years. Snakebite is a common health hazard in rural areas 24(66.7%). Agricultural labourers are the major sufferers with majority of bites occurring outdoor 30(83. 3%) and occurring over limbs, out of which 22 (61.1%) were lower limbs. Most bites occur in between 12 Noon to 6 PM(36.1%)patients. Out of 36 patients, 24 (66.7%) were poisonous snakebites, 12(33.3%) were non-poisonous snakebites. Among 24 (66,7%) poisonous bites, 9(25.0%) had neurotoxic manifestations and 15 (41.7%) had hemotoxic manifestations.

In neurotoxic venom poisoning, ptosis 9 (25.0%) was the most common and earliest feature followed by ophthalmoplegia 5 (13.9%), palatal and pharyngeal palsy 2 (5.6%), respiratory paralysis 4 (11.1%).

In hemotoxic poisoning, bleeding at the bite site 15 (41.7%) was the commonest manifestation followed by hematuria 6(16.7%), gum bleeding 6 (16.7%), ecchymosis 1 (2.8%).

Among complications of snakebite, acute renal failure 8 (22.2%) was the most common followed by respiratory paralysis 4 (11.1%), shock 2 (5.6%) and gangrene 1 (2.8%).

Average dose of Anti snake venom required in patients was 4 to 48 vials. Duration of ASV administration ranged from 1 hours to 10 days.

Adverse reactions to ASV were noted in 9 (25%) patients. Amongst them skin rashes 6 (16.7%) is most common followed by hypotension 3 (8.3%).

Total 4 patients died among 36 total patients, 3 deaths were due to acute renal failure,1 was due to respiratory paralysis.

Conclusion: Snakebite is one of the common hazards especially in rural setup as agriculture being the main occupation. Males are at more risk of bite than females due to their outdoor activity peak incidence of snakebite is observed between may to October as it is favouring climate for snakes. Snake bite can present with various manifestations at bite sites, neurotoxicity, hematotoxicity. Complication like acute kidney injury, respiratory failure, shock And lack of heath education, patients knowledge regarding snakebite and its complications, leading to delayed presentation to the hospital.

Hence early hospitalization and timely ASV administration were the corner stones in the treatment of snakebite.

Key words: Hemotoxic; Neurotoxic; Anti-snake venom.

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INTRODUCTION

Snake bite is the condition resulting from the bite of a venomous snake and characterized by variable symptoms (as pain and swelling at the bite site, blurred vision, difficulty in breathing, or internal bleeding).

Snakebite is a common medical emergency and an occupational hazard in most parts of India.

The mortality due to snakebite in India is around 1,300 to 50,000 per annum[1], which is much higher

The factors like favorable climate, rural predominance of the population and farming practiced in India are the major contributing factor for the snake bite. Hence India is also known as land of Exotic Snakebites.

Most parts of Karnataka also acts as a natural habitat for majority of snakes like cobra, viper, rat snakes.

Many species are mainly nocturnal (night hunters) e.g. kraits, but other species are mainly diurnal. People must be specially vigilant about snake-bites after rains, during flooding, at harvest time and at night and to be taken necessary precaution.

Most often snake bites are reported due to human interaction with the habitat of the snakes.

In India, there are about 216 species of snakes of which about 52 are venomous and of these only 5 varieties of snakes are commonly encountered as the cause of snakebite poisoning. They are,

1. Russell's viper - Doboia ruselli

2. Cobras - (Common cobra)- Naja Naja

3. Krait - Bungarus Caeruleus

Saw scaled viper - Echis Curinatus and Pit viper.

Approximately 2 lakh people are bitten by poisonous snakes in India annually, out of them about 20,000 die[2]. The annual mortality from snake bites in India is between 35000 to 50000. Annual snake bite incidence is about 66-163 per 100000 population. Morbidity is about 1.4 to 68 per lakhs and mortality is 1.1 to 2.4 per lakh population and case fatality rate is 1.7 to 20%[3].

There are four medically important venomous land snakes in India, the Indian Krait (Bangarus Coeruleus), the common Cobra (Naja Naja), the saw scaled viper (Echis Carinatus) and Russel's viper (Viper Russelli)[4]. The distribution of the snakes differs depending on the herpato fauna existing in any particular region and climatic conditions like temperature and rainfall. The pattern of bites also depends on occupation, recreational habits, clothing and season. Most of the snake bites occur in fields, usually during rainy season. Snake bites can be prevented to a certain extent by educating people working in fields to use protective gears like gumboots and gloves.

There are many causes attributed to high snake bite mortality, lack of adequate training and knowledge of doctors in rational use of anti snake venom is very important. Snake bite is completely treatable if treated in time. Immediate steps should be taken to shift the victim to the hospital as early as possible. Awareness and educating people regarding importance of early treatment following bite and avoiding of traditional methods of healing is necessary.

All cases of doubtful snake bites should be admitted in hospitals to watch the toxicity for proper treatment. Currently intensive work is being done on the pharmacological, pathological, toxicological and immunological aspects of snake venoms to give a better break to the snake bite victim, which has resulted in production of polyvalent and monovalent antisnake venoms though the latter is not yet freely available in India.

Snake bite is a major public health problem throughout the world. Snake poison is oldest known poison to mankind. Most of the Indian population resides in rural places and their main occupation is agriculture. The incidence of snake bite and scorpion sting is due to climate which favors large population of snakes.

The incidence of snake bite in Bijapur and its surroundings is high. Hence, this study is undertaken to study the snake bite, clinical presentation with special emphasis on complications and outcome.

AIMS AND OBJECTIVES

- To study the different clinical manifestation and coagulation profile following snakebite.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Some topics in medicine are as controversial or as influenced by tradition as the management of bites and stings from venomous[3] creatures. Because the incidence of serious bites and stings is relatively low in developing nations, may be due improper collection and maintenance of data, there remains a paucity of relevant clinical research and literature, and the therapeutic decision making is often based on anecdotal information. Furthermore, the responses of different species to various toxins make it difficult to extrapolate data from animal studies to clinical application.

The earliest reference[4] to Indian snakes available might be credited to **Dr. Patrick Rusell**, 1876, who may rightly be called "The father of Indian ophiology". The predict for distinguishing the venomous from the non-venomous snakes goes to him. It was he who focussed attention on Viper, viperal Russelli, which was appropriately named after him.

It is very difficult to find out exactly the incidence of snake bite in india and the number of people who die due to their bites. Most of the available data are based on hospital statistics with constitute a very small percentage of case of snake bite, because these cases still being treated by traditional healer rather than hospitals.

Studies of coagulation profile following Viper Bite conducted in Orissa by **Mohapatra** in 1992[5], along with clinical manifestations. They have found out that once the patient blood becomes defibrinated and in-coagulable, the activity of the haemorrhagins which damages the vascular endothelium and platelet abnormalities lead to haemorrhagic manifestations. However DIC was the principal coagulation

disorder in most cases (93%). Most of their patients presented with bleeding from one or more sites.

Exensive studies[6] about viper bites and its clinical features along with coagulation profile associated with it was done by **Bhat RN** in 1974. He found out that although coagulation remained defective, bleeding once it stopped, did not recur in patients who were treated without ASV, but were given blood transfusion. In this study 65% patients presented with haemorrhages. This was only next to the number of patients presented with local swelling (80%).

Joseph fayrer (Indian medical service) (1873):

"The destruction of life in India by snake-bite is so great, that, it probably destroys overs 20,000 human beings annually" (also affects domestic animals)

We have come a long way since 1873 but still scenario has not changed much due to many reasons in India.

In the study done by **Bijayeeni Mohapatra**[7] et al. conducted a nationally representative study of 123,000 deaths from 6,671 randomly selected areas in 2001–03. A total of 562 deaths (0.47% of total deaths) were assigned to snakebites. Snakebite deaths occurred mostly in rural areas (97%), were more common in males (59%) than females (41%), and peaked at ages 15–29 years (25%) and during the monsoon months of June to September. In the state of Karnataka Out of 6961 of all cases 41 death were by snake bite in the study period. Majority of death occur among males with 5 proportional mortality for 1000.

In the study done by **Francis N P Monteiro**[8] et al. in Kasturba Medical College, manifestations and treatment of cobra snakebite cases admitted to Kasturba Hospital, Manipal during August 2003 and November 2005. Twenty cases of cobra bite were reported during the study period. The victims of cobra bite predominantly were females. Mean age of victims was 41.9 years. Maximum cases occurred during the summer and pre-monsoon months, during daytime and involved the upper limbs. Ptosis was the chief neurotoxic feature followed by dysarthria. Cellulitis as a complication was observed in most of the cases. Polyvalent Anti Snake Venom (ASV) vials were used as specific treatment. No mortality was reported during the study period. Local only 30%,neurotoxic 20%, both local and neurotoxin 45%, none 5%.

In study done by **Dr. Nagnath Redewad**[9] **et al.** Government Medical College, Nagpur. Maharashtra-It was a prospective observational study of 203 patient of snake bite from June 2011 to September 2013 was done. Variable clinical presentations were noted starting from cellulitis (90.6%) followed by nausea and vomiting (70.4%), ptosis (19.2%), colour changes in form of bluish discoloration of bite site (12.8%), respiratory failure and haematuria (7.4%) to Hypotension (6.9%). Out of 203 cases studied 30, patients were died during the study period and overall mortality was 14.8%. Mortality in patients who received ASV more than 300 ml was higher than those who received anti-snake venom (ASV) less than 300 ml (p value < 0.001). In the study done by **H S Harshavardhana**[10] **et al.** Fifty patients consecutively admitted with history of snakebite were studied from May 2012 to November 2013 in a Kempegowda institute of medical sciences (KIMS), Bangalore, Karnataka, India 33 patients (66%) had fang marks, 20 patients had bleeding from the bite site (40%), 7 patients had bleeding gums (14%), 20 patients had hematuria (40%), swelling and

inflammation of the bite area was present in 45 patients (90%), 17 patients had breathlessness (34%). More than 20 ASV vials were given in 26 patients (52%), less than 10 were given in 11 patients (22%) and 10 to 20 vials were given in 13 patients. 31 patients (62%) had tachycardia (>100 bpm) and 18 patients (36%) had systolic blood pressure less than 100 mmHg at the time of presentation. 13 patients (26%) had Hemoglobin less than 10 gm% and 32 patients (64%) had total leucocyte count more than 11,000. 24 patients (48%) had platelet count less than 1,00,000. 28 patients (56%) had prothrombin time more than 15 seconds. 31 patients (62%) had activated partial thromboplastin time more than 30 seconds. 24 patients (48%) had INR more than 1.5. FDP was positive in 22 patients (44%). WBCT was more than 20 minutes in 30 patients.

In the study done by **Tejendra S Chaudhari**[11] et al. Out of 260 patients, 58 died and 202 survived. Mean age was 34.97 ± 14.07 years. One hundred and eighty‑six (71.5%) patients were from rural areas and 74 (28.5%) from urban. 63.4% of bites occurred during rainy season. One hundred and ninety‑seven (75.8%) had bite on lower limb and 62 (23.8%) on upper limbs. All 260 patients (100%) had pain at site of bite, local swelling in 252 (96.9%) and blackening of skin, blebs in 18 (6.9%). Seventy‑seven (29.6%) had bleeding tendencies. Ptosis was present in all the 65 patients with signs of neuroparalysis. Eighty (30.8%) patients had acute renal failure. The mean duration of stay in survivors was 7.50 + 4.13 days and in non‑survivors it was 3.45 + 3.02 days. Out of 58 who died 18 (31%) patients, succumbed within 24 hrs. On multivariate analysis, significant predictors mortality were bleeding tendency (P = 0.013), mean PTTK (sec) (P = 0.047), respiratory failure (P = 0.045), shock (P = 0.013), mean ASV dose (cc) (P < 0.001).

EPIDEMIOLOGY

India

The incidence is more in outdoor areas, rural areas and semi-rural areas. As the snakes are more active in Warm climate, majority of cases occur during months of May to September. Also the incidence is related to rainfall as the reptiles are found to come out of shelter and pits. Most bites occur between 6 am and Mid night corresponding to the period of more out door activity. People who are at risk from sea snake bite are fisherman who go on high seas for fishing and the sea snake bite among sea bathers is very rare.

The persons at greatest risk are Farmers and Agriculture labourers. Bush cleaners, construction workers, scientists and entertainers who handle the snake are also at increased risk. Snake bite is predominantly rural and occupational hazard of farmers and land workers.

Majority of victims of snake bite are found in the age group of 11-50 years by Sawai et al (1974). Males are twice more involved than females. Incidence of snake bit increases with age up to 50 years.

In the tropics most bites are on the foot, toe or lower leg because the victim is bitten through treading on or near the snake. According to Sawai et al (1974) the commonest site of bite is in lower extremities (68%) of which the feet is the most frequent site (41%). In the upper extremities, the most frequent site is finger (13.7%). In non tropics most bites are on the fingers or hands because the victim deliberately handles the snake. Severity of poisoning showed no significant variation according to the time of bite (in the light or dark), the breeding habits of the snakes. Regarding the age it is

more fatal in children and young people because large venom is injected in relation to the body surface area when compared to the adults.

According to Sawai et al Cobra is responsible for the most deaths and Krait is of secondary importance in India.[12] The fatality rate is low with Vipers. In only 6% of the hospitalized cases was the responsible snake identified.

Patrick Russell scientifically documented reference to Indian snakes; he distinguished the venomous from non venomous snakes and focused particularly on viper, viper russelli.[13]

Suchitra N, Pappachan JM conducted a study in Kerala in May 2005 to December 2006. Total of 586 cases were studied the results showed 200 (34%) were envenoming. Regional lymphadenitis occurred in 61%, mortality rate was 3%, 39.5% had complications with acute renal failure. Higher rates of complications were seen in those with severe coagulopathy, leucocytosis and those who received late anti-snake venom. The study proved early administrationof SAV reduces risk of complications. The presence of leucocytosis and severe coagulopathy can predict adverse outcomes.[14]

Atif Sitqwat Hayat et al conducted a study in Hyderabad/ Jamsharo where 100 cases were studied and they concluded 57 viper bites which presented with haemostatic abnormalities and 35 were elapid bites which presented with neuroparalytic symptoms, fang/ teeth marks noted in 90% of cases. Urban to rural ratio was 1:4.5 and male to female ratio was 4:1. Mean duration of hospital stay was 4 days. One patient had ARF and one had DIC. 3% cases of elapid bites needed assisted ventilation, 4 patients had adverse affects after antivenom. Overall mortality was 4%.[15]

Emam SJ, Nikzamir in a study conducted 103 patients of snake bite visiting Razi Hsopital in Iran concluded that 72 of them were males, 27 were females. 50.5% were found to have hemoglubinuria, 40.9% had proteinuria, 29.1% had bacteriuria, 33% had anemia, 74.8% had rhabdomyolysis, 45.6% had myoglobinuria, 12.7% had leucocytosis, 1.9% had thrombocytopenia, 65% had coagulopathy.[16]

Bawaskar et al in a study in Maharashtra, India 182 cases of snake bite were studied, out of these 55 (30.2%) were Echiscarinatus, 38 (20.8%) were Russel's viper, 48 (26.3%) were Krait and 41 (22.5%) were cobra.[17]

Mohapatra B, Warnell DA, Suraweera et al conducted a national study of 123000 deaths from 6671 randomly selected areas in 2001-2003 was conducted (0.47%) of total death was assigned to snake bites. Snakebite death occurred mostly in rural areas (97%) and were more common in males (59%) and females (41%). Peaked at age 15-29 years during months of June to September. The population represent about 45900 annual snake bite deaths randomly with highest rates in rural areas with highest snake bite rate in Andhra Pradesh.[18]

Nigami Tandon VK, Rajendra Kumar et al[19] (1973) conducted a study and found hemorrhagic snake bites were 63.6%, whereas neurotoxic bite 18.2% and cardiotoxic 18.2%, neurotoxic patients presented with ptosis 85%, ophthalmoplegia 43%, palatal palsy 71.4%, respiratory paralysis 42.8%, limb paralysis 7.15%, coma in 3.17%.

Aye-Aye Myint, Twn-Pe et al[20] conducted a study in Myanmar during 1998-2000 (3 years) and found that Russel viper bite constitutes 60% (fatility rate 8.2%), cobra 6% (8) green pit viper 5%, sea snake 0.4% and unknown 29% (3). Russel viper

bite occurred throughout the year with a definite seasonality. A majority of bites occur during the ploughing and harvesting seasons. The age of victims ranging from 6-76 years with a high number of snake bites (49%) and case fatality (5.6%) in 15 to 25 years old age group. Russel viper bite occurs at the at work in the field. A majority of bites occurs in lower limbs between 6 AM to 6 PM. The dead snakes brought by the victim suggests that Russel viper bites is most common followed by cobra bite.

SNAKES

Snakes belong to the Class of - Reptiles.

- Order – Squamata
- Sub order – Serpents (Ophidia)

There are about 2500 species of snakes in the world. In India there are 236 species of snakes of which 52 are poisonous and four species are dangerously venomous.[21]

There are five main families of poisonous snakes (Biggam and Wright)[22]

1. Colubridae (tree snakes).
2. Elapidae (Cobra and Kraits).
3. Hydrophidae (Poisonous sea snakes).
4. Viperidae (Russell's viper) and
5. Crotalidae (Pit viper).

Elapidae is most common type of family of poisonous snakes inhabiting India, especially the cobra and kraits. Crotalidae and Colubridae are not seen in India. Four medically important venomous land snakes in our country are – the Indian Krait (Bungarus caeruleus), the common cobra (Naja naja), the saw scaled viper (Echis

carinatus) and Russell's viper (Viper russelii). These four dangerously venomous snakes live in cohabitation with men.

The common non-poisonous snakes are natux piscator, rat snake, common whip snake, wolf snake, cat snake and Indian python.

Characters:

Snakes are limbless vertebrates with a head, elongated body and tail. On the head there are 2 eyes and two nostrils. The eyes have no lids, but is covered by a transparent scale-hence is steady stare. Snakes have no ears and are deaf but are sensitive to vibrations of the surface on which they lie. Snakes perceive the sense of smell by picking up odoriferous particles from the air and ground with its forked tongue and transferring them to Jacobsons organs situated in the roof of its mouth.

The constant flickering of the tongue in and out is to aid this special sense. Most land snakes feed on rodents and frogs, water snakes feeds on fishes and frogs and other smaller snakes and eels. Kraits and king cobras are exceptional in that they subsist mainly on other snakes. Snakes have the ability to store up fat in its body and some of them can live for months without feeding. Snakes have to swallow their prey whole as their teeth are adapted only for holding the prey and not for masticating a process facilitated by their greatly distensible jaws, skin and gut. Most snakes can climb and almost all can swim. One type can even glide (flying snake). sea snakes use their tails as paddles for propulsions and can hold their breath for long, upto five hours. Four different methods of locomotion have been described in snakes in which undulant or serpentine motion is important.

These are facilitated by rib movements by intercostal muscle action. Snakes are heterosexual and most (cobras-kraits) are oviparous-laying eggs which hatch in around 3 months. Vipers and sea snakes are viviparous. Snakes regularly cast of their

skin every 2 months at which time they are lethargic. Snakes are poikilothermic (cold blooded) and thus hibernate in winter, maximal activity is seen in the rainy months and late summers.[23]

Morphology of poisonous snakes:

The snakes have modified teeth called fangs, usually two in number. The fangs have channels for pouring venom either in the form of a gutter as in cobra or hallow with a tiny opening at the pointed end like a hypodermic needle as in Russel's Viper. At the base of fangs are the ducts connected to the poison glands. Poison glands are modified salivary glands situated on either side of upper jaw.[24]

Snakes have an elongated body. The body is divided into head, trunk and tail. The horny dry skin is covered by epidermal scales which vary in form, number and arrangement. The following nomenclature is commonly used for epidermal covering of snakes.[25]

1. The terms 'scales' is applied when they are small and over lapped.
2. Scales are called 'shields' when they are enlarged and touch only at their edges.
3. Scales on the back lying just above the vertebral column are called vertebrals and those on either side of vertebrals are called 'dorsals' or 'costals'.
4. The scales on the belly which touch the ground while crawling are called 'ventrals'.
5. Scales situated on the ventral side beyond the anus are called 'sub caudals'. Sub caudals may be single or double.
6. The head of the snake may be covered with scales or shields.

7. The shields present along the margin of the upper jaw are called ‘supra labials’ and those found along the margin of the lower jaw are called ‘infra labials’.
8. The region between the external nostril and the eye is known as loream and the pit present in this region is called the loreal pit.

Identification of poisonous snakes:

In poisonous marine snakes the tail is laterally compressed. In terrestrial snakes if the ventral scales are incomplete then it is a non poisonous snake.

If ventral scales are large transverse plates extending fully across the belly, the snake may be poisonous or non poisonous depending upon the following features.[26]

Poisonous:

1. If all the dorsal scales of head are small then it is a viper.
2. If ‘loreal pit’ between nostril and eye is present then it is a pit viper.
3. If the sub caudals are double and there is loreal pit then it is russel’s viper.
4. If dorsal side of head has both small and large shields and the third Supralabial shield touches the nostril and eye then it could be cobra, coral snake or king cobra.
5. If upper side of head has both small scales and large shields, no loreal pit, third supra labial shield does not touch eye, middle row of scales on back are larger than others and ventral side of lower jaw has fourth infralabial shield then it is a krait.[27]

Description of Common Poisonous Snakes in India:

Naja:

Names: English – Common Cobra, Indian Cobra; Kannada – Nagara havu.

Size: 1-2 meters.

Color: Dark brown or black to yellowish white above and white or yellow below. A well-defined spectacle mark on the expanded head and a dark spot on either side of the underside of hood and two or more broad black cross bands further below.

Head: Oblong shape, has a truncated frontal shield. 3 distinct small post ocular scales and 7 supra labials of which 3rd is the largest and touching eye and the nasal scale.[28]

Eye: Has rounded pupils.

Fangs: Small fangs with a gutter as channel for pouring venom.

Body: Dorsoventrally flattened and sub-cylindrical covered with 21-25 rows of smooth scales. Ventral scales cover the belly completely.

Tail: elongated.

Approximate yield of dry venom: 200mg (170-325 mg).

Lethal dose: 120 mg for I.V. dose 0.40 mg/Kg.

Figure 1 : Common Cobra (Naja Naja)

Habitat and Habit:

Cobra are remarkably adaptable snakes and found in all type of country; plains; jungles, open fields and even in the regions heavily populated by man. Their favourite hunts are the holes in embarkments, hollows of trees, old termite mounds, ruined buildings, rock piles and dens of small mammals. They are fond of water and prefer late afternoon and early evening hours for moving around and seeking food.

Cobras are not aggressive and tend to escape when encountered in wild.

- ✓ They strike only when accidentally stepped on or under extreme provocation.
- ✓ They feed on rats, mice, food and frogs but birds, eggs and other small snakes are also eaten.

Bungarus Caeruleus:

Names: English – Common Indian Krait; Blue Krait; Kannada – Kadambale.

Color and Pattern: Black or bluish black with about 40 thin white cross bars which may be indistinct or absent anteriorly. Upper lips and the belly are white. A white pre-ocular spot may be present.

Size: 1 to 1.75 meter.

Head: Flat head. Head shields are normal, 4 shields along the margin of lower lips 3rd and 4th supra oculars touching the eye.[28]

Eye: Small with rounded pupils.

Fangs: Short.

Body: Cylindrical, tapering towards tails 15-17 rows of highly polished scales cover the body. The ventral row distinctly enlarged and hexagonal.

Tail: Short and round.

Approximate yield of dry venom: 8-20 mg.

Lethal dose: 2-3 mg (I.V. LD50 0.09 mg/Kg).

Habitat and Habits:

The common Krait is essentially a plain snake and is usually found in the open country, cultivated area, and scrub jungles at low altitudes. Its favourable dwelling places are termite mounds, rat holes and bushes of other rodents, heaps of rubbish, manure or bricks in the open and gardens, roofs of hower and forsaken buildings and other cool spots in or near human dwelling. They enter the human dwelling frequently.

Figure 2: Common Indian Krait

The krait is strictly nocturnal. It becomes active at night and moves quickly. It feeds on small mammals. Lizard, frogs, toads and sometimes on snakes. They are remarkably quiet and inoffensive, biting only under severe provocation. When encountered in wild, it makes no attempt to escape or defend. But lies quietly and conceals the head in the will of its body.

Viper Russelii:

Name: English – Russell's Viper Kannada – Mandalada havu.

Color and Pattern: Light brown above and yellowish or marbled with brown below. Has 3 rows of large dark oval spots throughout its length. Head with 2 large black spots at the base and light 'V' shaped mark with its apex on the top of snout.

Size: 1 to 1.85 meter.

Head: Flat, triangular and covered with small scales, snout, short and bluntly pointed.

Eye: Large with vertical pupil.

Fangs: Fangs are big erectile and canaliculated.

Body: Stout, short and flattened dorsoventrally. Covered with 17 to 23 rows of strongly keeled scales.

Tail: Short.

Approximate yield of dry venom: 150 mg (130 to 250 mg).

Lethal dose: 150 mg (I.V. LD 50 0.08 mg/Kg).

Figure 3 : Russell viper(Viper Russelli)

Habitat and Habit:

The Russell's viper is found both in plains and hills even at elevations upto 3000 meters. In the plains it is found in the bushy areas, grasslands, farmlands, cultivated fields and rocky areas. It is a sluggish and quiet snake during most of the day although it remains alert always. It becomes active in the evening and at night when it wanders about in a slow, crawling motion. When disturbed, it does not move away quickly but holds the ground and emits a lucid hiss to indicate its annoyance. It can bite with force if injured or provoked. It has a highly efficient biting mechanism with large fangs.

Echis Carinatus:

Name: English – Saw Scaled Viper Kannada – Kallu havu.

Color and pattern: Brown, buff, sandy or greenish above and white below, speckled with brown or black. The usual pattern comprises a pale sinuous white line running down the back. Head has characteristic white cross-like marks.

Size: 30 to 809 cms.

Head: Triangular and very distinct from necks.

Eyes: Has a vertical pupil.

Fangs: Long and canaliculate.

Body: Round and stocky, have 27-37 rows of strangled keeled scales covering the body.

Tail: Short and stubby.

Approximate yield of dry venom: 20-35 mg.

Lethal dose: 5 mg (5 times more toxic than cobra and 16 times more toxic than venom of Russell's viper).

Figure 4 : saw scaled viper(Echis corinatus)

Habitat and Habit:

The saw-scaled viper prefers the sandy soil, sans jungles or thick vegetations. Its favorite haunts are small hills and scrub jungles. It seems to be fond of basking in the scorching heat of mid day sun. When alarmed, it throws itself into a double coil some what like a figure of 8 and rubs the sides of body, producing violent rustling sound. It is very nervous snake and quick to strike at slightest provocation. It flings in about 30 cm in the air to deliver the bite. Despite small size, this viper's habit of lying in the sand with only the head exposed poses a threat to the inhabitants of the desert area.

SNAKE VENOM

It is essential to understand the pharmacological actions of snake venom in order to devise a rational treatment for snakebite. The biochemical nature of the venom is very diverse and complicated. A single snake may contain several varieties of poison, for example there may be 5- 15 enzymes, 3-13 non-enzymatic proteins and peptides and half-a-dozen or more of other substances which have a poisonous actions.[29] The more lethal fraction of snake venom appears to be peptide and perhaps-certain non-enzymatic proteins and most important effects are produced on heart, nervous system, blood vessels, kidneys and respiratory system.

The biochemical constituents of snake venom can be broadly grouped into

(1) The enzymes (2) Non-enzymatic protein and polypeptide.

ENZYMES:

1. **Proteinases**:

It is a proteolytic enzyme that digests tissue proteins and peptide leading to marked tissue changes and destruction. The anticoagulant effect of several snakes venom may be attributable in part to the proteolytic disintegration of fibrinogen. Proteinases are abundantly present in viperidae venom, while elapidae have either very little or no proteolytic activity.[22]

2. **Hyaluronidase**:

It hydrolyses the hyaluronic acid, gets in the interstitial spaces of the cells and connective tissue and thus allows the penetration of other fractions of the venom into the surrounding tissues. This enzyme is responsible for the formation of edema, swelling and rapid absorption of the toxin at the site of bite. It is present in almost all snake venoms.

1. **Phosphodiesterase**:

This enzyme attacks DNA, RNA and also derivatives of arabinose. It has been found to responsible for the profound fall in the systemic arterial pressure. It is found in venoms of all poisonous snakes.

2. **Acetylcholinesterase**:

It is present in elapidae venoms and is shown to have direct action on the heart and at neuromuscular junction.

3. **Neucleotidase**:

It is a common constituent of all snake venom and specifically hydrolyzes phosphate monoesterase, which links with a 5' position of DNA and RNA. It is the most active phosphatase in the venom.

4. **Amino Acid Oxidase:**

It is found in the venom of all snakes. It is most active of the known amino acid oxidases. This enzyme is responsible for the yellow colour of the snake venom.[30]

5. **Arginine esteroser:**

It is a non-cholinesterase found in snake venom. The bradykinin releasing and perhaps the coagulant effects of certain venom may be related to esterase activity. It is substrate specific.

6. **Enzymes Affecting Coagulation Cascade:**

The venom can act as both procoagulant and anti-coagulant. It was Fontanna who first described certain interactions between snake venom and blood coagulation system. Subsequently, Mitchell and Riechert demonstrated that the altered coagulation was associated with a particular venom component the globulin fraction.[30]

There are number of different mechanisms that cause snake venom proteins to act either as procoagulant or anticoagulant.[31]

Procoagulant activities are:

- **Factor X-Activators**:

Found in venom of Russell's viper and activates factor X in the presence of calcium.

- **Factor IX Activators**:
- The same factor, which activates the factor X also activates, factor IX.
- **Indirect prothrombin activator**:

Viper Russelii venom also contains an indirect prothrombin activator that along with activated factor X converts prothrombin into thrombin.[32]

- **Direct prothrombin activator**:

The enzyme acts directly on the prothrombin and does not require calcium ions, phospholipid or factor V. It is found in venoms of elapids, viperids and colabrids but not in crotalids. Apparently one or two peptide bonds are cleaved by the venom enzymes during activation, generating a catalytically active intermediate. This intermediate is probably converted autocatalytically to normal thrombin.

- **Thrombin like enzymes**:

The venom of viperidae appear to contain significant amounts of thrombin like enzymes. These are glycoproteins and not inhibited by thrombin inhibitors or protease inhibitors. There is a formation of fibrinogen clot. There is little direct effect on other clotting factors and no activation of plasminogen. They also do not appear to affect any cellular constituents.[33]

There is secondary fibrinolysis following defibrinogenation by the thrombin like enzymes and this accounts for the increased levels of fibrin degradation products. The combination of defibrinogenation, the continuous presence of FDP and the anti-coagulant nature of the prothrombin intermediate formed by some of the venom enzymes lead to an anti-coagulant state despite coagulant nature of the enzyme.

- **Factor V Activator:**

There are isolated reports that V.Russelii venom contains a component that increases the activity of the clotting factor V.

- **Anticoagulant Activities:**

Most of the snake venom exhibit both anti-coagulant and coagulant effect in their pharmacological action. The mechanism of the anticoagulant activities:

- ✓ Inhibit one or more of the blood clotting factors or prevent activation of one of the clotting factors.
- ✓ Fibrinolytic or fibrinogenolytic action by direct action on fibrin or fibrinogen.
- ✓ Activate fibrinolytic mechanism by direct action on plasminogen or activation of a plasma proactivators of plasminogen.
- ✓ Inhibit clotting by direct action of the venom anticoagulant with phospholipids.

These venom activities appear to affect both extrinsic and intrinsic clotting ystem. The anticoagulant activity is noted predominantly with viper and elapid venom. Viper venom is fibrinolytic, whereas cobra venom are fibrinogenolytic.
The fibrinogenolysis sometimes observed following envenomation by viper might be attributable to primary pathological fibrinolysis as a result of direct activator.

Enzyme phospholipase probably does not hydrolyze the phospholipids necessary for blood coagulation, but rather it forms complex with the phospholipids making interaction with clotting protein difficult.

NON-ENZYMATIC:

A large number of enzymes with specific actions are shown to be present in venom, but play a little role in snakebite / venom lethality, at the most they play a facilitatory role. The constituents of venom that are found to be lethal by themselves are the non-enzymatic peptides, represented by:

1. Hemorrhagins
2. Cardiotoxins
3. Neurotoxins.

Hemorrhagins:

It plays a major lethal role in the viper envenomation. It is responsible for causing acute and rapid hemorrhage in the vital organs like the brain lungs, kidneys, heart and gastrointestinal tract. They cause severe vasoconstriction followed by vasodilatation of the micro-vessels and arterioles with hemorrhages in the capillary bed. Electron microscopic studies of the microvessels of the skeletal muscles injured with venom revealed endothelial gaps due to disintegration of the endothelial cells with intracellular edema, swollen mitochondria and dilated endoplasmic reticulum, separation of the intercellular junction of the endothelial cell and focal loss of basement membrane of the vessels leading to capillary and venous hemorrhage in the tissue.

Pharmacological studies have shown that the hemorrhagic principles induce the release of certain auto-pharmacological mediators such as histamine and 5-HT from various tissues which open up the endothelial cell junctions and disrupt the basement membrane thereby causing vascular damage and hemorrhage.[34]

Cardiotoxin:

Cobra venom contains a cardiotoxin, which is extremely toxic for the mammalian heart. It acts directly on the cell membranes, causing many effects on the skeletal, cardiac and smooth muscles, nerve and the neuromuscular junction, thus contributing to muscle paralysis, circulatory and respiratory failure and cardiac asystole. The pharmacological action of cardiotoxin has been shown to be due to an irreversible depolarization of the cell membrane transport mechanism and a systolic cardiac arrest possibly due to release of calcium from the surface membrane of the myocardium.[35]

NEUROTOXIN:

These toxins are found in the elapid venom. Neurotoxins of elapid venom cause neuromuscular block of non-depolarizing type similar to that of curare. However, the action differs from that of curare in that the onset of action is slower and are bound much more strongly to the receptors than curare and they are also more potent.[36]

According to the mechanism by which they block the neuromuscular transmission neurotoxins in the elapid venoms fall into two groups. The first group comprising of cobratoxin, alpha-bungarotoxin and probably neurotoxin in most other elapid and sea snake venom. They produce antidepolarizing neuromuscular block by acting on the post-junctional membrane of the motor end plate similar to d-tubocurarine. They depress the end plate potential without affecting the terminal nerve spike, resting membrane potential and action potential of the muscle. The neuromuscular blockade caused by this group can be reversed by neostigmine. The blockade caused by the short chain neurotoxin cobratoxin is more readily reversible than that with long chain toxins like alpha-bungarotoxin.

The second group comprises the beta-bungarotoxin. It has an exclusively presynaptic action and causes a severe reduction in acetylcholine output and produces neuromuscular block. It's action is similar to that of botulinum toxins. However, as in the case of botulinum toxin the time for neuromuscular block by beta-bungarotixin is dependent on the frequency of nerve stimulation. This would mean an early precipitation of neuromuscular paralysis by physical activities after the envenomation, while a restful muscle relaxation would retard the onset of neuromuscular block. Beta-bungarotoxin causes complete disappearance of miniature end plate potential

after a period of initial increase in the frequency of MEPPs. Neuromuscular block as well as abolition of end plate potentials takes place before the complete disappearance of MEPPs, since the conduction in motor nerve axon is unaffected by the acetylcholine releasing mechanism. So it is clear that the actions of elapid neurotoxins are highly selective, being confined to neuromuscular junction of skeletal muscle and not on the axonal conduction of the motor nerve.

CLINICAL FEATURES

Snake envenomation is a complex phenomenon manifesting as hematological, renal, cardiac and neurological features. The symptoms, signs and gravity of snake venom poisoning are dependent upon a number of factors:[19]

1. **Age**:

Younger patients are at a greater risk because of higher concentration of venom in relation to body volume available for its distribution. Elderly people may succumb to envenomation due to poor general health.

2. **Nature, Location, Depth and Number of Bites**:

Deeper the bite and more the number of bites, more lethal it is likely to be. Bite through clothing is less dangerous than bite on a bare limb.

3. **Amount of Venom Injected**:

This depends on factors like condition of the fangs and venom glands, like if a snake bites a man after having a recent kill of prey will be able to inject only small quantity. Other factors that determine the amount of venom injected are the kind of clothing through which the fangs pass, factors that motivate the snake to bite and length of the time the snake holds on.

4. **Species of Snake Involved**:

This will decide the symptomatology. Identification as poisonous and non-poisonous, as well species of poisonous snake will help appropriate monitoring and management of patient

5. **Victim's Sensitivity to Venom**:

It will vary from person to person. Based on this desensitization has been suggested as a form of protection against snakebite.

6. **Pathogens present in the Snake's Mouth**:

Snake's mouth contains usually anaerobic and gram negative organisms. They are responsible for the secondary infection of the wound following snakebite.

7. **Degree and Kind of First-aid Treatment and the subsequent Medical Care**:

Delay in the first aid measures or wrongly and over enthusiastically applied first aid measure by untrained persons, contribute substantially to morbidity and mortality, so also the delay in seeking medical help.

GENERAL SYMPTOMS

Fright:

Most common symptom following snakebite whether poisonous or nonpoisonous is fright, particularly the fear of rapid and unpleasant death. It is an emotional response occurring within minutes and present to varying degree in all victims. May manifest as sudden onset of weakness, difficulty in breathing or swallowing (non-paralytic), fainting attacks, or semi-consciousness. On examination victim may have cold clammy skin, feeble pulse and rapid shallow breathing. These symptoms usually resolve dramatically after a placebo therapy, but has to be properly differentiated from that due to envenomation.

LOCAL SYMPTOMS:

1. **Pain**:

After the bite there is some pain, which for most part is confined to the area of bite. The pain is extremely variable in severity and duration depending on the species of snake and amount of venom injected. The pain is most severe with viper bite, which usually appears within 5-10 minutes of bite. Following a cobra bite patient often complain of burning sensation at the site within 15 to 30 minutes. The pain may last for several days. Most of the nonpoisonous snakebites cause mild to moderate pain within few minutes of bite and subside within few hours after taking a mild analgesic. There are exceptions to this, like rat snake and fresh water snake, which cause severe pain after the bite and may require strong analgesics.

2. **Local Swelling**:

Most viper venom in man act predominantly on the haemostatic system, particularly on capillary endothelium. Locally this causes swelling, which starts within minutes of the bite. Massive swelling of whole limb may develop in the ensuing 48-72 hours and is often misinterpreted as resulting from venous thrombosis or bacterial infection from the mouth of the snake. Swelling with viper bites usually resolve completely in 2-3 weeks, occasionally it can take 2-3 months, and in exceptional cases limb may remain permanently swollen. A fair estimate of the dose of venom received can be made from the amount of local swelling i.e. the larger swelling of the limb the greater the quantity of venom injected.

Swelling after cobra bite usually starts from 1 to 3 hours and reaches a maximum in 24-48 hours, which is usually localized. The swollen part is painful and tender to palpation. Poisoning by Kraits or non-poisonous snakebites cause little or no swelling, unless it is secondarily infected. If occurrence of edema (swelling) has not

manifested within 4 hours after snakebite, it is generally safe to assume that the patient does not have pit viper envenomation.

3. **Ecchymosis and Erythema**:

They appear within few hours of the bite. Ecchymosis may occur along with edema and without bleb formation, depending on the amount of venom injected and species involved. In bites by the vipers, spontaneous systemic bleeding is rare whereas discoloration of the bitten limb is typical, The reverse is the case with E. Carinatus envenoming.

In viper bites extravasation of red blood cells as well as plasma into the subcutaneous tissue results in discoloration, which may not be appreciated in dark skin. Usually the discoloration is only around the bite, but in severe poisoning it may extend up the whole limb. It will be particularly evident in any area, where the skin rubs against itself such as between fingers or toes.

In cobra bite a dusky discoloration is seen around the bite marks, which extends in the area and deepens in color each day. About the third or fourth day the gray black area becomes encircled by a red raised rim sometimes studded with small blisters. After 4 or 5 days fluctuation is often evident and an incision on it releases red-yellow material and reveals necrosis of the subcutaneous tissue.

4. **Vesiculations and Hemorrhagic Bullae**:

They are commonly found in viper and cobra envenomation. In most patients they appear within 8-36 hours. Those with minimal envenomation will develop vesicles filled with clear serous fluid, whereas those with severe poisoning the bullae will become filled with blood and frequently rupture.

In case of viper bites blisters extending up the limb indicate a large dose of venom. In cobra bites sanguineous blisters develop over the middle of the dusky area and usually small, rarely exceeding 3cm in diameter.

1. **Local Necrosis**:

Local necrosis with viper bites often appear to be mainly ischemic, developing slowly over weeks and presenting like dry gangrene. It is usually superficial and involvement of tendons, muscles and bones is most exceptional. This necrosis is not due to increased intra compartmental pressure.

Local effects of cobra bites are different: Swelling does not usually appear until 2-3 hours after the bite, but necrosis develops rapidly presenting like wet gangrene within a few days with a putrid smell. Presumably it is caused mainly by a direct cytolytic venom effect. As with burns, the dead tissue provides ideal culture for secondary growth of anerobes, hence the importance of early excision.

Healing of local necrotic lesions requires at least a month and may take over 6 months, even with expert surgical attention.

2. **Bleeding from the Bite Site**:

Minimal bleeding from the wound is common following all snakebites whether poisonous or non-poisonous. Continues oozing from the bite site is common following viper bites.

3. **Fang Marks**:

The absence of discernible fang marks does not exclude snakebite, but the discovery of two discrete puncture marks does suggest a bite of venomous snake. As a rule, two lacerated punctures, about 1.25 cm deep in the case of colubrids and about 2.5 cm deep in the case of vipers[37]. An inverted ‘U’ shaped bite mark is caused by the teeth of a non-poisonous snake. Presence of marks by accessory fangs, other teeth and

sometimes multiple bites makes it difficult to identify the type of snake. The distance between the fang marks is proportional in the size of the snake.

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sometimes multiple bites makes it difficult to identify the type of snake. The distance between the fang marks is proportional in the size of the snake.

SYSTEMIC SYMPTOMS

Viper Envenomation:

Non-specific early systemic symptoms:

Within a few minutes of the bite, vomiting, headache, abdominal pain, explosive diarrhea, and collapse with un recordable blood pressure can occur. These features usually resolve spontaneously within 30-60 minutes, suggesting activation of the kinin system followed by inhibition of brady-kinin, rather than a direct venom effect.[19,38]

Shock:

Patients show varying degrees of signs of peripheral failure with or without signs of impending coma, hypotension, renal failure, dehydration and electrolyte disturbance. Shock starting later, as effect of envenomation is the main cause of death in viper bite. Hypovolaemia from loss of blood and plasma into the swollen limb is one causal factor. Further important factors in pathogenesis of shock are pulmonary intravascular clotting, pulmonary edema and cardiac effects as evidenced by abnormal ECG and serum enzyme levels.[19]

The shock usually develops after 30 minutes, most often seen between 6- 24 hours. But may occur as late as 3 or 4 days. Generally resolve within a week in patients surviving without antivenom.

Hemorrhagic Symptoms:

Hemorrhage is the cardinal manifestation of systemic viper poisoning. Spontaneous hemorrhage (or oozing) into a vital organ especially the brain, is often lethal and may be delayed upto several days after the bite. Although direct endothelial damage by hemorrhagins, coagulation defects and defibrinogenation are proposed mechanism, the available evidence suggest more important role for endothelial damage.

The earliest and almost diagnostic symptom of hematotoxicity in viper bite is the hemorrhagic bleb with uncontrolled bleeding from the site of the wound. Within 2 to 24 hours of bite patients may present with varying degrees of hemorrhagic manifestations like generalized ecchymosis, purpurae and hematoma. Painful large ecchymosis, purpurae, gangrenous particularly of lips, tip of the nose, fingers or toes is highly suggestive of Schwartzmann like phenomenon.

The systemic hemorrhagic manifestations include frank or microscopic hematuria, which has been observed to be the commonest symptom. Other bleeding manifestations like hemoptysis, bleeding from the gums, hematemesis, malena and cerebral hemorrhage are also common. According to Reid et al (1963) the commonest and earliest hemorrhagic manifestation which may be seen as early as 20 minutes after viper bite is hemoptysis. Hemorrhage into brain, the peritoneum or other vital organs and uncontrolled external hemorrhages may be fatal.[29]

SYSTEMIC ELAPID ENVENOMATION:

Presents with neurotoxic and cardiotoxic manifestation.

Neurotoxic Manifestation:

The earliest symptom of systemic elapid envenomation is a feeling of drowsiness or intoxication that starts from 15 minutes to 3 hours. There is selective neuromuscular block affecting mainly the muscles of eyes, tongue, pharynx, chest and finally limbs[19]. The symptoms and signs usually develop within 1 to 4 hours of bite. Bilateral ptosis is the earliest and commonest manifestation. Eyelids may remain completely closed despite normal ability to wrinkle the forehead. The eye movements may be impaired both in vertical and lateral direction, when the patient may have blurring of vision or double vision, or the eye may be central and fixed (immobile). The pupils are usually dilated but react normally to light except in the terminal stage. With small doses of venom, these eye signs may be the only evidence of muscle paralysis.

Following the onset of ocular symptoms, the patient may develop difficulty in speech, which may become nasal because of palatal palsy, difficulty in opening the mouth and moving the lips and difficulty in swallowing. According to the extent of envenomation the symptoms may progress insidiously or rapidly.

In severe or fatal poisoning the intercostal muscle paralysis occurs as shown by decreased outward rib movement and absence of intercostal bulge normally palpable during inspiration. Respiration then becomes entirely diaphragmatic and later complete paralysis supervenes over matter of hours. The respiratory failure manifests as confusion, stupor, shallow breathing, increase in pulse and respiratory rate and fall in blood pressure. Increased sweating and cyanosis sets in. At any time during this

phase of respiratory failure patient may go into deepening coma, non-reactive dilated pupils, twitching and convulsions and ultimately leading to death.

Limb weakness usually develops last. Varying grades of flaccid limb paresis, usually affecting proximal more than distal muscles. Patient has inability to sit up or lift up the limbs. Deep tendon reflexes remain normal in mild cases. Eventually a complete flaccid quadriplegia develops with loss of deep tendon reflexes. Bladder and bowel functions are normal. The pattern of involvement and sequence of signs and symptoms of neurotoxic envenomation bears a striking resemblance to myasthenia gravis.

CARDIOTOXIC SYMPTOMS:

The symptoms due to direct acting cardio toxin are usually of sudden onset appearing within 30 minutes to 20 hours of bite. Usually present with cardiovascular depression manifesting as sweating, cold extremities, tachycardia, hypotension and ECG changes usually in the ST segment or T-wave. These could often be followed by sudden hypotension, cardiac arrhythmia and cardiac arrest[38].

COMPLICATIONS

Renal Failure:

Acute renal failure may follow serious poisoning by all three types of venomous snake – viper, elapid and sea snake – and appears to be unusually common after V. russelii bites. Acute renal failure complicates the course in 5- 30% of victims of severe viper poisoning[39] cases. It usually becomes clinically evident towards the end of the first week after the bite. No consensus exists on the single mechanism causing acute renal failure after viper bite. The alterations that contribute to renal failure include a varying degree of bleeding, hypotension, circulatory collapse,

intravascular hemolysis and disseminated intravascular coagulation with or without microangiopathy.[40] A direct cytotoxic action of snake venom on the kidney is suspected, but convincing evidence is still lacking. Hypersensitivity to venomous or antivenomous protein occasionally causes acute renal failure. The renal lesions of clinical significance in envenomed patients are acute tubular and patchy or diffuse cortical necrosis.[41] Glomerulonephritis, interstitial nephritis, and papillary necrosis have been reported in rare patients. Clinical presentation is similar to the acute renal failure of any other cause manifesting with oliguria, associated fluid and electrolyte imbalances.

Respiratory Paralysis:

A complication of severe envenomation by cobra and krait, it is principle cause of mortality from these two species.[42] Snake neurotoxins that bind to acetylcholine receptor sites on the motor end plates produce effects similar to those of curare and myasthenia gravis.[43] Initially only intercostals are involved. Later it also involves diaphragm. The presentation in early stages will be with tachycardia, tachypnea and reduced tidal volume, which can progress to cyanosis, confusion, stuporousness, eventually leading on (if untreated) to coma, respiratory arrest and death. The respiratory failure in neurotoxic snakebites is acute type-II respiratory failure. In various degrees of presentations, the respiratory insufficiency and paralysis reported in 40-80% patients with elapid envenomation.

Gangrene:

Neglected local necrosis can result in gangrene of the limb. So the wound should be examined frequently for evidence of necrosis.[30] Early signs of necrosis include blistering, blackening or blanching of the skin, loss of sensation and a characteristic smell of putrefaction.[30] There is high risk of secondary infection and so

the necrotic tissue should not be allowed to slough spontaneously but should be debrided under local or general anesthesia. Cobra envenomation tends to produce a wet gangrene, whereas viper envenomation produces superficial dry gangrene.

Non-bacterial Thrombotic Endocarditis (NBTE):

Commonly occurs in patients with wasting disease (e.g., malignancy) or with valves damaged following trauma due to intracardiac foreign body, scarring or marked turbulence. DIC is well documented following viperine bite and the underlying mechanism of NBTE is thought.[44]

Guillain-Barre Syndrome:

Guillian-Barre Syndrome has been reported as an unusual complication after snake bite mainly due to krait bite. The patient presented with symmetric paresis and sensory signs in the upper and lower limbs, autonomic dysfunction, facial nerve involvement and mild elevated CSF protein at about 4 weeks after the bite. Electrodiagnostic studies, revealed profound sensory and motor polyneuropathy. Repeated electrophysiologic findings confirmed nerve regeneration. The patient reached satisfactory functional outcome after a shortterm intensive rehabilitation program despite severe axonal degeneration.[45]

Compartment Syndrome:

Hand compartment syndrome is a rare but potential complication of untreated crotala envenomations. It is due to direct intramuscular envenomation (compartment pressure greater than 30 mm of Hg).[46]

Rare Systemic Complications:

- ✓ Subarcahnoid hemorrhage.
- ✓ Hysterical paralysis.
- ✓ Second degree heart block.
- ✓ New dyselectrocytemic acute MI.
- ✓ Hypo-pituitarism.
- ✓ Bilateral thalamic hematoma.[47]

INVESTIGATIONS

I. Blood Investigations:

- ➢ Total Leucocyte count:- Neutrophil count above 20,000 cells/□L indicate severe poisoning.[38]
- ➢ RBC Count and hemoglobin and packed cells volume: In systemic Viperine poisoning there is usually no abnormal hemolysis, but anemia caused by internal loss of Red Blood cells into the bitten limb and from external bleeding may result in fall of hemoglobin and RBC count. Hemolysis is more commonly seen with bites of Australian land snakes and cobra bites.[48]
- ➢ Platelet Count: Platelet count may be normal but often reduced during the first few days after the bite although the bleeding time is normal.
- ➢ Bleeding Time: Usually normal in Viper bites. Prolonged if bleeding diathesis develops.
- ➢ Whole Blood clotting time: Prolonged if coagulation defect is present.[49]
- ➢ Non clotting blood Test: Non clotting of the blood indicates severe viper poisoning.
- ➢ Plasma Fibrinogen: It is severely depleted in Viper poisoning.
- ➢ Fibrin degradation products: Diagnostic of DIC.

- Reticulocyte count: Increased in hemolysis (Cobra).
- Red Cell Morphology: Spherocyte formation, acanthocytosis, Heinz body formation and Blurring of erythrocytes are readily demonstrated.
- Grouping and cross matching: This is considered whenever there are bleeding manifestations.
- Blood urea, serum creatinine: For assessment of renal function.
- Serum electrolytes: To assess the electrolyte balance of the patient. Serum potassium may be raised in sea snake poisoning due to muscle damage.
- Blood Lactate: To determine the lacltic acidosis in presence of Hypotension.
- Liver Function Test: Hemolysis produces raise of unconjugated Bilirubin levels.
- Serum Enzymes: raised CPK-MM-indicates skeletal muscle damage.

Raise of CPK-MB indicate Cardiac muscle damage.

Increased SGOT levels indicate Cardiac muscle damage.

Increased SGPT levels indicate damage to the liver.

II. Urine Examination:

A. Albumin:

Proteinuria lasting a few days is common in severe envenomations. It can also indicate renal involvement.

B. Bile salts and pigments: Positive in hemolysis (Cobra and Viper).

C. Microscopic Hematuria: Common with Viper bites.

D. Hemoglobinuria: Associated with severe hemolysis.

E. Myoglobinuria: Seen in sea snake poisoning.

F. Specific gravity: reduced in renal failure.

III. Stool Examination: Melena and occult blood may be seen in case of Viper Bites:

IV. Other Investigations:

1. **Immunodiagnosis:**

   a) Demonstration of sites of Venom localization by immuno fluorescence Technique: By this method the localization of venom and probably of its action can be demonstrated.[50]

   b) Micro Elisa: (Enzyme linked Immunosorbant Assay) By this technique quantification of the envenomation can be assessed. Snake venom levels upto 1-5 ng/ml can be detected. The assay is specific and further the specific anti body to the venom can also be demonstrated and can be carried out with serum, urine and other body tissues. The important application of this being- to make an accurate retrospective diagnosis so as to compile distinctive clinical patterns in bites of various poisonous snakes, in epidemiological study and in assessing the effectiveness of various antivenoms.[51]

2. **Lumbar Puncture:**

   C.S.F. is examined for any evidence of cerebral hemorrhage or sub archnoid hemorrhage.

3. **X –ray chest**:

   This may show pulmonary oedema or evidence of Haemorrhage into the lungs.

4. **ECG:**

   ECG changes are unusual. Sinus bradycardia, ST-T changes, Various degrees of AV block Can occur due to cardiotoxicity.[52]

5. **Fundus Examination:** For evidence of hemorrhage.

MANAGEMENT OF SNAKEBITE

The management of snakebite involves first aid by the patient or other present at the scene of the bite and later treatment by medically trained staff of a dispensary, health station or hospital.

First Aid:

Although this subject has stimulated much speculation and has generated an enormous literature, only the following principles are generally accepted.

1. Reassure the frightened patient.
2. Immobilise the bitten limb as far as is practicable with splint or sting.
3. Transport the patient to a place where he/she may receive medical attention.
4. Avoid harmful medicines and procedures.

1. Reassurance of Patient:

Most snakebite victims are terrified because they believe that rapid death is almost inevitable. This anxiety can produce misleading symptoms (tachypnea, sweating, dizziness, syncope, acroparaesthesia and carpopedal spasm) and interferes with rational management. The patient may behave irrelevantly to the extent of cutting of the bitten digit or limb. The basis of reassurance is the effectiveness of modern treatment for snakebite, the relatively slow progression to severe envenoming which usually allows time to reach hospital and the fact that venomous snakes often bite without injecting venom.

2. Immobilization:

Muscular contraction promotes spread of higher molecular weight venom components which are absorbed mainly into the lymphatics. Immobilization of the limb in a plaster spica delayed death and reduced symptoms of envenoming from tiger

snake and Russell's viper venom, but not cobra.[53] Venom splitting combined with crepe-bandaging of the bitten limb has also proved effective in delaying the absorption and promoting local neutralization of venom.

During the transit the body generally and the bitten limb in particular should be moved as little as possible, to minimize the spread of venom. If shifting to a hospital or clinic with antivenom facilities will take over 30 minutes, an absorption delaying compressive bandage, preferably crepe should be applied firmly, as for a sprain over the bite site and up the whole limb. The bandage should not be released during transit.[54]

Bite Wound:

Do not tamper with the bite wound in any way except to wipe it once with damp cloth to remove surface venom.

3. **Transport to Site of Medical Attention**:

This should be achieved as rapidly and comfortably as possible, saving the patient strenuous exercise. Very rarely death may occur as soon as 15 minutes after a viper or elapid bite. Usually however, the death time is hours for elapids and days for vipers, on their way to hospital patients may vomit, in which case they should lie on their side to avoid aspiration. The majority of patients (64%) die between 6 to 48 hours after the bite occurred. Victims of snakebite who receive medical attention within first 2 hours after a bite have an excellent chance of survival.

If the snake can be killed without endangering either the victim or another person, it should be brought to emergency department for identification. It has been observed that recently killed or dying snakes are still capable of biting. It is therefore

imperative not to handle the snake directly but rather to use a stick or place the snake's parts in a bag or other container.

4. Avoidance of Harmful Medicines and Other:

i) Drugs:

Aspirin given as an analgesic may lead to persistent gastric bleeding in patients with incoagulable blood. Paracetamol (acetaminophen) can be used for pain. Herbal remedies ingested or applied locally, have yet to prove beneficial but are widely used throughout the rural tropics. Many are emetics which may cause clinical confusion as vomiting is also a sign of severe envenoming by some species.

ii) Local Incision and Suction:

Incision, suction and cautery was first described by the Indian Physician Sushrutha in 600 BC[26]. This recommendation from several experts has remained unchanged with exception of cautery over last 2500 years. In experimental animals local incision and mechanical suction improved survival after eastern diamond back rattle snake envenoming only if it was performed within 10 minutes of subcutaneous venom injection.

The natural bites may inject the venom more deeply, however, and the possible benefit of these measures should be weighed against the risk of causing persistent bleeding in patients with incoagulable blood, and of introducing infection, particularly when a non-sterile instrument or mouth suction is used. Other dangers of incision include damage to vessels, tendons and nerves. Cauterization and excision of the bite wound are contraindicated for the same reasons. Amputation of bitten digit or extremity should never be considered as it would have to be done before it was evident whether or not

significant amounts of venom has been injected. The local injection or implantation of chemicals such as potassium permanganate, which inactivate venom toxins in vitro may cause local necrosis and should not be used.[54]

Currently best recommendations appear that incision and suction should not be performed as routine. If performed it should be done by medical professionals. An incision is made linearly through the skin, approximately 0.25 inches long to 0.125 inch deep over the fang puncture. The sooner incision and suction is performed, the more venom can be extracted from the bite. As mentioned, to be effective incision and suction should be performed only within the first 30 minutes of the envenomation under all aseptic precaution. Once antivenin is administered, incision and suction should be discontinued. In most instances at least 30 minutes or more elapse before snakebite victims are evaluated by medical personnel. Therefore, incision and suction rarely should be performed.[38]

iii) Tourniquets:

A firmly (but not tightly) applied broad band or ligature can impede the spread of the larger molecular weight viper toxins in lymphatic and superficial veins. This effect has not been proved to be clinically useful and may lead to congestion and edema of the limb, confusing signs suggesting envenoming where there may be none. In rabbits the use of a venous tourniquet did not increase the survival time after injection of venom. The danger of a tight tourniquet applied for more than 1-2 hours can cause ischemic damage to the limb. Loosening a tourniquet, by suddenly releasing pent up venom, may cause acute and disastrous envenoming unless adequate antivenom is given

first. Tourniquets also increase fibrin lytic activity in the occluded limb, which could enhance effect of venom coagulant. In restrained monkeys immobilization of the venom injected limb and crepe-bandaging proved almost as effective as arterial tourniquet in containing the venom.

It is suggested that a tight tourniquet or crepe bandage should be used (in addition to immobilization) only if the bite is known to have been inflicted by a dangerous elapid or sea snake and medical attention is likely to be delayed for up to two hours.

i) Cryotherapy:

Cooling of the bitten limb with ice packs may reduce discomfort and delay absorption of venom by producing vasoconstriction. But it appears to promote the necrotic effects of snake venom.[55]

Antivenom administration should not be regarded as a first aid procedure. Because of potential dangers of serum reactions, the limited indications for antivenom and requirement of intravenous route, this treatment should be given only by trained medical personnel.[30]

HOSPITAL TREATMENT

Snakebite is a medical emergency and ideally all patients bitten by snakes should be assessed quickly and promptly. Because of many uncertainties about the type, quantity and quality of venom injected, and variable time course for the development of signs of envenoming, all victims of snakebites should ideally be kept under medical observations for at least 24 hours. And level of consciousness, blood pressure, pulse rate and respiration should be monitored carefully.

Initial assessment is of great importance in correct management. If the patient was unable to bring the snake or failed to recognize it, details of the circumstances of the bite, and appearance and behavior of the snake may help species identification. For example bite inflicted on people sleeping in their huts at night strongly suggests common Krait in India. Physical examination should include assessment of local swelling. Significant envenoming by pit vipers results in swelling within 15 minutes, and by vipers within 2 hours. Some neurotoxic species such as kraits, produce virtually no local effects. Tender enlargement of regional lymph nodes draining the bitten area is an early sign of envenoming by viperidae. Spontaneous bleeding is most often detected in gingival sulci, and at venepuncture sites, from partially healed wounds and from nose and gastrointestinal or genitourinary tracts. Hypotension is an important sign of hypervolemia or cardiotoxicity. Ptosis is the earliest sign of neurotoxic envenomation. If procoagulant venom is suspected, hemostasis should be checked at the bedside. Complicated clotting tests are not required. Results of this rapid clinical assessment will determine whether the patient requires antivenom, additional supportive treatment or merely reassurance and/or a placebo.

ANTIVENOM

Anti-Snake Venom:

Indian ASV contains antibody and its half life is approximately between 80 to 100 hours.[56] This is the only specific cure for envenoming. In India it is polyvalent and prepared by hyper-immunizing equines against the venom of four common Indian snakes i.e. cobra, common krait, Russell's viper, saw scaled viper. The most important decision in the management of snakebites is whether or not to use ASV and if the decision of injecting ASV is made the questions to be answered are:

1. How much should be the initial dose?

2. How frequently and how long should ASV be given?

Unfortunately scientifically designed clinical trials on these aspects are hardly if any and hence rationalization is not seriously worked out.

The polyvalent antivenin is concentrated, purified and dispersed either in liquid form or lyophilized form. The potency is retained for about 2 years by fluid antivenin and for about 10 years by freeze dried or lyophilized antivenin. The latter is reconstituted by adding sterile water to the ampoule containing powder antivenin. Each ml of reconstituted serum neutralizes 0.6 mg of dried cobra venom, 0.45 mg of dried Krait venom, 0.6 mg of dried Russell's viper venom and 0.45 mg of dried saw-scaled viper venom.[38] In India it is manufactured by The Central Research Institute, Kasauli, Haffkine Biopharmaceutical Corporation Ltd., Bombay and Serum Institute of India, Pune. No monovalent anti-snake venom is available in India currently.[19]

Indications for Antivenom:

Because of the danger of antivenom reactions and high cost of antivenom, this material should not be used indiscriminately. Unfortunately in many hospitals around the world a standard small dose of antivenom is given to any patient who thinks that he/she has been bitten by a snake, irrespective of signs of envenomation and the identity of the biting or stinging animal. This practice exposes the majority of these patients, who have mild or no envenoming, to the risk of potentiality-fatal antivenin reactions, and squanders the limited supply of antivenin. Many patients bitten by venomous snakes develop no signs of envenoming and many other develop only mild or negligible envenoming.[30]

Treatment with specific antivenom is indicated as follows:

1. If there is evidence of systemic envenoming evidenced by:

   - ✓ Hypotension or other signs of cardiovascular toxicity such as abnormal ECG or cardiac arrhythmia.
   - ✓ Neurotoxicity or, in the case of bites by sea snakes and some Australian snakes, generalized myotoxicity (rhabdomyolysis).
   - ✓ Impaired consciousness.
   - ✓ Spontaneous systemic bleeding or incoagulable blood.

2. If, in the absence of evident systemic envenoming, there is massive local swelling (for example, involving more than half the bitten limb), especially following bites by species whose venom is known to cause local necrosis.
3. Much wider indications for antivenom are accepted in relatively wealthy countries, where the incidence of bites is low by Asian standards. Thus, it is claimed that in the case of bites by more dangerous rattle snakes antivenom should be given early, before systemic envenoming has become obvious. In this case rapid spread of local swelling is considered an indication for antivenom. The Common Wealth Serum Laboratories, Australia (CSL) recommend that antivenom be given to any patient with proved or suspected snakebite if there is any evidence of systemic spread. If spread of venom including finding of tender regional lymph nodes, and to anyone effectively bitten by an identified highly venomous species. In none of these special cases, is evidence provided to support the indication for antivenom.[30]

Supporting evidence for severe envenoming is an elevated peripheral leukocytosis of more than 20,000 per cumm., elevated serum enzymes such as creatinine phosphokinase, aspartate and alanine amino-transferases, hemo concentration, uremia, oliguria and acidosis.

Contraindications:

There is no absolute contraindication to antivenom treatment, but because of the increased danger of severe reactions, atopic individuals and those known to be hypersensitive to equine serum should be treated only if effects of envenoming are thought to be life threatening. Pregnancy is not a contraindication to the administration of antivenin. Early treatment may halt venom induced uterine contractions and abortion in cases of severe envenomation.

Timing of antivenom treatment:

Antivenom will neutralize the circulating venom but not the venom which is already fixed to the tissues. This leads to logical conclusion that antivenin treatment should be given as early as possible after the signs of envenomation become evident. Apart from this up to what time ASV treatment can be given remains an intelligent estimate only. Most authorities in the field believe that it is most effective if given within 4-6 hour and of questionable value after 24 hours. But others feel that it is never too late to try antivenom treatment, based on reports, that, sea snake envenoming has been reversed up to two days after the bite and blood coagulability in cases of saw-scaled or capet viper bite.[54]

Route and method of administration:

ASV can be administered by intramuscular, Subcutaneous or intravenous routes. First two routes, intramuscular and subcutaneous are rarely used. They have

disadvantages that they may cause hematoma formation, pressure necrosis of digits, etc. when injected into tissue compartments. Also would be impracticable to use the doses required due to its volume. Now it is accepted that intravenous route is much more effective and practical than any other.[38]

In intravenous route, it can either be given as infusion or slow intravenous injection (Pulse) of undiluted antivenom. For injection it can be diluted with normal saline, 5% dextrose water or Ringer's lactate. Infusion gives better control of speed of administration and there is in vitro evidence that diluted antivenom is less anticomplementary and so may be less likely to cause reactions and thrombocytopenia. Some experienced clinicians have formed the impression that infusion causes fewer reactions, but no controlled comparison of two methods has yet been performed.[54]

When patient arrives in hospitals with a tourniquet or other constriction band in place antivenin treatment if it is thought to be necessary, should be started before these are loosened or removed, as there is a risk of severe envenoming when the pent up blood from the occluded limb is released into the circulation. Whereas in a suspected case of non-poisonous snakebite the tourniquet can be removed as soon as the patient is brought to the hospital and watched for any development of signs of poisoning.

Dosage of ASV:

The exact dose of antivenin always remains a difficult question. Unfortunately scientifically designed clinical trials on dosage of ASV are hardly if any and hence

rationalization of its use is not seriously worked out. The appropriate initial dose of antivenom for patients has been established experimentally in very few cases.

The dose recommended by manufacturers is based upon mouse protection studies by scaling the antivenom dose up taking into account the venom yields. These calculations ignore the wide variability in the amount of venom injected into man by biting snakes, the difference in response of various species to venom, and different modes of death in small mammals compared to human victims of snakebite, and their design may not reflect the real life situation. Thus, those recommendations could be very misleading.[30] The variable time interval between the bite and patient presentation for treatment induces yet another difficulty into clinical study of antivenom. Experimentally, delay in administering antivenom results in steep increase in median effective neutralizing dose[54]. Both, Haffkine Biopharmaceutical Corporation Ltd., Mumbai and Serum Institute of India, Pune recommend a dose of at least 20 ml of reconstituted serum intravenously slowly and not over 1 ml per minute, repeating 2nd dose 2 hours of first dose or even earlier and further doses to be repeated every six hours till symptoms disappear.

Another way of making recommendations for dosage of ASV is based upon prior wide clinical observations.

Warrel recommends an initial dosage of 100ml of polyvalent antivenin to given to all Indian snake envenomation's. It should be given by intravenous injection at a rate of about 5 ml / min or diluted in isotonic fluid and infused over 30 to 60 minutes.[30]

An adequate initial dose of antivenin should be given as early as possible, depending upon the amount of envenomation. It should never be injected locally. The dosage schedule recommended: 2 to 5 vials (20-50 ml) for local swelling but no systemic symptoms. - 5 – 9 vials (50-90 ml) for swelling which has progressed beyond site of bite and mild systemic symptoms and/or presence of coagulation abnormalities. - 10-15 vials for severe bites associated with marked local as well as systemic effects.

ASV administered by intravenous infusion diluted in approximately 5-10 ml/ hr but of NS or 5% D over one hour to where effective blood concentration rapidly.[57]

Ghotekar analyzed previous Indian studies and felt that there is variation in requirement of ASV in different geographical areas of country probably due to interspecies variation and proposed that initial dose for viperine bites could vary from 20-100 cc according to regional requirements with repeat dose varying from 20-50 cc till normalization of clotting time, while recommendation for neurotoxic bites being 100-200 cc as initial dose.[58]

WHO has recommended which has been accepted by others, the initial dose of Indian polyvalent is 100 ml,[57,56,59]

Hoddad and Podgomy proposed a system of grading the severity of envenomation in pit vipers based upon symptoms and signs noted within four hours of bite to decide the initial dose of ASV[60]. An important randomized trial of ASV in snake envenomation with prolonged clotting time was done from India by Thomas and Jacob. They suggested that giving total of 7-9 ampoules of antivenom was as effective as high dose.[61]

Paul V et al observed 10 ml dose of ASV equally effective as high dose local administration of antivenom at the site is not recommended as it has not shown to be effective and extremely painful and may produce increase intra compartmental pressure.

Obviously, the scenario is quite confused and clinicians tend to follow the dosage schedule as per their own observation of local trends. It is impossible to provide a rule to calculate precisely the amount of antivenin to deliver. The clinician can analyze the needs of individual cases taking into account the type of envenomation, time of arrival, use of first aid measures and dosage requirements as per the regional geographical variations till the results of further trial are available.[62]

Sensitivity Testing:

Can be performed either by skin test / conjunctival test.

Skin Test:

Performed by injecting 0.02 ml of a 1:10 dilution of antivenin intracutaneously in the forearm. A simultaneous control test with equal amount of normal saline should be carried out in opposite forearm. Positive reactions occur within 5-20 minutes and consists of a large area of erythema. An occasional patient may develop anaphylactic shock even after the dose of skin test.[28]

Conjunctival Test:

The conjunctival test is relatively safe as it does not involve injection of antivenom into body tissues. One drop of a 1:100 dilution of antivenin is instilled into conjunctival sac of one eye with the control instillation of normal saline in other eye. A positive reaction is seen as the itching of the eye and eye lids with dilatation and

congestion of the conjunctival blood vessels and chemosis of eyelids. This occurs within few minutes and can be treated with eye wash with sterile water or normal saline followed by instillation of one drop of adrenaline 1:1000 dilution.[30]

Many authorities on snakebite have recommended the use of sensitivity testing but at the same time provide evidence of its unreliability and even potential lethality.[63] Others have considered this test to be useless. Neither opinion has been supported by prospective data. Results from 25 Nigerian and Thai patients prove that these conventional tests do not have any predictive value for occurrence of early reactions, even severe systemic anaphylaxis. It is not justifiable to delay antivenom treatment for 20-30 minutes to read result of sensitivity tests. As early reactions are common, unpredictable and occasionally life threatening all patients treated with antivenom must be regarded as reactive. Published reports with regards to late serum sickness type reactions provide no convincing evidence that they are predicted well by the results of sensitivity tests.

Antivenin Reactions:

Adverse effects of the serum are common and anaphylaxis can be fatal.

There are three types of reactions:

1. Early (anaphylactic) reactions
2. Pyrogenic reactions and
3. Late (serum sickness type) reactions.

1. **Early Reactions**:

Early reactions occur between 10-60 minutes after starting administration. Symptoms include cough, tachycardia, itching (especially of scalp) urticaria, fever,

palpitation, nausea, vomiting and headache. About 5% of patient with early reactions develop manifestations of severe systemic anaphylaxis such as hypotension, bronchospasm and angio-edema, but there are few if any reports of death reliably attributed to these reactions.

2. **Pyrogenic Reactions**:

Symptoms are those of an endotoxic reactions developing one or two hours after treatment. There is an initial chill with cutaneous vasoconstriction, gooseflesh and shivering. Temperature rises sharply during the rigors and there is intense vasodilatation, widening of the pulse pressure and eventually a fall in mean arterial pressure. Temperature falls with profuse sweating and there may be associated gastrointestinal symptoms such as vomiting and diarrhea.

3. **Late Reactions (Serum Sickness Type)**:

The incidence and speed of development of these reactions increase with the dose of antivenin. After seven days after treatment (range 5 to 24 days), there is itching, urticaria, flulike symptoms with fever, arthralgia which may include the temporomandibular joint, lymphadenopathy, periarticular swellings, albuminuria and neurological symptoms including neuralgic amyotrophy, mononeuritis multiplex usually of radial nerve, Guillian-Barre syndrome polyneuropathy and rarely encephalopathy.

There is convincing evidence that only reactions and late serum sickness type reactions to antivenom are related to complement activation by immune complexes (aggregates). But others believe that early reactions are immediate hypersensitivity reactions on the assumption that they represent type-I IgE mediated hypersensitivity to horse serum.

Prevention, Premedication and Management of Antivenin Reactions:

As antivenom serum is the most effective, if not the only effective treatment available for management of snakebite envenomation, increasing the safety of treatment with antivenom serum for snakebite victim is, therefore, a matter of high priority.

Methods used to reduce acute adverse reactions are:

1. **Monovalent Serum**:

There is now a trend towards use of monovalent serum. There is no evidence, however, that this would result in fewer adverse effects than polyvalent antivenom serum.[64]

2. **Immunotherapy**:

   Another possible treatment option is still at an experimental stage.

3. **Test Dose**:

   It is insensitive and can give rise to anaphylaxis by itself.

4. **Prophylactic use of hydrocortisone and antihistamines**:

   Administered before infusion with antivenom serum is also practiced. Antihistamines, however, counter only the effects of histamine release. Hydrocortisone takes time to act, and hence it will not be effective against acute adverse reactions that can develop immediately after serum treatment, which is very often administered urgently to snakebite victims.

5. **Adrenaline**:

   The prophylactic use of 1:1000 adrenaline in a dose of 0.25 ml given subcutaneously immediately before infusion of antivenom serum significantly reduces the risk of acute adverse reactions. Fears of development of hypertension or CVA seem unfounded.

Treatment of Anaphylaxis:

Adrenaline 1 in 1000 in a dose of 0.5 to 1ml for adults, 0.01 mg/Kg for children. It should be given by subcutaneous injection at the first sign of reaction. It should be given IM/IV/intra cardiac in appropriate situation. It should also be accompanied by administration of antihistamine.[63]

Though antivenin treatment remains corner stone of envenomation, it is not necessary in all bites and neither complete treatment itself. Other measures play equally important role. They are:

1. **Reassurance**:

   Reassurance is one of the most important measures in general treatment.

2. **Care of the Wound**:

   The bitten area may be washed with soap and water and blotted dry with a sterile gauze. No covering or dressings should be applied. The blisters should be let alone, they will break spontaneously and will quickly heal without infection provided there is no underlying necrosis. But as soon as local necrosis is obvious slough should be excised. Normal saline is best local application.

3. **Tetanus Prophylaxis**:

   Although clostridium tetani have not been isolated from the fangs or mouths of snakes, one ampoule of adsorbent tetanous toxoid is routinely recommended in all types of snake bites.

4. **Antibiotics**:

   Most of the local effects of snakebites are attributable to cytolytic and other activities of the venom itself, but there is always a risk for infection from fangs, oral cavity of snake or skin of patient.[65] So it is a common practice to use broad spectrum

antibiotics including metronidazole. But recent evidences speaks against the use of prophylactic antibiotic as it was noted in controlled trials[66] and meta-analysis of data that infection rate was very low, antivenin itself has antibacterial activity.[67]

5. **Analgesics**:

Pain in the bitten limb may be severe. Oral paracetamol is preferable to aspirin or other analgesics, as they may cause gastric erosion and persistent bleeding in patients with incoagulable blood.

6. **Sedation**:

Frightened patients occasionally become extremely agitated and even hysterical, simulating coma. Treatment is by reassurance and mild sedation with diazepam 5 mg BID provided patient does not have respiratory depression.

Other Specific Measures:

Elucidation of toxicology and pharmacological actions of snake venom have provided the possibility of employing specific pharmacodynamics approach in the management of poisonous snakebite.

Neuroparalysis:

Neurotoxins produce the neuromuscular block by acting on the post junctional membrane of the motor end plates. This action is similar to curare and can be removed by neostigmine. Neostigmine is given in doses of 0.5 mg I.V. half-hourly for first five doses and thereafter the interval is increased depending upon clinical response. Atropine 0.6 mg usually precedes neostigmine to block muscuranic side effects of latter on the gland cells, smooth muscle and heart.

Best results are obtained by starting neostigmine as soon as neuroparalytic signs and symptoms appear and continuing till there is complete neurological

recovery. A premature discontinuation carries risk of relapse of neuromuscular paralysis. The therapeutic benefit is both in terms of high survival and significantly faster pace of recovery. The neuromuscular block is reversible only as long as block is partial.[68]

Management of Complication of Snakebite:

The complications i.e. shock, acute respiratory failure and acute renal failure are managed on same lines, as that for any other cause.

Mortality and morbidity:

The overall mortality rates for venomous snakebites are low in areas of the world with rapid access to medical care and appropriate antivenom, where mortality rate is < 1%.[69] But the mortality in developing countries is high ranging from 4-28% in various studies and epidemiological reports.[80]

Prevention:

1. Protective clothing, boots, socks, long trousers should be worn when walking in agricultural fields and deep sand. Light should always be carried at night. Particular care should be taken while collecting firewood, moving logs, boulder, boxes or debris likely to conceal a snake and climbing rocks and trees covered with dense foliage.

2. Domestic animals such as chickens and rodent pests attract snakes into human dwellings. Snakes can be discouraged by rodent proofing by removing unnecessary junk and litter and by using solid building material. Various toxic chemical such as naphthalene, sulphur, insecticide e.g. DDT and fumigants are lethal or repellent to snakes.

3. Snakes should never be disturbed, attacked or handled unnecessarily even if they are thought to be harmless species or appear to be dead. Venomous species should never be kept as pets or as performing animals.

Incidence of snakebite can be greatly reduced by taking these simple precautions. Unfortunately these methods are not followed either because of ignorance or practical difficulties.

Prophylaxis:

Venom toxoids (venoids) have been used to immunise farmers at high risk of snake bite. Elsewhere, there has been some progress in producing venoids to protect against Russell viper bite. In this case, rapid development of renal damage, irreversible by antivenom is a strong argument for pre-exposure prophylaxis.

The production and modification of venom antigen by genetic engineering is an exciting new development, which could lead to production of snake venom vaccines.

MATERIALS AND METHODS

1. SOURCE OF DATA:

The information for the study was collected from snake bite patients admitted to BLDEU'S Shri B.M Patil Medical college Hospital and Research Centre, Vijayapur between December 2014 to march 2016.

2. METHOD OF COLLECTION OF DATA:

Information was collected through prepared proforma from each patient. All patients were interviewed as per the prepared proforma and then complete clinical examination was done.

Inclusion criteria :

- ✓ History of snake bite.
- ✓ Patients with presence of fang marks.
- ✓ Patients with one or more clinical manifestation of snakebite like local swelling, haemorrhages, blisterformation, vomiting, abdominal pain, regional lymphadenopathy etc.

Exclusion criteria :

- ✓ Patients with bites other than snakebites.
- ✓ A patient who is a known case of any bleeding disorder.
- ✓ Chronic alcoholics.
- ✓ Individuals with acute or chronic liver disease.
- ✓ Pregnant females.
- ✓ Patients on anticoagulation therapy.

3. TYPE OF STUDY:

Hospital based study

4. SAMPLE SIZE:

- Hospital based study.
- Incidence rate of snake bite in Karnataka = 0.5% [5/1000 population]
- Level of significance = 99%
- Margin of error = 3
- Formula for estimating sample size:

$$n = \frac{Z\alpha^2 \times P \times (1-P)}{d^2}$$

Zα = Z value for α level = 99%

P = incidence rate of snake bite

d = margin of error

- Hence calculated sample size "n" is 36
- Hence in this study 36 cases of snake bite will be included.

Statistical Method

Data were presented using diagrammatic and mean SD,

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. If the p-value was < 0.05, then the results will be considered to be significant. Data were analyzed using SPSS software v.23.0.

Investigations required in this study are routine standardized procedures.

INVESTIGATIONS :

1. Hb%,
2. TC,
3. DC,
4. URINE ROUTINE
5. BLOOD GROUPING AND TYPING
6. ESR
7. FBS/PPBS/ RBS
8. BLOOD UREA
9. SERUM CREATININE
10. BLEEDING TIME-sensitive measure of platelet function.
11. CLOTTING TIME-measure all stages of coagulation in intrinsic system.
12. PROTHRMBIN TIME-screens extrinsic or tissue factor dependent pathway.
13. APPT-screens intrinsic limb of coagulation and tests for adequacy of factor VII, IX, XI, XII, HMWK and PK
14. PERIPHERAL SMEAR
15. ELECTROLYTES
16. ECG
17. LFT

RESULTS

During the study period from December 2014 to March 2016. 36 patients were admitted in. B.L.D.E.U's SHRI B.M PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, Vijayapur, With alleged history of snakebite were included in the study.

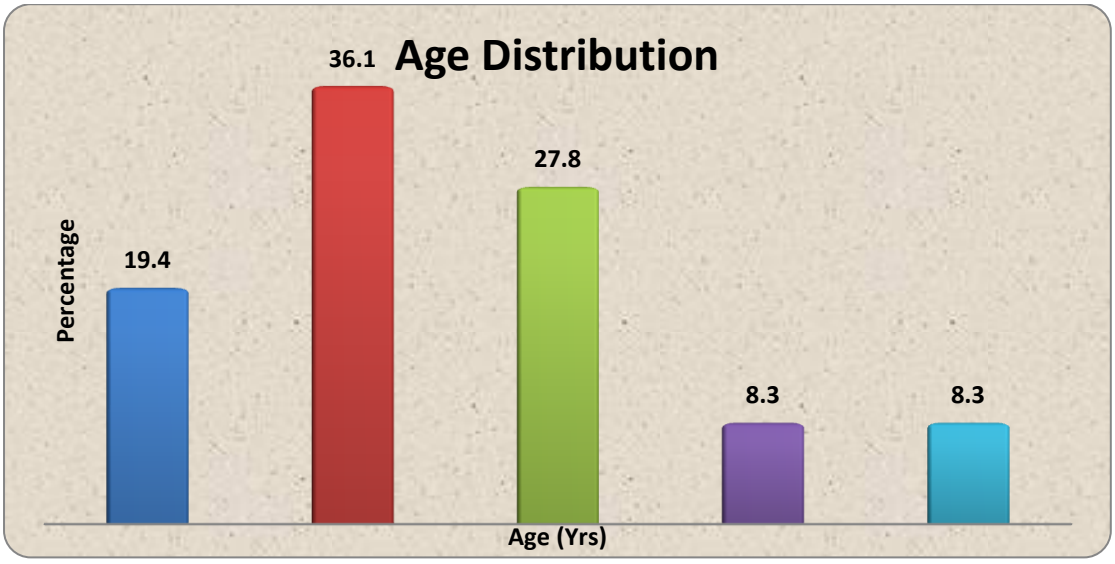
Age wise distribution of snakebites

Table:1

Age (Yrs)	No. of patients	%percentage
16-19	7	19.4
20-29	13	36.1
30-39	10	27.8
40-49	3	8.3
≥50	3	8.3
Total	36	100.0

Diagram: 1

Age wise distribution of snakebites



The snakebites were observed in all age groups. The youngest patient was 16 years old and oldest was 69 years. The majority of patients were between the age group 20 to 29 years, which constituted of 13(36.1%) patients, next commonly affected age group was 30 to 39 years, with 10(27.8%) patients. This higher incidence in these age groups seem to be contributed due to higher occupational activities in these group of people.

Gender wise distribution of snakebites

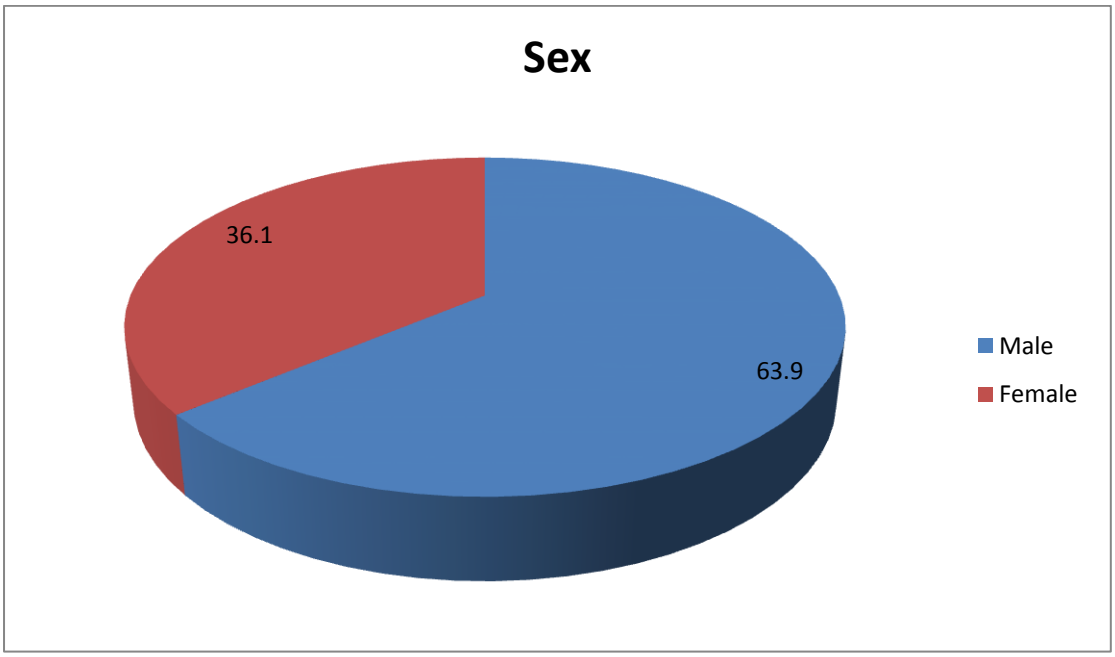
Table:2

Gender wise distribution of snakebites

Sex	No. of patients	%percentage
Male	23	63.9
Female	13	36.1
Total	36	100.0

Diagram:2

Gender wise distribution of snakebites



In our study, the snakebite was more commonly seen in males in 23(63.9%). The male to female ratio was approximately 2:1.

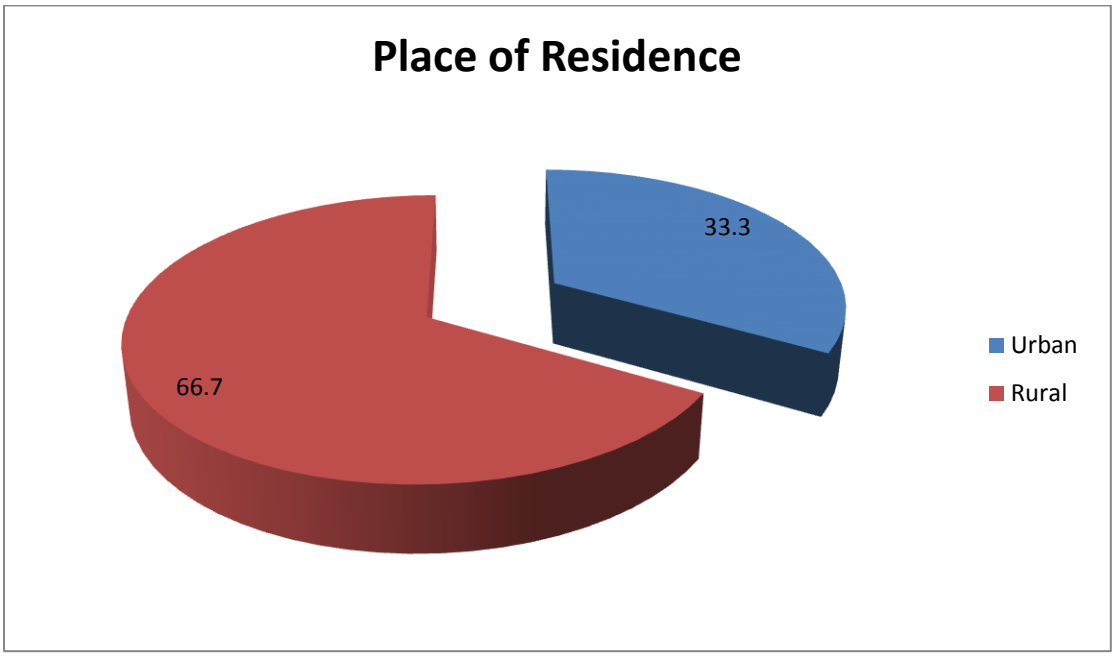
Distribution of snakebites by Place of Residence

Table : 3

Place of Residence	No. of patients	%percentage
Urban	12	33.3
Rural	24	66.7
Total	36	100.0

Diagram: 3

Distribution of snakebites by Place of Residence



In our study snakebite was mainly seen in rural area consisting of 24(66.6%) cases, while the rest 12 (33.3%) were from urban places. This distribution may be explained due to agriculture being the main occupation in rural areas in our country.

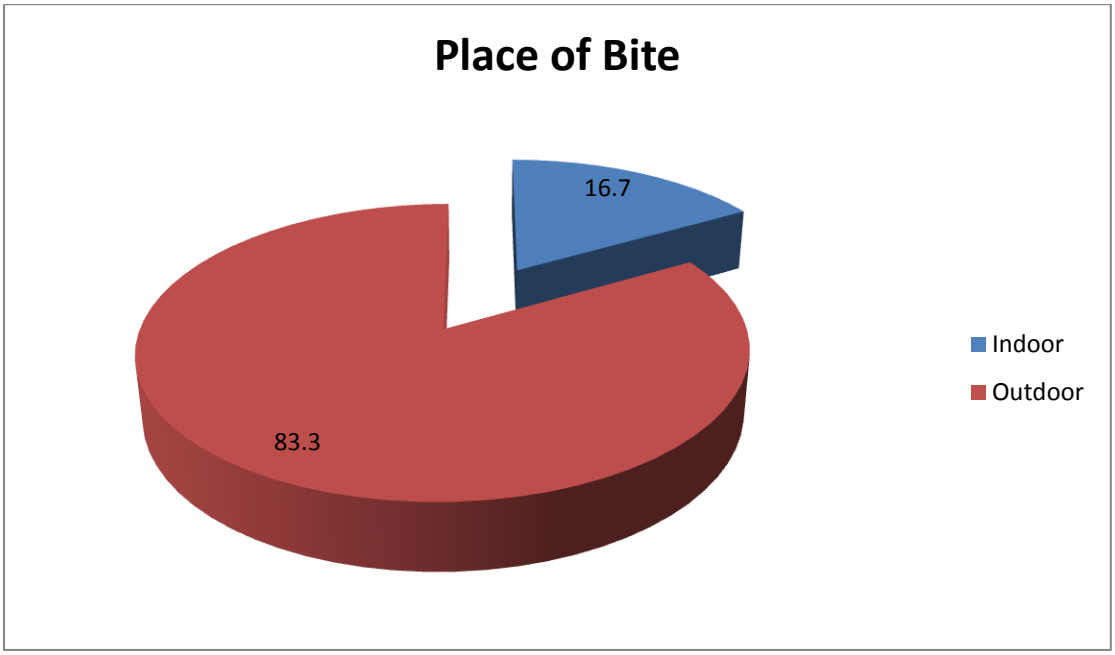
Distribution of snakebites by Place of Bite

Table: 4

Place of Bite	No. of patients	%percentage
Indoor	6	16.7
Outdoor	30	83.3
Total	36	100.0

Diagram: 4

Distribution of snakebites by Place of Bite



Among 36 patients, the bites have occurred predominanty during outdoor activites that is 30(83.3%).

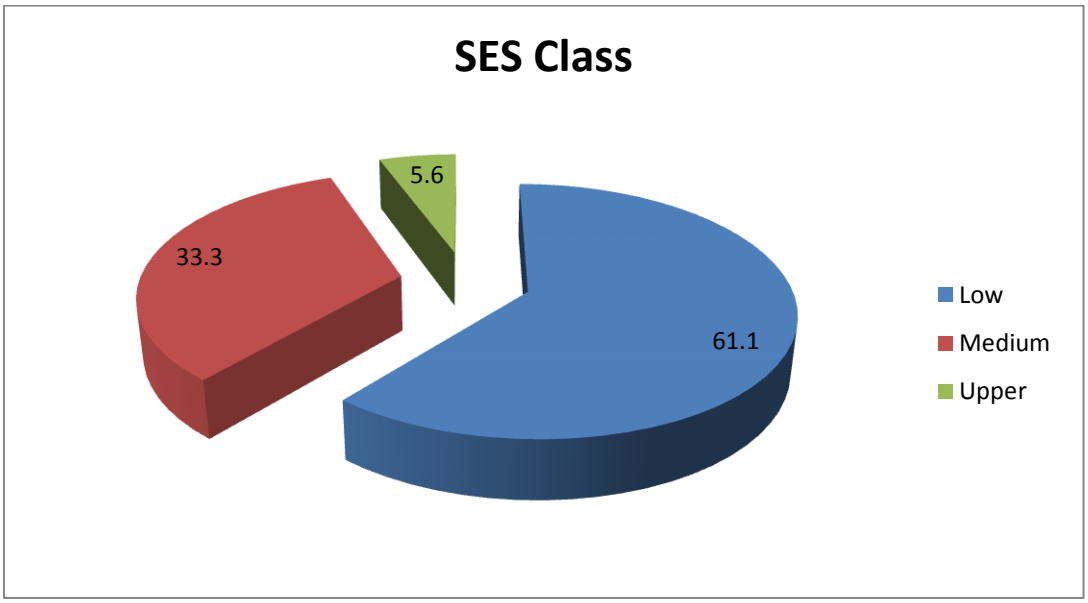
Distribution of snakebites by SES Class

Table: 5

SES Class	No. of patients	%percentage
Low	22	61.1
Medium	12	33.3
Upper	2	5.6
Total	36	100.0

Diagram:5

Distribution of snakebites by Place SES Class



Though the snakebite did not spare any socioeconomic class, the major burden of the disease was borne by low socioeconomic population that 22 (61.1%) patients, followed by middle class 12 (33.3%). Snakebite was very rarely noted in upper socioeconomic class, that is in 2 (5.6%) patients.

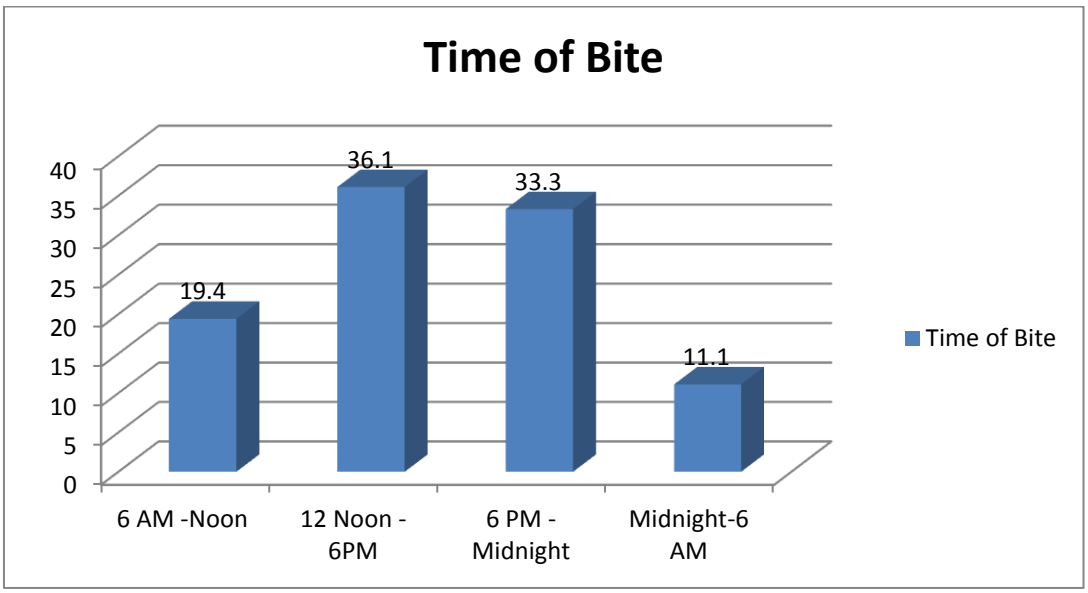
Distribution of snakebites by Time of Bite

Table:6

Time of Bite	No of patients	%percentage
6 A.M. – Noon	7	19.4
12 Noon – 6 P.M.	13	36.1
6 P.M. – Midnight	12	33.3
Midnight – 6 A.M.	4	11.1
Total	36	100.0

Diagram:6

Distribution of snakebites by Time of Bite



In our study, the maximum number of bites were noted between 12 noon to 6 PM that is in 13 (36.1%) patients, corresponding to maximum outdoor and agricultural activity during this time. Between 6 PM to 12 midnight, snakebites were noted in 12(33.3%) patients. Overall maximum bites occurred between 12 noon to midnight, 25 (69.4%) patients out of 36 patients.

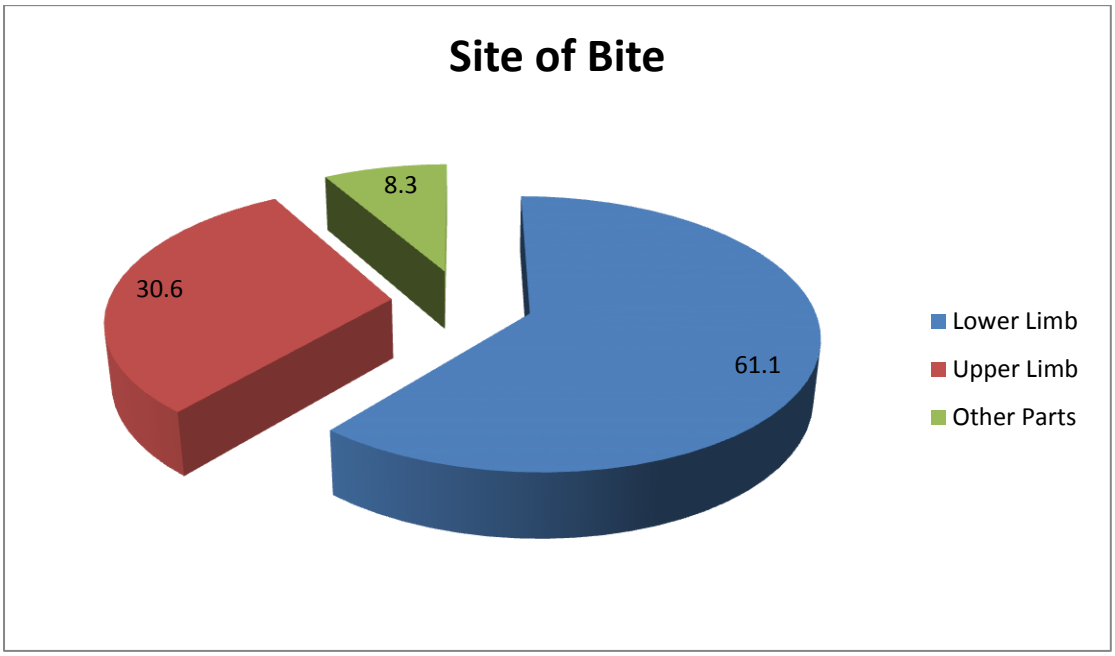
Distribution of snakebites by Site of Bite

Table:7

Site of Bite	No. of patients	%percentage
Lower limb	22	61.1
Upper limb	11	30.6
Other parts	3	8.3
Total	36	100.0

Diagram:7

Distribution of snakebites by Site of Bite



Snakebites were commonly observed on limbs that is in 33 (91.7%) patients. Among the limbs, lower limbs were commonest site noted in 22 (61.1%) patients, followed by upper limb in 11 (30.6%). Bite at unusual sites were noted in 3(8.3%) patients, two on face and one over back, all three bites occurred while patients were asleep.

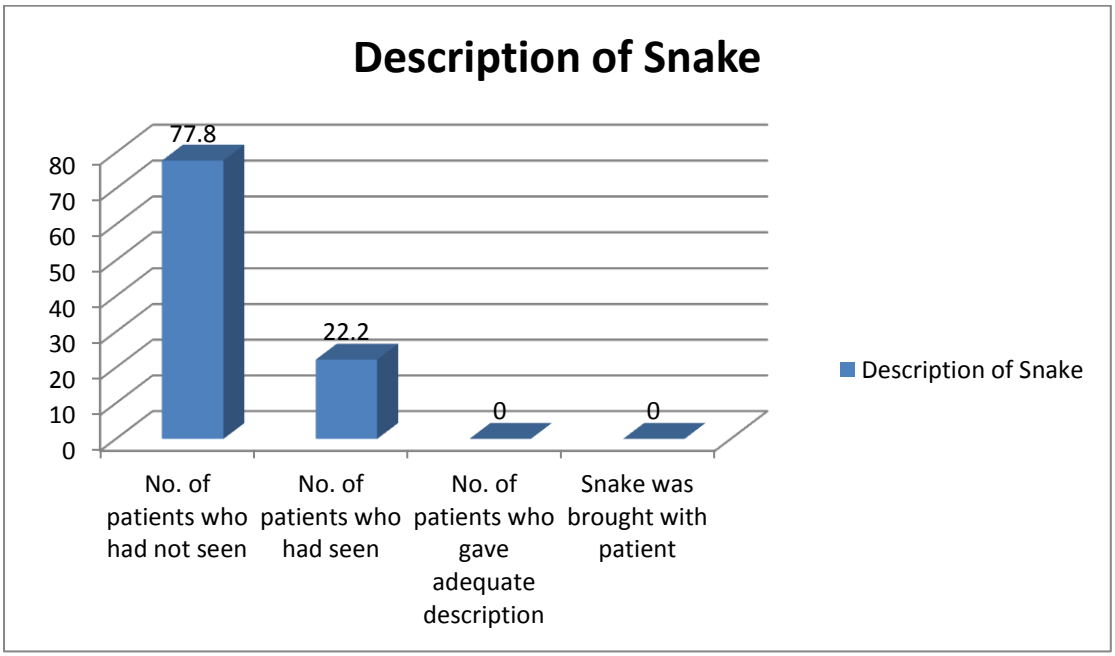
Distribution of snakebites by Description of Snake

Table:8

Description of Snake	No. of patients	%percentage
No. of patients who had not seen	28	77.8
No. of patients who had seen	8	22.2
No. of patients who gave adequate description	0	0.0
Snake was brought with patient	0	0.0
Total	36	100.0

Diagram : 8

Description of snake



Among 36 patients, 28(77.8%) patients had not seen the snake though some information about biting species was available in 8 (22.2%) patients of cases, the information given was inadequate to identify the type of snake. No patient had brought the snake to the hospital for identification.

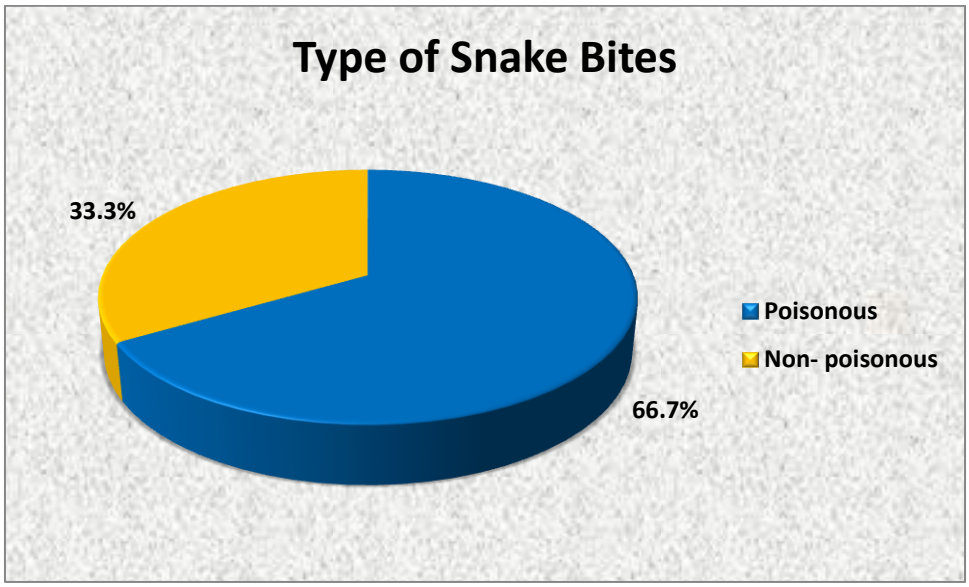
Table:9

Type of Snake Bites

Type of Snake Bites	No.of patients	%percentage
Poisonous	24	66.7%
Non- poisonous	12	33.3%
Total	36	100.0%

Diagram:9

Type of Snake Bites



Among all snakebites, majority of cases were due to poisonous snakebites that is 24 patients (66.6%). In 33.3% of patients the biting snake was nonpoisonous.

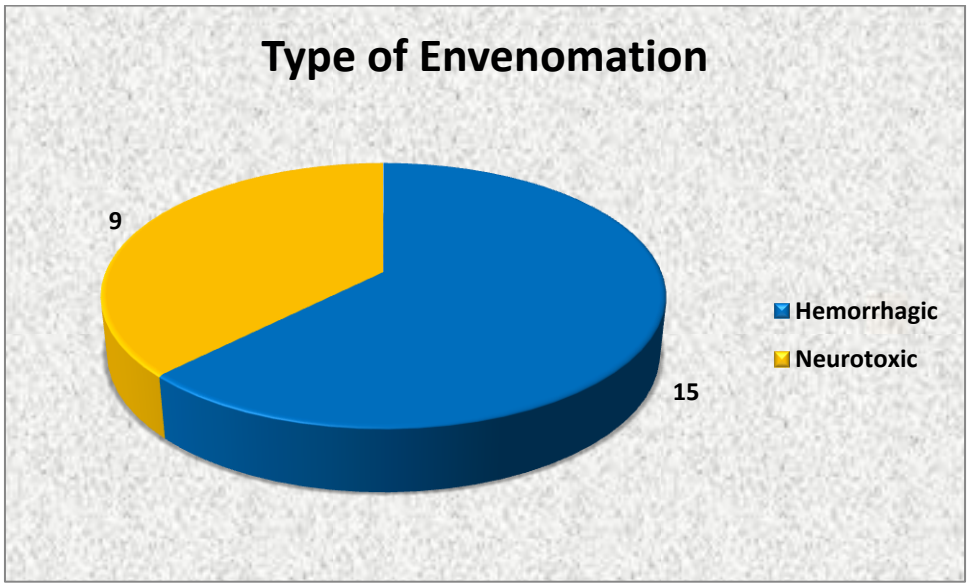
Table: 10

Distribution by type and Envenomation

Type of Envenomation	No.of patients	%percentage
Hemorrhagic	15	41.7%
Neurotoxic	9	25.0%
Cardiotoxic	0	0.0%
Total	24	66.7%

Diagram: 10

Distribution by type and Envenomation



The incidence of venomous snakebites was 24 (66.7%), whereas nonpoisonous constituted only 33.3%. Among poisonous bites, hemorrhagic manifestations 15 (41.7%) were more common than neurotoxic manifestations 9 (25.0%).

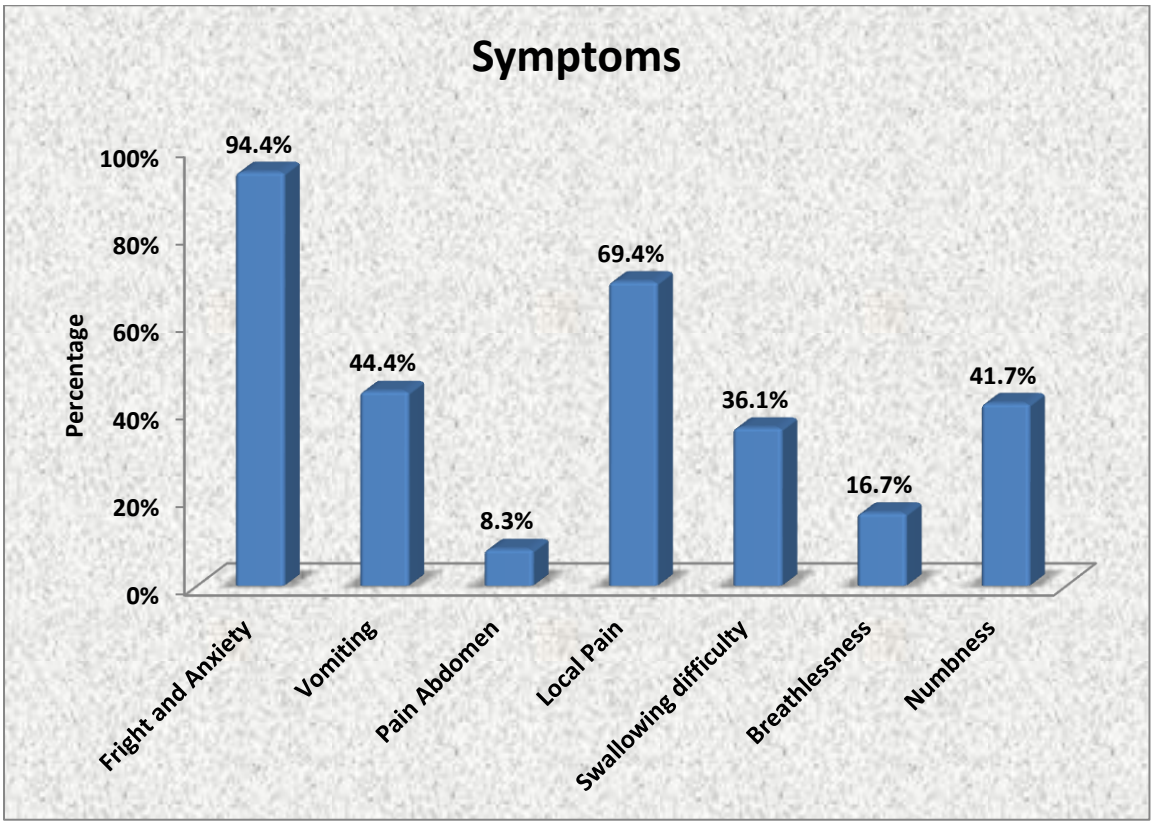
Table:11

Distribution by Symptoms

Symptoms	No. of patients	%percentage
Fright and Anxiety	34	94.4%
Vomiting	16	44.4%
Pain Abdomen	3	8.3%
Local Pain	25	69.4%
Swallowing difficulty	13	36.1%
Breathlessness	6	16.7%
Numbness	15	41.7%

Diagram:11

Distribution by Symptoms



After the snake bite, the predominant symptoms noted were fright and anxiety in 34(94.4%) patients usually developed soon after the bite noted in both poisonous and non poisonous snake bite.

Pain at the site of bite was noted in 25(69.4%) patients,swallowing difficulty 13(36.1%) patients was noted and numbness in 15(41.7%) patients.

Respiratory sympotoms like breathlessness was seen in 6(16.7%) patients. Gastrointestinal symptoms like vomiting, pain abdomen were seen in 16(44.4%) patients and 3(8.3%) patients respectively.

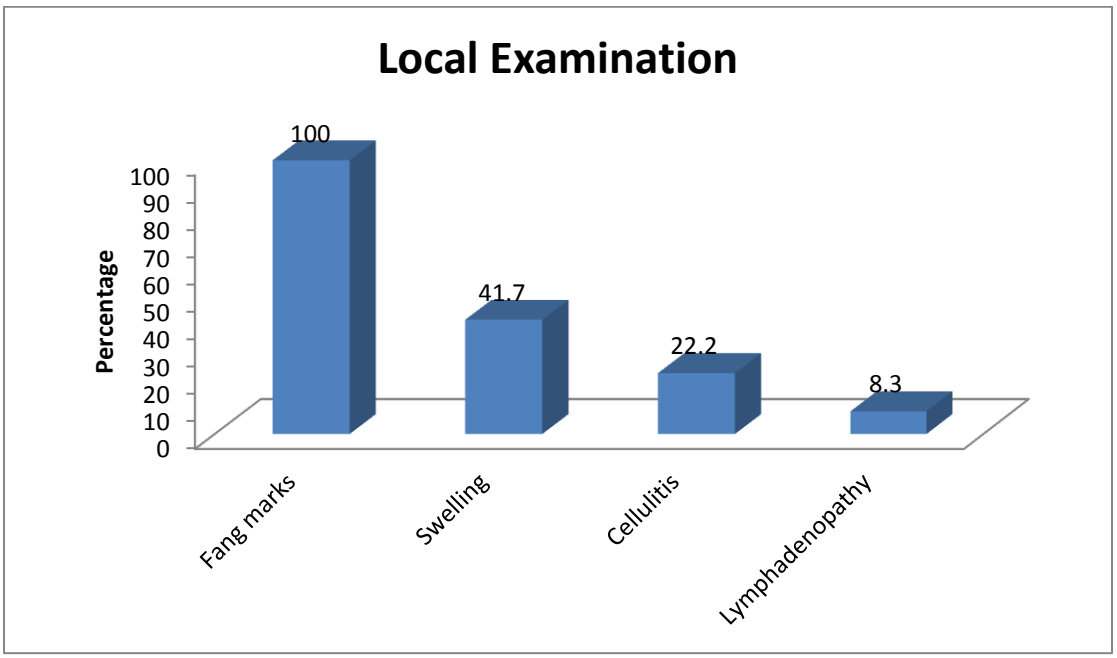
Table: 12

Distribution of cases by Local Examination

Local Examination	No.of patients	%percentage
Fang marks	36	100%
Swelling	15	41.7%
Cellulitis	8	22.2%
Lymphadenopathy	3	8.3%

Diagram:12

Distribution of cases by Local Examination



On local examination of 36 patients brought to hospital all patients presented with fang marks, swelling in15(41.7%) patients was the second most common finding seen on local examination, patients also presented with cellulitis 8(22.2%) patients, least was lympadenopathy in 3(8.3%) patients..

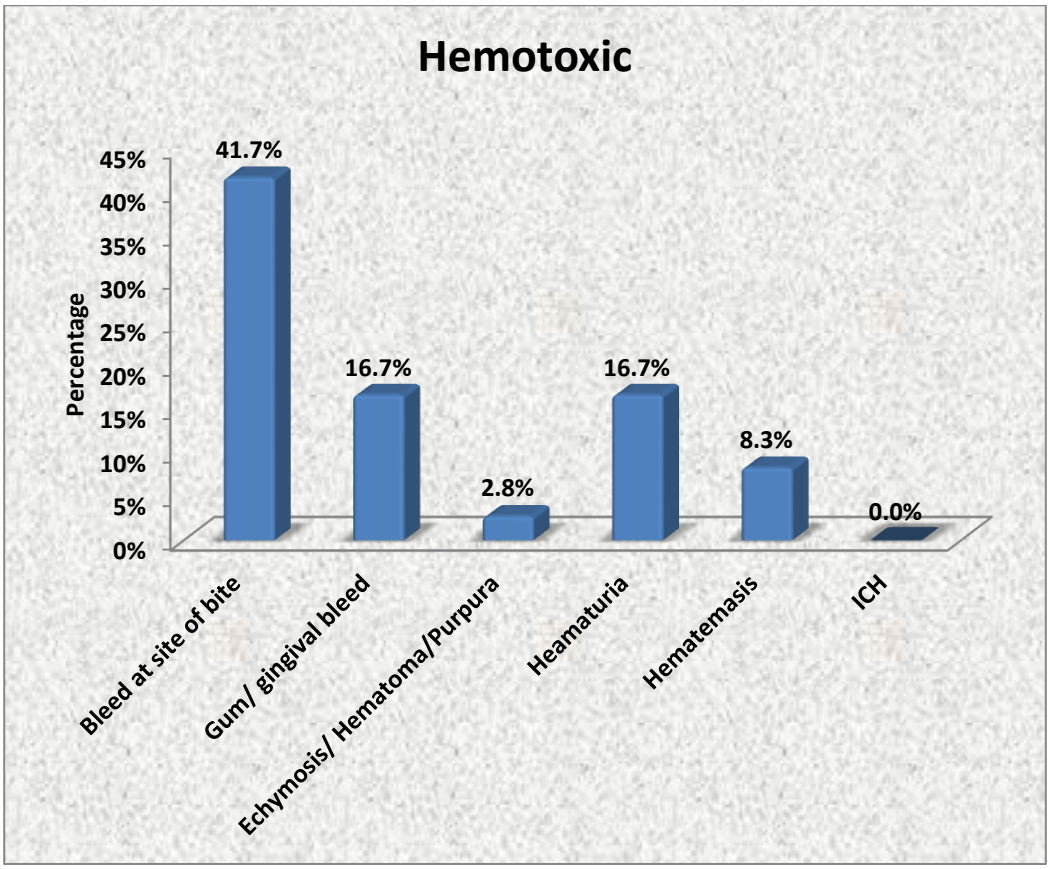
Table:13

Distribution by Hemotoxic manifestation.

Hemotoxic	No.of patients	%percentage
Bleed at site of bite	15	41.7%
Gum/ gingival bleed	6	16.7%
Echymosis/ Hematoma/Purpura	1	2.8%
Heamaturia	6	16.7%
Hematemasis	3	8.3%
ICH	0	0.0%

Diagram: 13

Hemotoxic manifestation.



Out of 15 patients associated with hemotoxic manifestaion, bleed at the site was the most common noted manifestation in 15 (41.7%) patients followed by heamaturia and gum/gingival bleed in 6 (16.7%) patients and hematemais was noted in 3(8.3%) patients then the least one was to present is echymosis/hematoma/purpura 1(2.8%) patients.

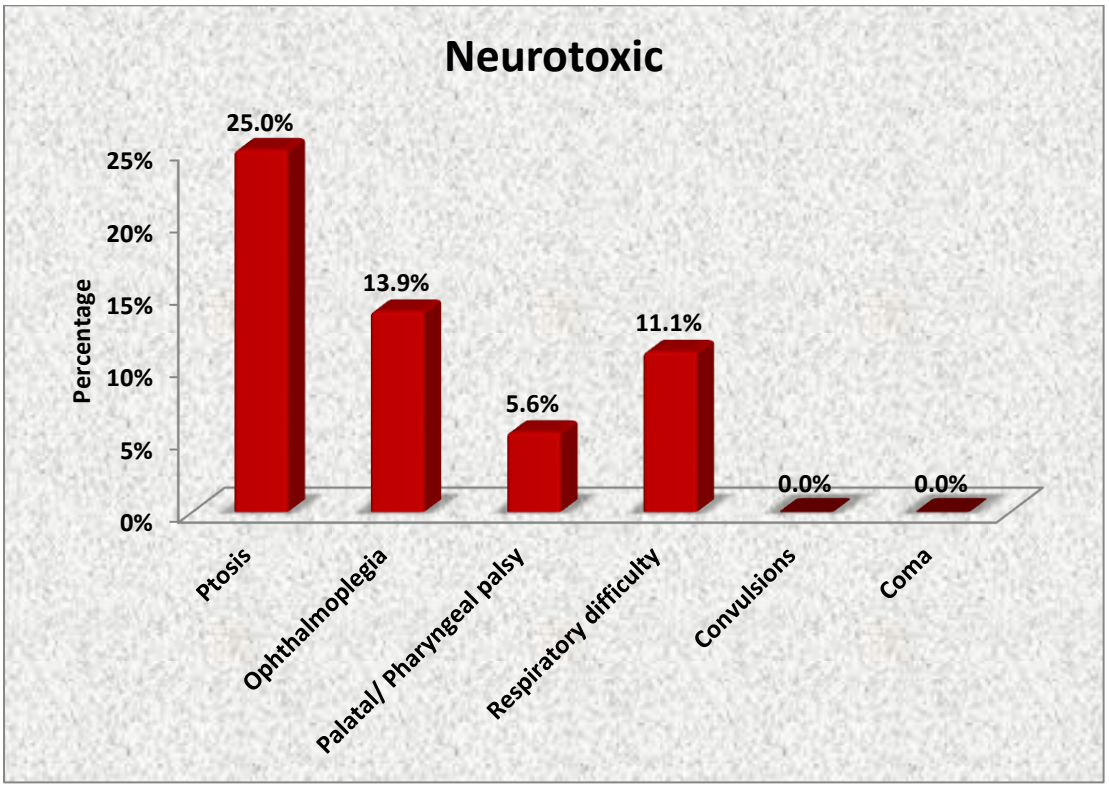
Table:14

Distribution by Neurotoxic manifestation.

Neurotoxic	**No.of patients**	**%percentage**
Ptosis	9	25.0%
Ophthalmoplegia	5	13.9%
Palatal/ Pharyngeal palsy	2	5.6%
Respiratory difficulty	4	11.1%
Convulsions	0	0.0%
Coma	0	0.0%

Diagram:14

Neurotoxic manifestation



Out of 9 patients associated with neurotoxic manifestations, ptosis was the most common noted manifestation, in all 9(25.0%) patients, followed by ophthalmoplegia in 5(13.9%) patients and respiratory difficulty 4(11.1%) patients. palatal/ pharyngeal palsy in 2(5.6%).

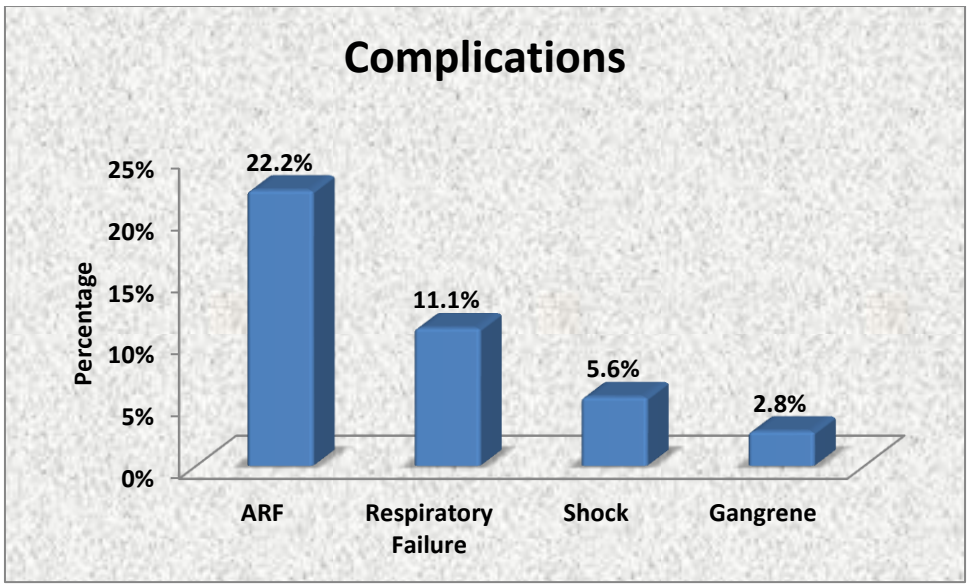
Table:15

Distribution by complications observed

Complications	No. of patients	%percentage
ARF	8	22.2%
Respiratory Failure	4	11.1%
Shock	2	5.6%
Gangrene	1	2.8%

Diagram:15

Complications



Most common complication was acute renal failure, noted in 8(22.2%) patients. 4(11.1%) patients had respiratory failure. Through shock was observed in 2(5.6%) patients. It was mainly attributed to blood loss rather than cardiotoxicity.

Table: 16

Investigations

Investigations	No. of patients	Min	Max	Mean	SD
BT (min)	36	3.48	9.32	6.3	1.7
CT (min)	36	1.2	10.2	6.7	1.9
PT (sec)	36	15	22	16.8	1.8
Hb (gm/dl)	36	7.4	15	11.2	1.9
TLC (C/dl)	36	92	220	114.1	25.3
Blood Urea (mg/dl)	36	20	338	69.0	85.3
S-Creatinine (mg/dl)	36	0.6	11.2	2.5	3.3
Platelet count x 1000/ cumm	36	80	300	190.4	62.3

Bleeding time, clotting time, prothrombin time were seen to be prolonged in patients with hematotoxic manifestation mean BT was 6.3 minutes, mean CT was 6.7 minutes and mean PT was 16.8 seconds.

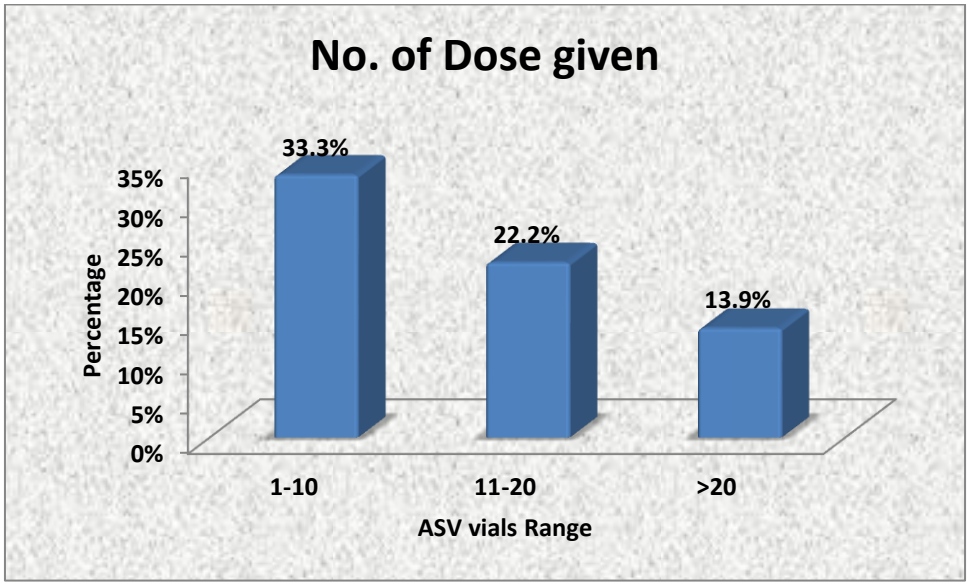
Table:17

No. of Dose given

No. of Dose given		
N	**ASV vials Range**	%
12	1-10	33.3%
8	11-20	22.2%
5	>20	13.9%

Diagram: 16

No. of Dose given



Antisnake venom was administered to patients with all venomous bites, minimum 4 vials and maximum 48 vials were given 12(33.3%) patients recived 1 to 10 vials of antisnake venom, 8(22.2%) patients recived 11 to 20 vials and 5(13.9%) patients recieved more than 20 vials.

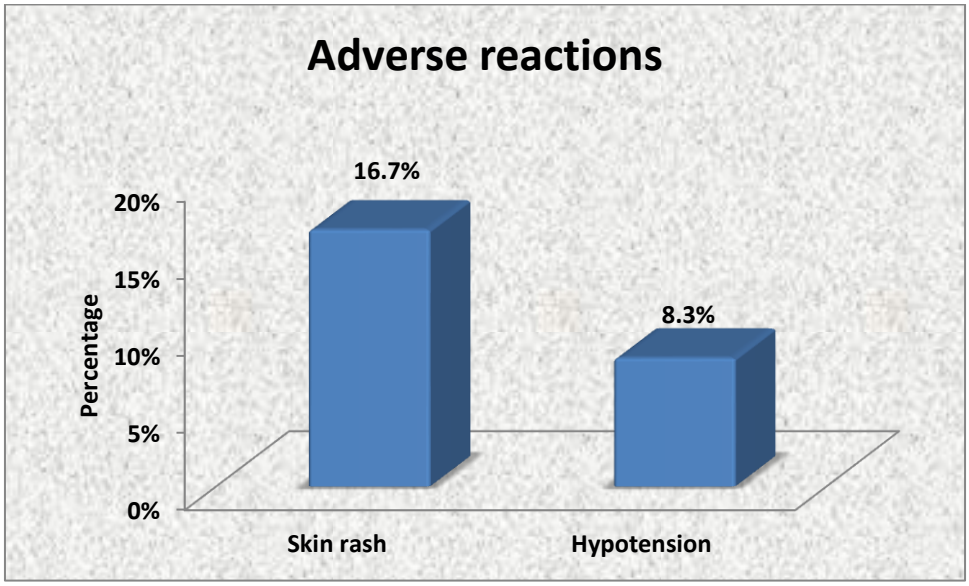
Table:18

Adverse reactions

Adverse reactions	No. of patients	%percentage
Skin rash	6	16.7%
Hypotension	3	8.3%

Diagram:17

Adverse reactions



The ASV was administered immediately after admission to hospital, after sensitivity testing either intradermal or intravenous. In all cases it was administered by intravenous infusion.

Duration of ASV administered ranged from 4 hours to 3 days. Most patients received ASV for 12 hours after subsidence of manifestations, none of the patients required restarting of ASV for recurrence of manifestations.

Adverse reaction to ASV were noted. 6(16.7%) patients had skin rash, 3(8.3%) patients had hypotension. No late reactions were noted to ASV during study period.

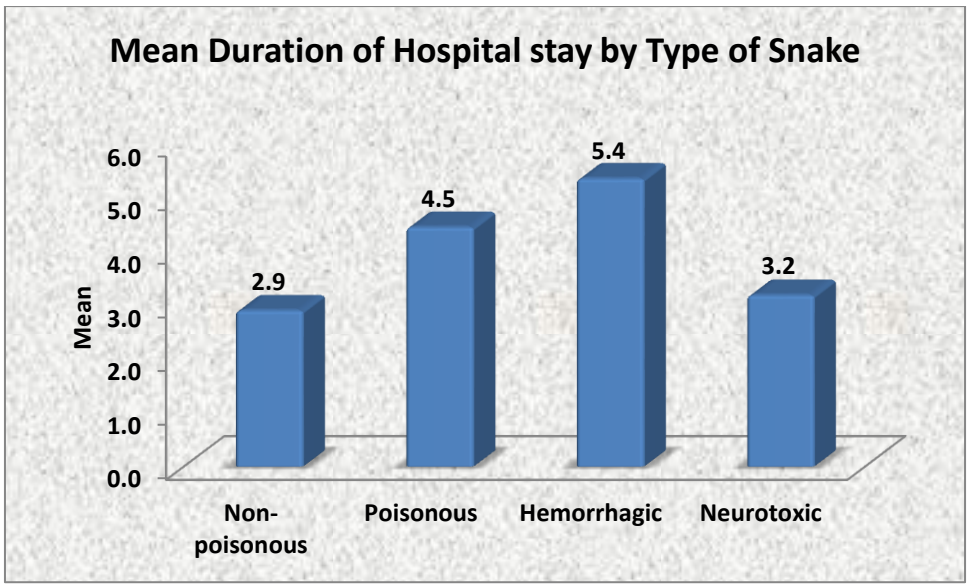
Table:19

Comparison of Mean Duration of hospital stay

Type of Snake	No. of patients	Range	Mean (Days)	SD	p value (with compare to Non- poisonous)
Non-poisonous	12	1-9	2.9	2.4	--
Poisonous	24	1-14	4.5	3.1	0.136
Hemorrhagic	15	1-14	5.4	3.7	0.059
Neurotoxic	9	1-4	3.2	1.3	0.739
Total	36	1-14	3.9	2.9	

Diagram: 18

Comparison of Mean Duration of hospital stay



On an average, patients stayed in hospital for 5days ranging from a minimum of 1 day to maximum of 14 days for treatment. The mean duration for hemorrhagic snake bite is 5 days, and for neurotoxic is 3 days. Type of snake bite manifestations were found to be statistically insignificant with duration of hospital stay.

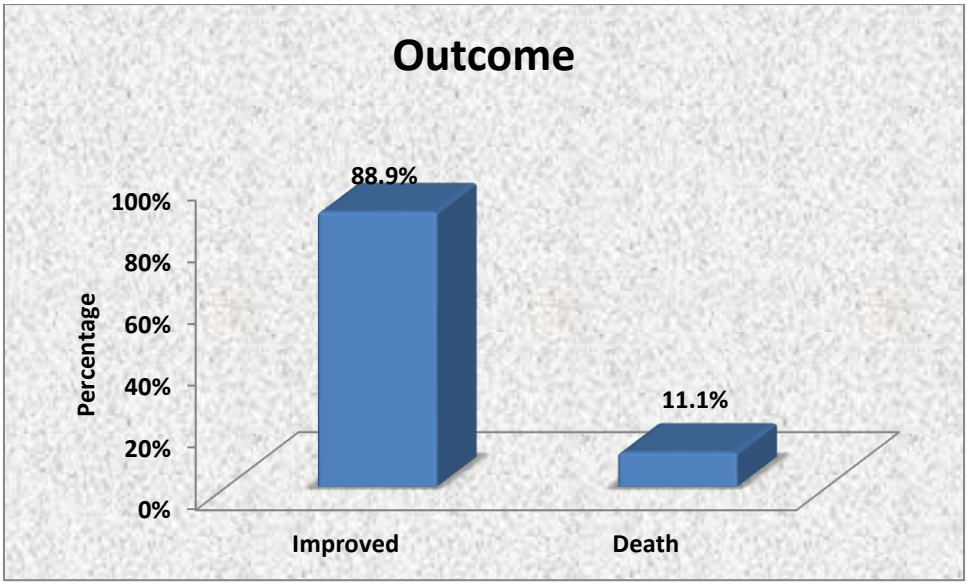
Table: 20

Outcome

Outcome	No. of pateints	%percentage
Improved	32	88.9%
Death	4	11.1%

Diagram:19

Outcome



In this study, out of 36 patients, 32(88.9%)patients were improved. Where as mortality was noted in 4(11.1%) patients, could be due to complication following snakebite.

Table:21

Distribution of snakebites by Mortality

Total		**No.of patients**	**Mortality**	**% (out of N)**
		36	4	11.1
Sex	Male	23	3	13.04
	Female	13	1	7.7
Site of Bite	Lower limb	22	3	31.64
	Upper limb	11	1	9.09
	Other parts	3	0	0.0
Cause of Death	Acute renal failure	8	3	37.5
	Respiratory paralysis	4	1	25
Time lapse between bite and admission	< 24 hours	23	3	13.0
	> 24 hours	13	1	7.6

- ✓ Out of 36cases of snakebite 4(11.1%) patients died.
- ✓ Among 23 male patients, 3 (13.04%) died and out of 13 female patients, 1 (7.7%) died.
- ✓ When the site of bite was in lower limb, mortality was 3 out of 22 (31.64%), and when it was in the upper limb mortality was 1 out of 11 (9.09%).
- ✓ Acute renal failure was the cause of death in 3 out of 8 patients (37.5%) and respiratory failure was the cause of death in 1 out of 4 patients (25%).
- ✓ When the time lapse between the bite and admission was <24 hours, mortality was 3 out of 23 (13.0%) and when it was >24 hours, mortality was 1 out of 13 cases (7.6%).

DISCUSSION

Snakebite is one of the major medical emergency and hazard to life and health of people in the predominantly agricultural country like ours.

In this study, 36 cases of snakebite were reported in our hospital during the period of December 2014 to March 2016. But exact incidence of snake bite cannot be concluded based on these numbers due to different geographical distribution and lack of awareness and preference to traditional healer.

In our study, snakebite was observed in all the age groups. The maximum number of patients were in the age group 10-39 years, they constituted 80% patients, which is comparable to that of Sawai[12] (70.28%) and Nigam P[19] (83.3%). Biyajenee Mohapatra et al[7] also concluded that snakebite and deaths peaked at ages 15-29 years Maximum number of cases were seen in 10 to 39 years age group.

The incidence of snakebite is more common among males shown in our study as well as others. It is obviously due to the increased risk of exposure to the snake bite occupationally.

Snakebite is mainly the disease of the rural population. In the present study, 24 (66.7%) patients were from rural population and 12(33.3%) from urban population. The findings are consistent with finding of Bhat RN[6].

An incidence of 30(83.3%) of snakebite was reported during out door activities in the present study. A similar high incidence was also reported by Bhat RN[6]

The incidence varies in different regions of India due to various factors, main among them being the rainfall, pattern of agricultural activity. Seasonal variation was also noted with high incidence in rainy season. In our study, high incidence was noted between May to October. This is consistent with findings of Bhat RN[6] and Nigam P[19] and Bijayeeni Mohapatra et al[7]. In most studies, the highest incidence corresponds to months of rainy season. When rain water compel the snake to come out of their dwellings.

Our study showed that maximum number of bites i.e., 13(36.1%) occurred between 12 Noon to 6 PM and 12(33.3%) bites occurred between 6 PM to 12 midnight, which is similar to findings of Sawai[12](64%).

Afternoon bites correspond to peak agricultural activity, while evening bites are combination of activity and poor lighting.

In our study, maximum number of bites occurred on lower extremities 22 (66.1%). The lower and upper extremities constituted 33 (91.7%), bite sites suggesting the site of the bite was predominantly determined by accidental or inadvertent contact of the snake during the activities. The incidence in our study is similar as observed by Sawai[12] (97.90%).

The hemorrhagic type 15(41.5%) was found more frequently than neurotoxicity 9(25.0%).which is similar to Nigam P[19], Sarangi A[52], Bawaskal et al[17] and Emam SJ[16] et al who all reported a high incidence of hemorrhagic manifestations. No cardiotoxicity was noted in our study. It is due to the fact that relative prevalence of toxic varieties of snakes could vary in different region of country depending on prevalence and distribution of snakes.

In the present study, bleeding from bite site was most common 15(41.7%), followed by hematuria 6(16.7%), gum bleeding 6(16.7%) and ecchymosis 1 (2.8%). Sarangi A[52] reported bleeding from bite site in (44.4%) which is similar to our study Sarangi et al[52] also reported hematemesis (39%), echymosis (27.7%) and gum bleeding (27.7%). Contrary to above studies, Saini[33] reported hematuria as most common presentation (83.3%) followed by bleeding from bite site (50%), bleeding gum (41.6%), and hematemesis (33.3%).

In our study, all the patients who preinted with neurotoxic manifestations had ptosis 9(25.0%) was commonest manifestation of neurotoxic bites. Frequency of ptosis was 80% in study by Sarangi A[52] & 85% in Nigam P[19] study. It was also noted to be the earliest manifestation.

Palatal and pharyngeal palsy was present in 2(5.6%) patients in our study, while Nigam P[19] and Sarangi A[52] found it in 71.4% and 60% cases respectively.

Ophthalmoplegia was present in 5(13.9%)in present study but Nigam P[19] found it in only 43% patients.

Among 36 patients, 5(13.9%) of our patients reported within four hours to hospital, while only 2% patients came to hospital with in four hours in study by Bhat RN[6]. The delay may be due to less awareness and poor transport facilities.

Analysis of ASV Treatment:

In our study, 24(66.7%) patients were given ASV. In general, the mean dosage requirement ranged between 4 to 48 vials.

Duration for which ASV was administered ranged from 1 hours to 10 days, which is comparable to the study reported by Saini et al[33].

A high number of patients developed adverse reactions to ASV therapy that is 9(25.0%)patients. But severe reactions were noted in only 6(16.7%)patients that is

skin rash, 3(8.3)% patients showed hypotension, that were treted with antihistamine, steroids and IV fluids. No death in the study was attributable to ASV adverse reaction.

Mortality:

In the present study, 4(11.1%) patients died. Three patients expired due to acute renal failure the other one patients expired due to sudden respiratory arrest,compared to Nigam P[19] (45.4%) and Sarangi A[52] (27.2%).

Mortality in relation to time lag between bite and admission:

Nigam P[19] reported 03 deaths all of whom were admitted within 24 hours. Sarangi A[52] reported two death, though they were admitted within 3 hours of bite.

In present study, one patient died though the patient admitted within 3 hours, due to sudden respiratory arrest. One patients who died were admitted after a delay of 24 hours to 14 days of bite.

All the patients, who died were in the age group of 20-39 years. Thus, out of 23 males 3 died and out of 13 females, 1 died. All who died had single bite. Out of them 3 had bite in lower extremity and 1 had bite on the upper extremity. Total number of patients bitten on the lower extremity were 22 (61.1%), out of whom 3 died. Total number of bites on the upper extremity were 11 (30.6%), out of whom 1 died.

CONCLUSION

Snake bite though preventable in principles, remains to be one of the common medical emergency being more frequent in rural agricultural and farm workers. Most common age group is 20-39 years. Males are more prone to the bites Maximum bites were noted in rainy seasons (May to October) and during daytime. Poisonous bites are more common than non-poisonous. In neurotoxic envenomation, ptosis was the commonest and earliest symptom while in hemotoxic envenomation, most common symptoms were bleeding from bite site and hematuria

Antivenom is the boon for snakebite patient if it is given in appropriate time. Though associated with adverse reaction in some patients, it remains safe and effective when given in hospital setup. Average dose of ASV required was 4 to 48 vials. ASV was administered in a duration of minimum 1 day to Maximum of 10 days.

The commonest complications were acute renal failure and respiratory paralysis, shock and gangrene were also noted in some patients. Maximum mortality was observed in patients who were admitted after 24 hours. Early hospitalization and timely ASV was the corner stone in the treatment of snakebite.

Still majority of the patients do not seek medical attention immediately. Most of them visit traditional healers. Thus there is a need for giving health education regarding the snakebites, their toxic effects, effectiveness of hospitalization, ASV therapy in bites and prevention of snakebite by appropriate measures. This will definitely reduce the incidence and complications of snakebites.

SUMMARY

A total of 36 patients of snakebites admitted in B.L.D.E.U's SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, Vijayapur from December 2014 to March 2016 were studied.

- Snakebite occurs at any age but was found to be more common in the range of 20-39 years (60%).
- Snakebite was commonly noted in males 23(63.9%)patients. Male: female ratio is approximately 2:1.
- Snakebite is common in rural setup 24 (66.7%), with agricultural labourers and people from low socioeconomic group being the major sufferers. Majority of snakebites occurred outdoor 30(83.3%).
- The peak incidence was during the month of May to October.
- The majority of bite were on limbs 33(91.7%), the lower limb being more frequent site 22(61.1%), upper limb in 11(30.6%) patients and other parts like face and back 3 patients (8.3%).
- Poisonous snakebite 24 (60.7%) was more common than non-poisonous bite 12 (33.3%). Among 24 poisonous snakebite, 9(25%) presented with neurotoxic manifestations and 15(41.7%) with hematotoxic manifestation.
- Commonest neurotoxic symptom was ptosis, present in 9(25.0%) patients while hemotoxic, commonest symptom was bleeding from bite site and hematuria which was present in 15(41.7%)patients and 6(16.7%) patients respectively.
- Fright and local pain were two most common symptoms in both venomous and non-venomous bites.

- Clotting time, bleeding time were useful bedside tests in predicting hemorrhagic tendency and to monitor response to therapy. Mean BT was 6.3min, mean CT was 6.7min and mean PT was 16.8sec.
- Acute renal failure developed in 8 patients (22.2%) but only 4 patients of them required dialysis. Out of 8 patients, three patients expired.
- Respiratory failure 4(11.1%) was noted, among them, 3 patients recovered well, 1 patient expired due to sudden respiratory arrest.
- Depending upon the degree of envenomation, ASV was given as early as possible after test dose. General supportive measures, corticosteroids, antihistamine were given to prevent the late complications of serum sickness and to prevent the allergic manifestations of venom itself.
- During antivenom therapy, 9 (25.0%) of the patients developed reactions like hypotension, skin rash. They were treated with antihistamines and steroids and IV fluids.
- Neostigmine – Atropine protocol was found very useful in early reversal of neurotoxocity used in all 9 (25.0%) patients with neurotoxic bite.
- Overall mortality was 4(11.1%) out of 36 patients Cause of death in 3 patients was acute renal failure and in 1 patient respiratory failure.
- Patient education regarding snakebite, complication early hospitalization and early use of ASV particularly within 24 hours of venomous snakebite will prevent morbidity and mortality because of snakebite.

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ANNEXURES

ETHICAL CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 574/14
Date 21/11/14
BLDE U's Shri B.M. Patil Medical College

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "clinical and coagulation profile in patients with snake bites in a tertiary care hospital"

—x—x—x—x—

Name of P.G. student Dr Sagar.S.Biradar.
Dept of Medicine

Name of Guide/Co-investigator Dr G.S. Mahishale
Associate prof of medicine

for
DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

CONSENT FORM

Informed consent for participation in dissertation/research

I, the undersigned,_____ S/O D/O W/O_____, aged_____ years, ordinarily resident of _____do hereby state/declare that DR SAGAR S BIRADAR of BLDEU'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR, has examined me thoroughly on _____at _____ (place) and has been explained to me in my own language _____ that I am suffering from _____disease (condition) and this disease/condition mimic following diseases _____.

Further Dr. SAGAR S BIRADAR informed me that she is conducting dissertation/ research title "**CLINICAL AND COAGULATION PROFILE IN PATIENTS WITH SNAKE BITES IN A TERTIARY CARE HOSPITAL**" under the guidance of DR G. S. MAHISHALE requesting my participation in the study. Apart from routine treatment procedure the pre-operative, operative, post-operative and follow-up observations will be utilized for the study as reference data.

DR SAGAR S BIRADAR has also informed me that during conduct of this procedure _____adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available. Further doctor has informed me that my participation in this study help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and

also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

In the view of anticipated / unexpected complications during the course of study, that I will be treated free of cost, as explained by the investigator.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt _____ under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:
Witness: 1.
2.
Date:

Place:

PERFORMA

"CLINICAL AND COAGULATION PROFILE IN PATIENTS WITH SNAKE BITES IN A TERTIARY CARE HOSPITAL"

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Occupation:

Residence:

Presenting complaints with duration:

History of present complaints:

Past History:

History of hypertension

History of diabetes mellitus

Personal History:

Diet/appetite

Sleep

Bladder and bowel habits :

Smoking/Tobacco chewing/Snuff Inhalation

Duration

Number of cigarettes/beedis pack year smoked

Amount of tobacco chewed/snuff inhaled

Alcohol

Duration

Quantity/Frequency

Type

Sexual History

History of multiple sexual partners

Family History:

History of suggestive of Ischemic Heart Disease/hypertension diabetis mellitus

Treatment History :

General Physical Examination

Height :

Weight :

Body Mass Index :

Vitals

PR:

BP:

RR:

Temp:

Hair :

Eyes :

Nose :

Ears :

Oral Cavity :

Neck :

Upper Limbs :

Chest :

Abdomen :

Genetilia :

Lower Limbs :

Skin :

SYSTEMIC EXAMINATION.

- Respiratory System
- Cardiovascular System
- Central Nervous System
- Per abdomen

INVESTIGATIONS

HAEMATOLOGY –

Haemoglobin	gm %
Total WBC counts	Cells/mm^3
Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
ESR	mm after 1 hour

BIOCHEMISTRY–

Random blood sugar	
Blood Urea	
Serum creatinine	

URINE EXAMINATION -

Albumin	
Sugar	
Microscopy	

BLEEDING TIME-sensitive measure of platelet function.

CLOTTING TIME-measure all stages of coagulation in intrinsic system.

PROTHRMBIN TIME-screens extrinsic or tissue factor dependent pathway.

aPPT-screens intrinsic limb of coagulation and tests for adequacy of factor VII, IX, XI, XII, HMWK and PK

PERIPHERAL SMEAR

ELECTROLYTES

ECG

LFT

FINAL DIAGONOSIS

KEY TO MASTER CHART

Sl.no	: Serial number
Ip.no	: In- patient number
M	: Male
F	: Female
R	: Rural
U	: Urban
I	: Indore
O	: Outdoor
S	:Seen
NS	: Not seen
UL	: Upper limb
LL	: Lower limb
D	: Days
+	: present
-	: Absent
+	: Occupation + = Agriculture
-	: Occupation - = Non agriculture
RR	: Respiratory rate
BP	: Blood pressure
BPM	: Beat per minute
CPM	: Cycle per minute
ICH	: Intra cranial hemorrhage
AKI	: Acute kidney injury
V	: Venomous
NV	: Non venomous

H	: Hemotoxic
N	: Neurotoxic
BT	: Bleeding time
CT	: clotting time
PT	: Pro thrombin time
HB	: Hemoglobin
TLC	: Total leukocyte count
LFT	: Liver function test
ECG	: Electrocardiogram
ASV	: Anti snake venom
HP	: Hypotension
SR	: Skin rash
ADR	: Adverse drug reaction
EXP	: Expired
CR	: Completely recovered
IVF	: I V Fluids
TH	: Treatment from traditional healers