"CLINICAL PROFILE OF TOXIC SNAKE BITE CASES IN PATIENTS ADMITTED AT DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI. A ONE YEAR CROSS SECTIONAL STUDY."

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This is to certify that the dissertation entitled **"CLINICAL PROFILE OF TOXIC SNAKE BITE CASES IN PATIENTS ADMITTED AT DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI. A ONE YEAR CROSS SECTIONAL STUDY."** is a bonafide research work done by **Reg. No. BG0115011**

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ABSTRACT

Background and objectives

Toxic snake bit remains an important health hazard in the public, especially in developing countries like India. Though, supportive treatments have increased over the years with advancements in medical field, primary treatment remains with the anti snake venom only, whose regimen and effectivity continous to be a matter of debate. This study was intended to study the clinical manifestations developing after a toxic snake bite among the patients admitted in a tertiary care hospital.

Methodology

This one-year study was done from January 2016 to December 2016 in the Department of Medicine of a tertiary care hospital in North Karnataka. Prior to the commencement, ethical clearance was obtained. A total of 50 patients of toxic snake bite presenting to the medicine department were included. Detailed history and examination was done of any patient of suspected toxic snake bite. Patients were subjected to complete blood count, coagulation profile, and renal profile investigations for further study.

Results

Majority of the patients were males (70%) and the commonest age group involved was those between 20-40 years. Agricultural section of population is the most commonly affected (50%), lower limbs were affected more commonly (84%). Pain (98%) was the most common symptom, followed by local swelling (80%) and active bleeding from site of bite (44%). Most common snakes in the region was found to be Russell’s viper (58%) and saw-scaled viper (20%).

Neurotoxic snakes like cobra (8%) and krait (2%) were encountered less frequently. Cellulitis was the most common complication observed (68%), followed by acute kidney injury (32%). Mortality was seen in only 2% of the cases.

Conclusion and interpretation

In the present study, it was found that hematotoxic snake bite cases are much more common as compared to neurotoxic snake bite cases, resulting in cellulitis and acute kidney injury being the most frequent complications. Mortality is relatively less among the hematotoxic snake bite victims.

Keywords

Toxic snake bite, anti snake venom, coagulation profile, cellulitis.

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INTRODUCTION

Snakes are ubiquitous species of reptiles and their bites, whether poisonous or otherwise are major medical emergencies requiring immediate attention and exercise of considerable judgment. More so in this country, as India is estimated to have highest snakebite mortality in the world.

World Health Organization estimates, place the number of bites to be 83000 per annum, with 11000 deaths.

Most of the fatalities are due to the victims not reaching the hospital in time where definite treatment can be started at the earliest. In India, the awareness in community about occupational risks and the simple measures to prevent these are lacking. In addition to this, people still continue to adopt harmful first aid measures, such as tourniquet application, cutting, suctioning etc.

In the study done by Simpson et al in 2008, it has been revealed that primary care doctors do not treat snakebite patients mainly due to lack of confidence. At the secondary and tertiary level hospitals, multiple protocols are being followed for the administration of polyvalent antisnake venom (ASV), which is mainly based on western textbooks.

In response, the Government of India, Health and Family Welfare department has prepared a national snakebite management protocol to provide doctors and the general public regarding the best possible, evidence based approach to deal with this problem in this country.

India has a very large proportion of its population exposed to snakebites during farming, fishing and herding. This group of population is relatively young, active and crucial for the country's economy. Community education regarding snakes

is strongly recommended for preventing snakebites and also preventing in any delay in initiation of treatment at the right place.

Antivenom is the only effective element of the treatment of systemic envenoming, though may be insufficient in saving a patient's life in critical conditions. Antivenom is relatively expensive, and at times unavailable or short of supply at many primary and secondary hospitals across India. In the absence of antivenom, judicious use of conservative treatment options can help save a patient's life. It is recommended that antivenom should be used only in patients in whom the benefits are considered to exceed the risks of reactions due to antivenom hypersensitivity. Skin/conjunctival hypersensitivity testing does not reliably predict early or late antivenom reactions and hence not recommended. Whenever possible, antivenom should be given by slow intravenous injection or infusion. Epinephrine (adrenaline) should always be kept ready in case of hypersensitivity, though no method has been proved effective in preventing antivenom reactions.

Dialysis, in some cases of Russell's viper, hump nosed viper and sea snake bites which cause direct renal toxicity, can prove life saving measures.

Fasciotomy should be performed only when hemostatic abnormalities have been corrected and clinical features of intracompartmental syndrome are present.

OBJECTIVE

1) To study clinical profile of various types of toxic snake bite patients admitted at Dr. Prabhakar Kore, charitable hospital, Belagavi.
2) To study various complications and outcome of toxic snake bites.

REVIEW OF LITERATURE

History:

Man's association, fear and hatred of snake is as ancient as history, land. Shiva has cobra in his neck as ornament. Lord Vishnu rests on snake in the middle of an ocean. King Parixit, the grandson of Pandav was bitten by snake and was told to have just a few days to live before succumbing to snake venom.

The written legend of Eden is assumed to date from about sixth century B.C. The symbol of two inter wined serpents was used in Babylonia to connote wisdom and healing. Same has been taken as its symbolic by Indian Medical Association. The knowledge about snake venom also dates back in to history. "Suchikbhasma" is an ancient preparation of cobra venom used as a cardiotoxic agent.

Antivenom treatment for snake bite was first introduced by Albert Calmette at the Institute Pasteur in Siagoin the 1890s. Holden and Kellaway (1932) described the action of snake venom on the neuro muscular junction which led to its trial in artificial respiration in the treatment of neuromuscular block.

In India had mentioned that anticholinesterase given very good results in Elapidae bites but no firm base was there. Banerjee et. al[1] studied neostigmine in elapidae bite and all patients showed dramatic response in neuroparalysis. When used in early stages, neostigmine reverse the neuromuscular block produced by snake venom and came to be used clinically.

Use of anticoagulants like heparin came in vogue in the treatment of defibrillation caused by snake venom. Later showed that heparin could increase the lethal dose of E. carinatus venom by 20 times when given simultaneously.

Epidemiology

The fundamental problem in India is that snake bite treatment remain domain of traditional, herbal on ayurvedic practitioner and unfortunately some time with 'Tantriks'. Majority of snake bites do not seek modern medicine on treatment.

WHO has strongly recommended that snake bite should be made specific notifiable disease in all countries.

Morphological features of snakes[2]:

Snakes are poikilothermic animals having no appendages. The body is covered with scales and have no legs. The eyes consists of a singular cornea without eyelids. Hearing is conducted through the ground. The upper and lower jaws do not articulate as in man, and this allows wide opening of the mouth, enabling it to swallow animals 3 to 4 times its size. They have a poor vision. They are short sighted and vision is restricted mainly to moving objects.

The venom apparatus of snake consists of three important structures –

i. The venom glands

ii. The ducts and

iii. The fangs

i. The venom glands

They are highly modified maxillary salivary glands. The venom is modified saliva which serves the dual purpose of defense mechanism, killing the prey and initiating digestion. Snakes cannot chew; they swallow the prey once it is dead. The toxin of snake venom is the third most powerful toxin in the world, next to botulism toxin and tetanus toxin. The minimum lethal dose of purified Cobra neurotoxin is 0.4

mg- 0.6 mg per kg body weight compared to 10 mg per kg body weight for sodium cyanide.

ii. The ducts

The ducts convey the venom from the glands to a papilla which opens at the base of the fang.

iii. The Fangs

The fangs are modified teeth of the upper jaw (maxillary teeth). These are three different types of venomous dentition.

a) Opisthoglyphodonts or "back fanged"- The fangs are in the rear of the mouth and are grooved posteriorly. They are ill adapted for piercing human skin and majority of the venom is spilled.
b) Proglyphodonts or "front fanged"- the fangs are anteriorly situated and mobile. They are turned outwards when the snake opens its mouth for a bite.

The venom apparatus if the vipers is the most advanced and effective. The maxillary bone is so shortened that it is wider then its length. The two rows of maxillary teeth are replaced by two huge fangs which are tubular with a central canal. The fang may be 1 inch in length or even longer. The mouth opens by 180^0 and the fangs move out to point right at the tip of its mouth. When the snake closes its mouth for a bite the muscles of the jaw squeeze the venom glands and the venom is injected into the tissue of the victim with tremendous force, the whole apparatus acting like a high pressure syringe.

Fang replacement: to keep the fangs sharp and functional they are constantly being replaced once every 10-15 days on alternative sides. The snakes therefore may have only one fang and very often a single fang mark is seen on examination.

Identification of snakes[2]

Since as many as 90.00% of snakes are nonpoisonous, it is very important to distinguish between poisonous and nonpoisonous snakes. The type of snake can be identified by

i. Direct examination of a killed specimen.

ii. Patients description of the snakes and identification from specimen or coloured photographs.

iii. Knowledge of common native names of snakes.

iv. Knowledge of symptomatology and clinical manifestation of different snake bites.

The four common poisonous snakes of India are the Cobra, Krait, Russell's viper and E. carinatus.

INDIAN COBRA: Monocled (Naja Naja Kaouthia)

Spectacled (Naja Naja Naja)

The two snakes are similar but the monocle cobra has a single ring design on its hood while a spectacled cobra has a pair of connected rings. The length ranges from 1 to 2 meters. The colour varies from black to dark brown to yellowish white, with ragged bands of white or yellow. The bands are thin and may not be noted. The head is rounded with large scales. The third supralabial touches both the eyes and the nostril. The hood characterizes cobra. They are very active during rainy season prefer to move at night.

KING COBRA (Ophiophagus Hannah)

The largest poisonous snake in the world and may measure upto a maximum of 6 meters. It is yellowish, olive green or black in colour, with distinct light cross bands mainly on the forebody.

It is found in dense forests of Western Ghats, Nigiris, Himalayas, Bengal and Andamans. Their venom glands are huge with enough venom to kill an elephant.

KRAITS: There are two type of Kraits

1. Common Krait
2. Banded Krait

The common Krait (Bungaerus caeruleus): It is found all over India, including Karnataka, and is about 1 meter in length with a maximum of 1.75 meters. Its head is rounded with large scales on the dorsum. There are four infralabial scales, the fourth being the largest. The body colour varies from dark blue black to bluish gray. It has 30-40 thin inconspicuous white bands across its back.

The Banded Krait (Bungaerus fasciatus): It is found mainly in Eastern India and is a little larger in length 1.5 meters with broad conspicuous yellow and black bands over the body. Kraits are very active at night and often enter human houses.

RUSSELL'S VIPER (Vipera russelli)

They are heavy, thick, rough scaled snakes with an average length of 1 meter. The maximum length is 1.8 meters. The body is brown to yellow in colour with dark, round spots forming a characteristic chain pattern on its dorsum. The head is triangular with small scale. Found all over India. It is highly poisonous and is found in the fields.

SAW SCALED VIPER (Echis carinatus)

It is small in size with a length of 30-80 cms. It is highly active and bites vehemently. It has a small triangular head with small scales. The body is relatively stocky, yellowish brown to grey in colour, with a conspicuous dark zig-zag pattern on the back. The head has a characteristic cross or lance mark, "Trishul", at its centre. It

is found in fields, dense thickets, thorny buses, hay stacks, amongst dried cow-dung cakes, dry timber, garbage heaps and underneath the stones.

SNAKE VENOMS [3, 4, 5, 6, 7,8]

Venom composition:

Modern techniques of "venomics" (proteomics as applied to venoms) such as high performance liquid chromatography, SDS- PAGE ans mass spectrometry are revealing the enormous complexity of snake venoms. More than 90% of snake venom (dry weight) is protein. Each venom contains more than a hundred different proteins. Enzymes (constituting 80-90% of viperidae and 25-70% of elapid venoms), non-enzymatic polypeptide toxins, and non-toxic proteins such as nerve growth factor. Nonprotein ingredients include carbohydrates and metals (often part of glycoprotein metalloprotein enzymes), lipids free amino acids, nucleosides, and biogenic amines such as serotonin and acetylcholine.

Venom enzymes:

These include digestive hydrolases (proteinases, exopeptidase, endopeptidases, phospholipases), hyaluronidase (spreading factor), and activators or inactivators of Physiological processes, such as kininogenases. Most venoms contain L- amino acid oxidase (containing a riboflavin 5'- nucleotidase, DNAase NAD – Nucleosidase, phospholipase A_2, and peptidases.

Zinc Metalloproteinases/ Metalloproteases (metalloproteinase- like disintegrin- like, cysteine-rcih) haemorrhagins (snake venom metalloproteinases, SVMPs): degrade basement membrane components, leading to endothelial cell damage and contributing to spontaneous systemic bleeding.

Procoagulant enzymes:

Venoms of Viperidae and some Elapidae and Colubridae contain serine proteases and other procoagulant enzymes that are thrombin- like or activate factors V, X, prothrombin and other clotting factors. These enzymes stimulate blood clotting with formation of fibrin in the blood stream. Paradoxically, this process results in incoagulable blood because most of the fibrin clot is broken down immediately by the body's own plasmin fibrinolytic system. Sometimes within 30 minutes of the bite, the levels of clotting factors have been so depleted that the blood will not clot("consumption coagulopathy"). Some venoms contain multiple anti-haemostatic factors. For example, Russel's viper venom contains toxins that activate factors II(prothrombin), V, X, IX and XIII, fibrinolysis and protein C and cause platelet aggregation, anticoagulation and haemorrhage.

Phospolipases A_2 (lecithinase):

are most widespread and extensively studied of all venom enzymes. They damages mitochondria, red blood cells, leucocytes, platelets, peripheral nerve endings, skeletal muscle, vascular endothelium, and other membranes, producing presynaptic neurotoxic activity, cardiotoxicity, myotoxicity, necrosis, hypotension, haemolysis, haemorrhage, plasma leakage (oedema- induction), opiate-like sedative effects and autopharmacological release of histamine and other autacoids. They are anti-coagulant, either by hydrolyzing plasma or platelet membrane phospholipids, or by interacting with different coagulation factors.

Acetylcholinesterases: although found in most elapid venoms, may cause fasciculation.

Hyaluronidase: promotes the spread of venom through tissues by increasing permeability but can also contribute to tissue damage.

Proteolytic enzymes (metalloproteinases, endopeptidases or hydrolases) and polypetidecytotoxins ("Cardiotoxins") : increase vascular permeability causing oedema, blistering, bruising and necrosis at the site of the bite.

Venom polypeptide toxins (neurotoxins)

Postsynaptic (α) neurotoxins such as α-bungarotoxin and corbotoxin, consists of 60-62 or 66-74 amino acids. They bind to acetylcholine receptors at the motor endplate. Presynaptic (β) neurotoxins such as β-bungarotoxin, and taipoxin, contain 120-140 amino-acids and a phospholipase A subunit. These release acetylcholine at the nerve endings at neuromuscular junctions and then damage the endings, preventing further release of transmitter.

Variation in venom composition within species:

The composition of snake venoms, and hence their antigenicites in inducing specific neutralizing antibodies during antivenom manufacture, varies greatly between different species, but also within an individual species, as the snake matures (ontogenic variation), seasonally, between sexes, and throughout the geographical range[7]. The two important implications of venom variation are 1- envenoming by juvenile and adult snakes may cause qualitatively different clinical effects and 2- envenoming by a snake in one part of its geographical range may not be neutralized by an antivenom raised using venom from another part of the range.

Quantity of venom injected at a bite, "dry bites"

This is very variable, depending on the species and size of the snake, the mechanical efficiency of the bite, whether one or two fangs penetrated the skin and whether there were repeated strikes. The average dry weight of venom injected at a strike is approximately 60 mg in *N. naja*, 13 mg in *E. carinatus* and 63 mg in *D. russelli*. In the case of *D. siamensis* in Myanmar, the total yield of desiccated venom

extracted by milking ranged from 21-268 mg(127 +/- 13 mg), mean +/- 1 SE) in adults (mean total length 111 +/- 1.8 cm) and 8-79 mg (45 +/- 7 mg) in juveniles (mean total length 79 +/- 2.8 cm). Adults inject 45% of the venom glands content in the first bite[9]. Either because of mechanical inefficiency or the snake's control of venom discharge, a proportion of bites by venomous snakes does not result in the injection of sufficient venom to cause clinical effects. About 50% of bites by Malayan pit vipers and Russell's vipers, 30% of bites by cobras and 5-10% of bites saw-scaled vipers do not result in any symptoms or signs of envenoming. Snakes do not exhaust their store of venom, even after several strikes, and they are no less venomous after eating their pray[10].

Variations in venom composition within individual species of snakes:

Although large snakes tend to inject more venom than smaller specimens of the same species, the venom of smaller, younger vipers may be richer in some dangerous components, such as those affecting haemostasis because venom composition varies (ontogenically) with the snake's age and hence size[11].

Pathophysiology of human envenoming

Local envenoming

Swelling and bruising result from increased vascular permeability attributable to venom endopeptidases, metalloproteinase hemorrhagins, membrane- damaging polypeptide toxins, phospholipases, and endogenous autacoids released by the venom, such as histamine, 5-HT, and kinins. Local tissue necrosis results from the direct action of myotoxins and cytotoxins, and ischemia caused by thrombosis; compression of blood vessels by first-aid methods such as tight tourniquets; or by swollen muscle within a tight fascial compartment. Myotoxins damage the muscle cell plasma membrane directly. Most are PLA2s, either enzymatically active (aspartate-49) or

enzymatically inactive (lysine-49). Cobra cardiotoxins are low-molecular weight polypeptides with cytotoxic action.

Hypotension and shock

After viper bites, leakage of plasma or blood into the bitten limb and elsewhere or massive gastrointestinal haemorrhage, may cause hypovolemia. Vasodilation, especially of splanchnic vessels, and a direct effect on the myocardium may contribute to hypotension. Profound hypotension is a part of autopharmacological syndrome that occurs within minutes of bites by D. siamensis, D. russelli, and Australasian elapids, attributable to oligopeptides (ACE inhibitors and BPPs) and vasodilating autacoids. In some cases, direct myocardial effects of venom may be suggested by electrocardiographic (ECG) changes and autopsy findings of epicardial or endocardial haemorrhages and histopathological evidence of cardiac myonecrosis.

Bleeding and blood clotting disturbances

Snake venoms affect haemostasis in several ways. Procoagulant enzymes activate intravascular coagulation, producing consumption coagulopathy and incoagulable blood. Procoagulants of Colubridae, Australasian Elapidae, Echis and Daboia species activate prothrombin, whereas those in venoms of Daboia russelli and D. Siamensis also activate factors V and X. Thrombin –like enzymes in pit-viper venoms have a direct action on fibrinogen. Some venoms cause defibrinogenation by activating the endogenous fibrinolytic (plasmin) system. Anticoagulant activity is attributable to venom phospolipases. Platelet activation or inhibition results in thrombocytopenia in victims of *Trimeresurus* and *Viridovipera* species. Calloselasma *rhodostoma, Denagkistrodon acutus*, and *Daboia siamensis*. Potentially lethal

spontaneous systemic bleeding is attributable venom haemorrhagins (Zn metalloproteases).

Complement Activation:

Elapid and some colubroid venoms activate complement via the alternative pathway ("Cobra venom factor" is the snake's C3b), whereas some viperidae venoms activate the classic pathway. Complement activation affects platelets, the blood coagulation system, and other humoral mediators.

Neurotoxicity

Neurotoxic polypeptides and PLA2s of snake venoms cause paralysis by blocking transmission at the neuromuscular junction. Patients with paralysis of bulbar muscles may die of upper airway obstruction or aspiration, but the most common mode of death after neurotoxic envenoming is respiratory paralysis. By prolonging activity of ACh at neuromuscular junctions, anticholinesterase drugs may improve paralytic symptoms in patients bitten by snakes with neurotoxins that are predominantly postsynaptic in their action (e.g. cobras and Australasian death adders [genus Acanthophis]). Some patients bitten by elapids of vipers are drowsy in the absence of respiratory or circulatory failure. This is unlikely to be an effect of neurotoxic polypeptides, which do not cross the blood- brain barrier.

Myotoxicity

PLA_2myotoxins and metalloproteinases are principally responsible. They are present in venoms of most species of sea snakes, many terrestrial Australasian elapids, some species of krait (Bungarus), and Viperidae, such as the Sri Lankan Russell's viper(D. russelli). Release into the bloodstream of myoglobin, muscle enzymes , uric acid, potassium, and other muscle constituents is an effect in humans of presynaptic

neurotoxins. Patients may die of bulbar and respiratory muscle weakness, acute hyperkalaemia, or acute kidney injury.

Acute kidney injury

A wide range of renal histological changes has been described after snakebite. Acute tubular necrosis is the most common, but proliferative glomerulonephritis, interstitial nephritis, toxic mesangiolysis with platelet agglutination, fibrin deposition , ischemic changes and distal tubular damage ("lower nephron nephrosis), suggesting direct venom nephrotoxicity attributable to venom PLA_2 and metalloproteases, and bilateral renal cortical necrosis with subsequent calcification are also reported. Antivenom can cause immune-complex-mediated kidney injury. Acute tubular necrosis may result from prolonged hypotension and hypovolemia, DIC, direct toxic effect of venom on the renal tubules, haemoglobinuria, myoglobinuria and hyperkalaemia. Russell's viper venom produces hypotension, DIC direct nephrotoxicity, and in Sri Lanka and India, intravascular haemolysis and rhabdomyolysis. In Burmese patients envenomed by Russell's vipers (D. siamensis), high urinary concentrations of β2 –macroglobulin, retinal binding protein and N-acetyl glucosaminidase suggested failure of proximal tubular reabsorption and tubular damage. High plasma concentrations of active renin suggested that renal ischemia with activation of the renin-angiotensin system was involved in development of renal failure. A massive but transient capillary and glomerular leak of albumin was an early sign of oliguric renal failure. Snake venom-induced DIC may result in deposition of fibrin on vascular endothelium that has been activated by, for example, metalloproteinases, producing microangiopathic hemolysis. Although the clinical picture is reminiscent of haemolytic uraemic syndrome(HUS) and thrombotic

thrombocytopenic purpura (TTP), there is no evidence of depleted ADAMTS-13 levels and therefore no justification for cryo supernatant plasmapheresis.

Generalized increasein capillary permeability

Venoms of some viperidae, such as D. russelli and D. siamensis, can cause a generalized increase in vascular permeability, resulting in pulmonary edema, serous effusions, conjunctival, periorbital, facial and retinal edema, bilateral parotid enlargement, albuminuria and haemoconcentration. The likely cause is metalloproteases that damage vascular endothelium.

Saw-scaled vipers do not cause renal failure whereas Russell's viper and hump-nosed pit viper do. Russell's viper can also manifest with neurotoxic symptoms in a wide area of India which can cause confusion. Further work is necessary to determine the areas in which this species exists. The neurotoxic symptoms in Russell's viper are believed to be due to presence of a presynaptic toxin like that in common Krait.

All the patients should be kept under observation for a minimum of 24 hours. Many species, particularly the Krait and the hump-nosed pit viper are known for delayed appearance of symptoms which can develop after 6-12 hours.

Essentials:

Most published data, based on hospital returns are incomplete because many patients are treated by traditional healers. However, three large, well-designed, national, community-based studies from Bangladesh, Indian and Sri Lanka have produced reliable estimates. Data are inadequately reported so snakebite should be made a notifiable disease in all South-East Asia Region countries. Death certification should use International Classification of Diseases code T63.0 (Toxic effect of contact with venomous animals- snake venom and sea-snake venom) (ICD-10 version: 2015 http://apps.who.int/classifications/icd10/browse/2015/en#/T63.0).

Incidence of snakebite varies diurnally and seasonally. It is highest during agricultural activities and seasonal and seasonal rains. Most bites are inflicted on the feet and ankles of bare-footed agricultural workers who tread on snakes inadvertently while walking in the dark or working in fields and plantations. Snake species differ in their inclination to strike when disturbed. Notoriously "irritable" species include Russell's and saw-scaled vipers. Cobras and kraits enter human dwellings. Kraits bite people who are asleep on the ground at night. On average, about 50% of bites by venomous snake cause no envenoming ("dry bites"), a figure ranging 5-80% with different species.

Snakebite epidemics follow flooding, cyclones and invasion of snakes habitats for road building, irrigation schemes and logging. These activities cause long term changes in climate and ecology and encourage influx of human settlers. Males are more often bitten than females. Peak incidence is in children and young adults. Pregnant women and their fetuses are at increased risk of dying. Snakebite is an occupational disease of farmers, plantation workers, herders, hunters, fishermen, fish farmers, snake restaurant workers and snake charmers. Factors contributing to fatal snakebite include problems with choice and dosage of antivenom, delay from visiting traditional healers, transportation difficulties, death in transit, airway obstruction, failure to attempt assisted ventilation or problems in carrying it out, failure to treat hypovolemia, complicating infections, failure to observe deterioration in hospital. Hours usually elapse between bite and neurotoxic deaths from elapid envenoming and several days or longer. From viper envenoming.

India: Medically important species include N. naja, N. kaouthia; B. caeruleus; D. russelli, E. carinatus; Hypnalehypnale, Trimeresurus. Registrar General of India's "Million Death Study" assigned causes of all deaths in about 7000 randomly chosen

sample areas, each with a population of about 1000 throughout the whole country. Verbal autopsy (questioning bereaved relatives and neighbours about the circumstances of the deceased's death), proved reliable for an event as distinctive, dramatic and memorable as snakebites fatality. Results were independent of hospital underreporting and were nationally representative.

Direct estimate of deaths attributable to snakebite in 2005 was 46 000 (99%Cl 41 000-51 000), (1 snakebite death for every 2 HIVIAIDS deaths). Snakebites caused 0.5% of all deaths, 3% in 5-14 year-olds. 97% died in rural areas, only 23% in health facilities. The highest numbers of deaths were in Uttar Pradesh (8,700), Andhra Pradesh (5,200) and Bihar (4,500).

True scale of mortality from snakebite is just beginning to be revealed. Thanks to three large, well designed community based studies that has been published recently [12,13,14].

Types of snakes:

The poisonous snakes belong to 4 families

i) Elapidae - Cobra, Krait (India), Mambas (Africa)
Coral snakes (Australia and S. America)

ii) Viperidae - They are divided into 2 sub- families

a. Viperinae – The "True vipers" or "old world vipers". e.g. Russell's viper and saw scaled viper.

b. Crotalidae – "Pit vipers". These are "Rattle snakes" the commonest of snales in America.

iii) Hydrophidae - These are the sea snakes.

iv) Colubridae – These form 80.00% of all snakes. The two commonest species are :

(a) Boomslangs (Dispholidus Types)

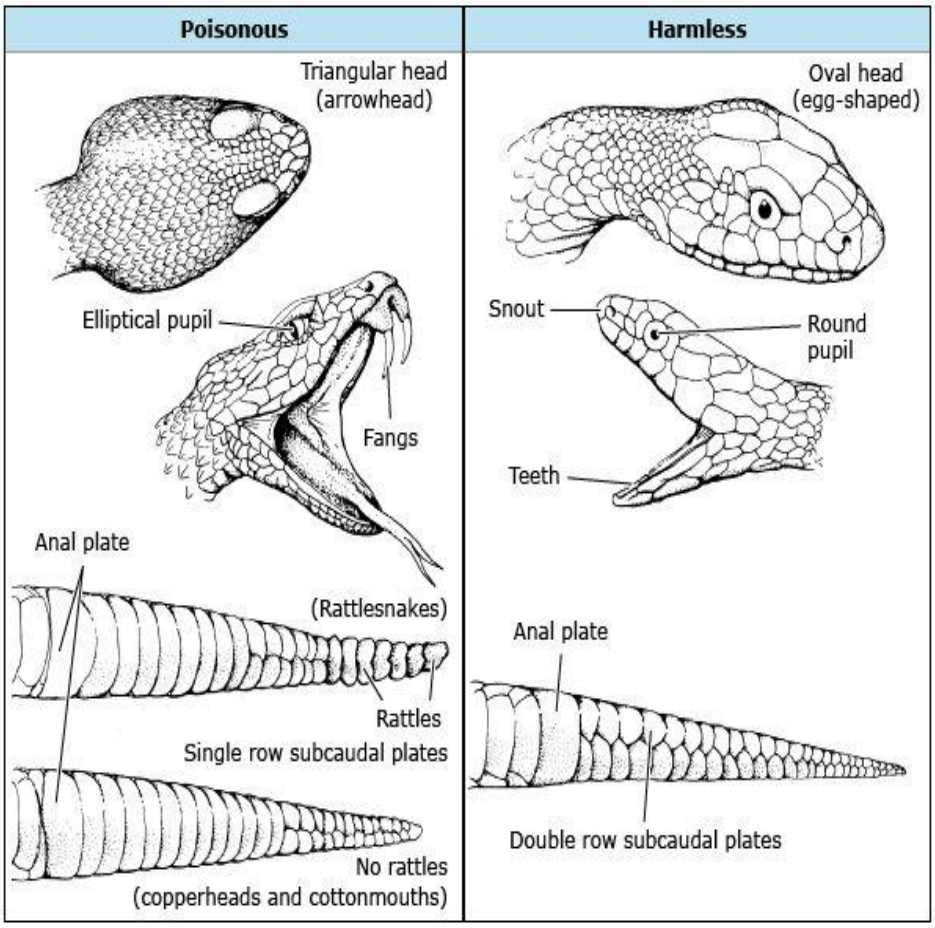
(b) Bird snakes (Thelotormiskertlandii)

Both of them are found only in Africa.

The 4 common snakes of India- the so called “BIG FOUR” are:

(i) Cobra, (ii) Krait, (iii) Russell’s viper, (iv) Saw scaled viper or echiscarinatus.

While Echis carinatus and cobra are by far the commonest, the cobra and Krait are the most poisonous and deadliest.



Clinical effects of snakebite

In patients with suspected snakebite there may be

1. Puncture Mark(s)
2. Local pain /swelling at bite site
3. Local and /or systemic envenoming affecting organs and tissues distant from bite site.
4. Signs of extreme anxiety

1. Local envenoming:

Increasing local pain at the site of the bite (krait bites usually painless), local swelling proximally, tender, painful swelling of regional lymph nodes draining bite site. Other signs: fang mark, persistent local bleeding, bruising, lymphangitis, inflammation (swelling, redness, heat), blistering (blebs, bullae, vesicles), infection, abscess formation, necrosis.

2. **Systemic envenoming:** nausea, vomiting, malaise, abdominal pain, weakness, drowsiness, prostration.
3. **Cardiovascular (Viperidae):** visual disturbances, dizziness, faintness, collapse shock, hypotension, cardiac arrhythmias, myocardial damage. Generalized increase in capillary permeability: facial, periorbital, conjunctival oedema (chemosis), bilateral parotid enlargement, pleural and pericardial effusions, pulmonary oedema, massive albuminuria, haemoconcentration. Bleeding and clotting disorders(Viperidae): local traumatic bleeding from recent and partly-healed wounds and venepuncture sites; spontaneous systemic bleeding.
4. **Neurological (Elapidae, Viperidaeeg Russell's viper D. russelli, Gloydius species):** bilateral ptosis, external ophthalmoplegia, descending paralysis progressing to generalized flaccid paralysis.

5. **Acute kidney injury:** loin (lower back) pain, haematuria, haemoglobinuria, myoglobinuria, oliguria/anuria, uraemia.
6. **Acute pituitary insufficiency (Russell's viper):** acute- shock, hypoglycaemia; chronic- weakness, loss of secondary sexual hair, loss of libido, amenorrhoea, testicular atrophy, hypothyroidism etc.

Another source of symptoms and signs not caused by snake venom is first aid and traditional treatments[15]. Constricting bands or tourniquets may cause pain, swelling and congestion that suggest locale envenoming. Ingested herbal remedies may cause vomiting. Instillation of irritant plant juices into the eyes may cause conjunctivitis.

Incisions, cauterization, immersion in scalding liquid and heating over a fire can result in devastating injuries.

Cerebral arterial thrombosis (Russell's vipers Daboia Russell and D. siamensis)

Thrombotic strokes, confirmed by angiography or imaging are increasingly recognized after envenoming by D. russelli in India, Sri Lanka[16] and Taiwan.

Neurological (Elapidae, Viperidaeeg. Russell's viper D. russelLi, Gloydium species)

Drowsiness, paraesthesia, abnormalities of taste and smell, "heavy" eyelids, ptosis , external ophthalmoplegia, paralysis of facial muscles and other muscles innervated by the cranial nerves, nasal voice or aphonia, regurgitation through the nose, difficulty in swallowing secretions, respiratory and generalized flaccid paralysis.

Renal (Viperidae, sea snakes)

Loin (lower back) pain[17], haematuria, haemoglobinuria, myoglobinuria, oliguria/anuria, symptoms and signs of acute kidney injury/uraemia (acidotic breathing, hiccups, nausea, pleuritic chest pain etc. see below)

Endocrine(acute pituitary / adrenal insufficiency from infarction of the anterior pituitary – (Russell's viper in Myanmar and several parts of India)[18,19,20,21,22,23]

Hyponatremia has been observed in victims of krait bites in the area of Hanoi and around Ho Chi Minh City in Vietnam [24]

Limitations of syndromic approach:

The more carefully the clinical effects of snakebites are studies, the more it is realized that the range of activities of a particular venom is very wide. For example, some elapid venoms, such as those of Asian cobras, can cause severe local envenoming, formerly thought to be an effect only of viper venoms. In Sri Lanka and India Russell's viper venom causes paralytic signs (ptosis etc.)

Envenoming by the greater black krait (B. niger) can cause generalized rhabdomyolysis leading to acute kidney injury [25,26,27,28].

Long term complications (sequelae) of snakebite:

1. At the site of the bite, loss of tissue may result from sloughing or surgical debridement of necrotic areas or amputation.
2. Chronic kidney disease (renal failure) may occur after bilateral cortical necrosis (Russell's viper and hump-nosed pit viper bites)[29]; and
3. Chronic panhypopituitarism or diabetes insipidus after Russell's viper[22,30]
4. Depression and anxiety, impaired functioning, post – traumatic stress disorder and unexplained residual physical disability were reported[31]. Chronic musculoskeletal disabilities have been reported.

Management of snakebites in South- East Asia

First Aid:

Do not apply a tourniquet[32]. Do not wash the bite site with soap or any other solution to remove the venom. Do not make cuts or incisions on or near the bitten area[33]. Do not use electrical shock[34]. Do not freeze or apply extreme cold to the area of bite. Do not apply any kind of potentially harmful herbal or folk remedy. Do not attempt to suck out venom with your mouth[35]. Do not give the victim drink, alcohol or other drugs. Do not attempt to capture, handle or kill the snake and patients should not be taken to quacks. There has been some initial research which suggests that a "Pressure Pad" at the site of bite may be of benefit[11]. This however, needs to be evaluated in field in India to assess its efficacy. Speeding up transport to hospital, by improving free ambulance services[36] or by recruiting village-based motor cyclist volunteers who transport the victim propped upright between the driver in front and a supporting pillion passenger behind. This has proved effective in villages in the Nepal Terai[37,38].

The special danger of rapidly developing paralytic envenoming after bites by some elapid snakes has prompted the use of pressure-bandage immobilization[39] and pressure-pad immobilization[35,40] requires equipment (long elasticated bandages and splints)[41,42] and skill.

Tight bands, bandages and ligatures:

They should not be released until the patient is under medical care in hospital and antivenom treatment has been arted[43].

Treatment in the dispensary or hospital [44]:-

Snakebite is a medical emergency: history, symptoms and signs must be obtained rapidly so that appropriate, urgent and life-saving treatment can be given.

Rapid primary clinical assessment and resuscitation: ABCDE approach

Airway

Breathing (respiratory movement)

Circulation (arterial pulse)

Disability of the nervous system (level of consciousness)

Exposure and environmental control (protect from cold, risk of drowning etc.)

Early clues that a patient has severe envenoming:

1. Snake identified as a very dangerous one or a large specimen.
2. Snake colouration its pupil size and bite marks are unreliable means to identify[45].
3. Widely spaced fang puncture marks or evidence of multiple strikes.
4. Rapid early extension of local swelling from the site of the bite.
5. Early tender enlargement of local lymph nodes, indicating spread of venom in the
6. Lymphatic system
7. Early systemic symptoms: collapse (hypotension, shock), nausea, vomiting, diarrhea, severe headache, “heaviness” of the eyelids, inappropriate (pathological) drowsiness or early ptosis/ ophthalmoplegia.
8. Early spontaneous systemic bleeding.
9. No urine passed since the bite.
10. Passage of dark brown / black urine

Clinical Features:

Feature	Cobra	Kraits	Russell viper	Saw-scaled viper	Humped-nose viper
Local pain / tissue damage	Yes	No	Yes	Yes	Yes
Ptosis, neurological sign	Yes	Yes	No	No	No
Hemostatic abnormality	No	May occur	Yes	Yes	Yes
Renal complication	No	No	Yes	No	Yes
Response to neostigmine	Yes	±	No	No	No
Response to ASV	Yes	Yes	Yes	Yes	No

All the patients should be under observation for 24 hours at least in hospital as Krait and hump nose pit vipers symptoms can be delayed.

General Examination

Examine the skin and mucous membranes for evidence of peptechiae, purpura, discoid haemorrhages and ecchymoses, the conjuctivae for haemorrhages and chemosis and the optic fundi for retinal haemorrhages. Examine the gingival sulci thoroughly using torch and spatula / tongue depressor as these may show the earliest evidence of spontaneous systemic bleeding. Examine the nose for epistaxis. Abdominal tenderness may suggest gastrointenstinal or retroperitoneal bleeding. Loin (low back) pain and tenderness suggest acute renal ischemia (Russell's viper bites). Subarachnoid haemorrhage is suggested by neck stiffness(meningism).

Intracranial haemorrhage is suggested by lateralising neurological signs, asymmetrical pupils, convulsions or impaired consciousness (in the absence of respiratory or circulatory failure).

Neurotoxic envenoming:

To exclude early neurotoxic envenoming, ask the patient to look up and observe whether the upper lids retract fully. Ask about diplopia and test eye movements for evidence of early external ophthalmoplegia. Check other muscles innervated by the cranial nerves (facial muscle, tongue, gag reflex etc.) The muscles flexing the neck may be paralysed, giving the "broken neck sign".

Can the patient swallow or are secretions accumulating in the pharynx, an early sign of bulbar paralysis? Ask the patient to take deep breaths in and out. "Paradoxical respiration" indicated that the diaphragm is still contracting but that the intercostal muscles and accessory muscles of inspiration are paralysed. Single-breath counting test (SBC). SBC measures how far the patient can count at two numbers per second in a normal speaking voice after taking a maximal inhalation.

Conventional tests of brain death can prove misleading[46]

Generalized rhabdomyolysis:

Russell's vipers in Sri Lanka and South India, muscles, especially of the neck, trunk and proximal part of the limbs, may become tender and painful on active or passive movement and later may become paralysed.

Myoglobinuria may be evident 3 hours after the bite.

Examination of pregnant women

Uterine contractions and fetal heart rate should be monitored continuously. Lactating women should be encouraged to continue breastfeeding.

Species Diagnosis:

Even experienced medical personnel may mistake harmless mimics for venomous snake, or they may confuse different venomous species[47,27]. As a result hump nosed pit viper (Hypnalehypnale) bites may be mistaken for saw-scaled viper (Echis carinatus) bites in SW India[48].

As polyvalent serum in India does not cover the hump nose pit viper[27]. The victim will continue to bleed for 3 weeks or so. (Editorial Management of Snake bite in India, JAPI, August 2016).

Investigations:

20 minute whole blood clotting test

(20 WBCT)[49]

However, the commonly used recycled glass antibiotic bottles can be made suitable and reliable, provided that they are cleaned by washing with "normal 0.9% saline" for intravenous infusion, without any added detergent of other cleansing agent, followed by hot air drying.

Other test for blood coagulation

More sensitive laboratory test that are rapid and relatively simple to perform are plasma prothrombin time (PT) or activated partial thromboplastin time (aPPT) and measurement of fibrinogen related antigens, also known as fibrin degradation products (FDP) or fibrin split products (FSP), by agglutination of sensitized latex particles or of D-dimer (cross-linked fibrin fragments).

An abnormal INR result is 1.2 or above.

Thrombo- elastography (TEG) and thromboelastometry (TEM, ROTEG, ROTEM) have been suggested as a simple bed-side method for assessing coagulopathy in snakebite victims but the equipment is expensive

Other laboratory tests

Haematocrit: a transient increase indicated haemoconcentration resulting from a generalized increase in capillary permeability (e. g. Russell's viper bite)

More often, there is a decrease reflecting blood loss or in the case of Indian, Thai and Sri Lankan Russell's viper bite, intravascular haemolysis.

White blood cell count: an early neutrophil leukocytosis is evidence of systemic envenoming by any species. Lymphopenia has been described in patients envenomed by Australasian Elapidae.

Blood film: ("helmet cell", schistocytes) are seen when there is microangiopathic haemolysis or thrombotic microangiopathy (TMA) and acute kidney injury. It is associated with envenoming by Russell's vipers, hump-nosed pit vipers and Australian Elapidae.

Biochemical abnormalities: Plasma creatinine, urea/ blood urea nitrogen and potassium concentrations are raised in the acute kidney injury of Russell's viper, hum-nosed pit- viper and sea-snake envenoming. Aminotransferases and muscles enzymes (creatine kinase, aldolase etc.) will be elevated following massive extravasation of blood. Early hyperkalaemia may be seen following extensive rhabdomyolysis in seas snakebites. Hyponatraemia is reported in victims of krait bites.

The urine should be tested by dipsticks for blood or haemoglobin or myoglobin. Microscopy will confirm whether there are erythrocytes in the urine. Red cell casts indicate glomerular bleeding. Massive proteinuria is an early sign of the generalized increase in capillary permeability in Russell's viper envenoming and an early indicator of acute kidney injury. Urine eosinophilia suggests acute interstitial nephritis, but this can be confirmed only by renal biopsy[50].

Other investigations:

Radiography: Chest radiography is useful for detecting pulmonary oedema (e.g. after bites by Vipera and Daboia species), pulmonary haemorrhages and infarcts, pleural effusions, and secondary bronchopneumonia.

Ultrasound: Ultrasonography can be useful for detecting deep vein thrombosis and for detecting pleural and pericardial effusion.

Electrocardiography: ECG in snakebites victims include tachyarrhythmias, sinus bradycardia, ST-T wave changes, varying degrees of atrioventricular block, and evidence of hyperkalaemia. Shock may induce myocardial ischaemia or infarction in patients with diseased coronary arteries.

Antivenom treatment

Antivenom is the only specific antidote to snake venom. A most important decision in the management of a snak

Monovalent (monospecific) antivenom neutralizes the venom of only one species of snake. Polyvalent (polyspecific) antivenom neutralizes the venoms of several different species.

Indian antivenom manufacturers," polyvalent anti-snake venom serum" is raised in horses, using the venoms of the four most important venomous snakes in India(Indian Cobra, Naja naja, Indian krait, Bungarus caeruleus; Russell's viper, Daboia russelli; saw-scaled viper, Echis carinatus). But other species are also important in certain regions [e.g. Echis carinatus sochureki in Rajasthan[51]; Trimeresurus (Craspedocephalus) malabaricus in southern India; Trimeresurus (Peltopelor) macrolepis (ref) in hilly regions of Tamil Nadu and Kerala; Trimeresurus (T). Erythrurus in Assam and Sikkim; Naja Kaouthia in North east India; Bungarus sindanus in W and NW India B. walli and possibly B. niger in NE India[25,2,52] .

No monovalent anti snake venom serum available in India.

Indications of antivenom

Antivenom treatment is recommended if and when a patient with proven or suspected snakebite develops one or more of the following signs:

1. Haemostatic abnormalities:
2. Neurotoxic signs
3. Cardiovascular abnormalities
4. Acute kidney injury (renal failure)
5. Haemoglobin / myoglobinuria
6. Local swelling involving more than half of the bitten limb (in the absence of a tourniquet) within 48 hrs of the bite. Swelling after bites on the digits (toes and especially fingers).
7. Rapid extension of swelling (for example beyond the wrist or ankle within a few hours of bites on the hands or feet)
8. Development of an enlarged tender lymph node draining the bitten limb.

Inappropriate use of antivenom:

In some parts of the world, a small standard dose of antivenom is given routinely to any patient claiming to have been bitten by a snake, irrespective of symptoms or signs of envenoming[53].

Antivenom treatment should be given as soon as it is indicated. It may reverse systemic envenoming even when this has persisted for severe days or in the case of haemostatic abnormalities for two or more weeks. Give antivenom for as long as evidence of the coagulopathy persists.

Antivenom reactions:

A substantial proportion of patients develop reactions, either early (within a few hours) or late (5 days or more) after being given antivenom[54,55,56,57,58,59,60,61]. The risk of antivenom reactions is dose-related (usually).

1. Early anaphylactic reactions:

Usually within minutes and up to 180 minutes after starting antivenom. Dry cough, fever, nausea, vomiting, abdominal colic, diarrhea and tachycardia. A minority of these patients may develop severe life-threatening anaphylaxis: hypotension, bronchospasm and angioedema.

2. Pyrogenic (endotoxin) reactions:

Usually develop 1-2 hours after treatment. Symptoms include shaking chills (rigors), fever, vasodilatation and a fall in blood pressure. Febrile convulsions may be precipitated in children. These reactions are caused by pyrogen contamination during the manufacturing process.

3. Late (serum sickness type) reactions:

Develop 1-12 (mean 7) days after treatment. Clinical features include fever, nausea, vomiting, diarrhea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteneinuria with immune complex nephritis and rarely encephalopathy.

Prevention of antivenom reactions:

One of only two systematic reviews carried out in the field of snakebite treatment concluded that routine prophylactic adrenaline for antivenom known to have high adverse event rates seemed sensible, based on only one trial[62] and that antihistamine appeared to be of no obvious benefit, again based on one trial[63].

However the risks of adrenaline make it less attractive for prophylaxis[64,62,65,66,67] tested parallel pre-antivenom infusion of placebo, hydrocortisone alone or hydrocortisone plus chlorpheniramine in 52 patients. The results did not achieve statistical significance and the study was underpowered.

A large and well-designed study was carried out in Sri Lanka. Placebo-controlled trial of adrenaline (0.25 ml of a 0.1% solution subcutaneously) promethazine (25 mg intravenously), promethazine (25 mg intravenously) and hydrocortisone (200 mg intravenously) each alone and in all possible combinations. The interventions or matching placebo, were given immediately before infusion of antivenom. Patients were monitored for at least 96 h[68]. Compared with placebo, adrenaline significantly reduced severe reactions to antivenom. Adding hydrocortisone negated the benefit of adrenaline.

Speed and dilution of intravenous antivenom administration

In Sri Lanka, 104 patients were randomly allocated to receive antivenom by intravenous infusion over 20 minutes and 94 by infusion over 2 hours. There was no difference in the incidence of early severe anaphylactic reactions in the two groups[69].

Recommendation:

Based on the results of a powerful and well-designed trial in Sri Lanka, routine use of prophylactic adrenaline is recommended before antivenom treatment, except in those older patients in whom there is evidence or suspicion of underlying cerebrovascular disease and when the particular antivenom in use has a proven low incidence of reactions (<5%). The adult dose of epinephrine (adrenaline) is 0.25 ml of 0.1% solution (0.25 mg) by sub-cutaneous injection (children 0.005 ml/kg body weight of 0.1% solution)

Treatment of antivenom reactions:

Epinephrine (adrenaline) is given intramuscularly (ideally into the upper lateral thigh) in an initial dose of 0.5 mg for adults, 0.01 mg /kg body weight for children. The dose can be repeated every 5-10 minutes if the reaction persists or the symptoms become worse. After epinephrine (adrenaline), patients with bronchospasm should be given an inhaled short-acting β agonist bronchodilator.

Corticosteroid do not reduce the risk of recurrence (biphasic) anaphylaxis[70].

Anaphylaxis unresponsive to intramuscular epinephrine

a. Patients who remain shocked and hypotensive should be laid supine with their legs elevated and given intravenous volume replacement with 0.9% saline (1-2 litres rapidly in an adult). Intravenous epinephrine (adrenaline) infusion should be considered [adult doe 1 mg (1.0 ml) of 0.1% solution in 250 ml 5% dextrose or 0.9% saline- i.e. 4 μ(micro) g /minute(15-60 drops/ min using a microdropper burette chamber), increasing to maximum 10μ(micro) g/min and in patients who remain hypotensive , vasopressor agent such as dopamine [dose 400 mg in 500 ml 5% dextrose or 0.9% saline infused at 2-5 μ(micro) g/kg/min].
b. Patients who remain dyspnoeic should be propped up at 45 degrees and given supplemental oxygen with optimal nebulized / inhaled and /or parenteral bronchodilator (β2 agonist)[71].

Completion of administration of antivenom dose:

After the patient has recovered from the early anaphylactic or pyrogenic reaction, the indications for antivenom therapy should be critically re-examined. If antivenom is still indicated, intravenous administration should be cautiously resumed until the total dose has been given.

Treatment of late (serum sickness) reactions:

Late (serum sickness) reactions may respond to a 5- days course of oral antihistamine. Patients who fail to respond within 24-48 hours should be given a 5-day course of prednisolone.

Selection:

Immunisation of a horse or sheep with venoms of several related species of snakes (e.g. Viperidae) may produce an enhanced antibody response to common antigens, making the resulting polyvalent antivenommore rather than less potent than a monovalent antivenom[72].

Dosage of antivenom:

India: there have been many publications on treatment of snakebites with national polyvalent antivenoms, but there is little reliable evidence to guide initial dosage. Indian national snakebite protocol (Directorate General of Health Services, 2009) and previous editions of WHO guidelines recommend immediate administration of 5 vials,and a recent consenus 4-6 vials in the case of Echis carinatus; and 10 vials for patients envenomed by the other species, with repeated dosing if the patient fails to improve to a maximum of 20 vials. There are no adequately designed dose finding studies that selected snakebites by identified species, controlled for clinical severity, were randomized and employed defined clinical end points including measurement of antigenemia[73]. In clinical practice, the dose of antivenom used is very variable. In government hospitals where antivenom is freely available, higher doses of antivenom are prescribed, often exceeding 20 vials. Several randomized controlled trials from such hospitals claimed to demonstrate that lower doses were equally effective in victims of predominantly haemotoxic snakebites in South India in[74,75,76,77,58,52].

However, these studies without exception, had severe limitation sin patient selection and case definition , snake species identifications, design end-points and power, rendering their results uninterpretable.

Observation of the response to antivenom:

a) **General :** the patient feels better

   Nausea, headache and generalized aches and pains may disappear.

b) **Spontaneous systemic bleeding:** usually stops within 15-30 minutes.

c) **Blood coagulability** usually restored in 3-9 hours. Bleeding from new and partly healed wounds usually stops much sooner than this.

d) **In shocked patients:** blood pressure may increase within the first 30-60 minutes and arrhythmias such as sinus bradycardia may resolve.

e) **Neurotoxic envenoming:**of the post synaptic type (cobra bites) may begin to improve as early as 30 minutes after antivenom (Faiz et al. cobra bites in press). But may take several hours. Envenoming by presynaptic toxins (kraits and sea snakes) will not respond in this way.

f) **Active haemolysis and rhadbomyolysis** may cease within a few hours and urine colour returns to normal.

Recurrence of systemic envenoming:

This is attributable to

- Continuing absorption of venom from the “depot” at the site of the bite.
- Redistribution of venom from the tissues into the vascular space, as the result of antivenom treatment[78].

Criteria for repeating the initial dose of antivenom

Criteria for giving more antivenom

- Persistence or recurrence of blood incoagulability after 6 hr or of bleeding after 1-2 hr.
- Deteriorating neurotoxic or cardiovascular signs after 1 hr.

In patients who continue to bleed briskly, the dose of antivenom should be repeated within 1-2 hours.

In case of deteriorating neurotoxicity or cardiovascular signs. Repeat the initial dose after 1 hour if the patient's condition is deteriorating.

Repeating doses of antivenom after the patient is paralysed and being ventilated has no proven value, increases the risk of reactions, is expensive and wastes a valuable resource.

Conservatives treatment when no antivenom is available.

Neurotoxic envenoming with respiratory paralysis. Manual ventilation where no mechanical ventilator available .

Haemostatic abnormalities: Strict bed restto avoid even minor trauma including intramuscular injection; transfusion of clotting factors and platelets; ideally fresh frozen plasma(FFP) or cryoprecipitate with platelet concentrates or, if these are not available, fresh whole blood.

Shock, Myocardial damage:

Hypovolemia should be corrected with colloid / crystalloids, controlled by observation of the central venous pressure. Ancillary pressor drugs (dopamine or epinephrine-adrenaline) may also be needed. Patients with hypotension associated with bradycardia should be treated with atropine.

Acute Kidney injury: conservative treatment or dialysis.

Dark brown urine (myoglobinuria or haemoglobinuria): correct hypovolemia with intravenous fluid, correct acidosis with a slow intravenous infusion of 50-100 mmol of sodium bicarbonate,

Severe local envenoming: local necrosis, intracompartmental syndromes and even thrombosis of major vessels is more likely in patients who cannot be treated with antivenom. Prophylactic broad spectrum antimicrobial treatment is justified.

Trail of anticholinesterase:

Potentially very useful effect in patients with neurotoxic envenoming, especially those bitten by cobras[79,80,81] but not usually in those envenomed by kraits[82]. However, recent claims that intra-nasal neostigmine might provide a universal first-aid method for snakebite victims[83,84].

- Atropine sulphate (0.6 mg for adults; 50µg/kg for children) or glycopyrronium is given by intravenous injection followed by neostigmine by intramuscular injection 0.02 mg/kg for adults, 0.04 mg/kg for children. Short acting edrophonium chloride (Tensolon) is ideal for this test but is rarely available.
- The patient is observed over the next 30-60 minutes (neostigmine) or 10-20 minutes (edrophonium) for signs of improved neuromuscular transmission. Ptosis may disappear and ventilator capacity (peak flow, FEV-1 or maximum expiratory pressure) may improve.
- Patients who respond convincingly can be maintained on neostigmine mehylsulphate, 0.5-2.5 mg every 1-3 hours up to 10 mg / 24 hours maximum for adults or 0.01-0.04 mg/ kg every 2-4 hours for children by intramuscular, intravenous or subcutaneous injection together with atropine to block muscarinic side effects. Patients able to swallow tablets may be maintained on atropine 0.6

mg twice each day, neostigmine 15 mg four times each day or pyridostigmine 60 mg four times each day.

Passive leg raising test: another way of assessing fluid responsiveness is to sit the patient in a 45 degrees head-up semi-recumbent position. Lower their upper body to the horizontal and passively raise their legs at 45 degrees up, increasing circulating volume by about 150-300 ml. the maximal effect of this "auto-infusion" occurs at 30-90 seconds, measured by clinical features of improved cardiac output (e.g. increase in pulse pressure and decrease in heart rate)[85].

In victims of Russell's viper bites in Myanmar, India and Sri Lanka, acute pituitary adrenal insufficiency resulting from haemorrhagic infarction of the anterior pituitary may contribute to shock. While neurological manifestations of hypoglycaemia, such as impaired consciousness, extensor posturing and other involuntary movements may be presenting signs that respond to a test dose of intravenous 50% dextrose injection[19] Hydrocortisone, fluid and electrolyte replacement may needed acutely in these patients. In chronic cases, addition of thyroxin, oestrogen or testosterone may be needed[86,87,88].

Indications for dialysis:

a) Clinical uraemia (Encephalopathy, pericarditis etc.)
b) Fluid overload not responding to diuretics.
c) Plasma potassium concentration > 7 mmol/l (or hyperkalaemic ECG changes.)
d) Symptomatic acidosis.
e) Blood biochemistry – one or more of the following Creatinine > 4 mg / dl (354 micromol/l).

   Urea > 130 mg / dl (46 mmol/l)

Caution: biochemical criteria alone is not sufficient to start dialysis.

Haemostatic disturbances:

Bleeding and clotting disturbances usually respond satisfactorily to treatment with specific antivenom, but the dose may need to be repeated several times, at six hourly intervals, before blood coagulability (assessed by the 20WBCT) is finally and permanently restored.

In exceptional circumstances, patients can be given fresh frozen plasma, cryoprecipitate (fibrinogen, factor VIII), fresh whole blood or platelet concentrates. Heparin is ineffective against venom-induced thrombin and may cause bleeding on its own account. It should never be used in cases of snakebites.

Antifibrinolytic agents are not effective and should not be used in victims of snakebite[76]

Treatment of the bitten part

1. Excessive elevation:

   May reduce arterial perfusion pressure in a tensely swollen limb and increase the risk of intra-compartmental ischaemia.
2. Blisters / bullae/"blebs" may be large and tense but they should not be de-roofed and require aspiration only if they threaten to rupture.
3. Amputation may be indicated in case of gangrene of toes or limbs.
4. In Asia, local bite wound infections may be due to single or multiple bacteria including gram-positive aerobes (Staph, aureus, coagulase-negative Staphylococcus and Enterococcus), aerobic gram-negative bacterial (E. coli, Klebsiella, Pseudomonas, Enterobacter, Morganella morganii), anaerobic bacteria (P.streptococcus) and Bacteroides fragilis)[89,90].

   Prophylactic antibiotics were not effective in a controlled study in Brazil[91]. Interference with the wound (incisions made with an unsterilized razor blade /

knife etc.) creases a risk of secondary bacterial infection and justifies the use of immediate broad spectrum antibiotics (e.g. gentamicin with benzyl penicillin, amoxicillin or a cephalosporin plus a single dose only of gentamicin- to avoid the risk of kidney injury- plus metronidazole) and tetanus prophylaxis. Other possible antibiotics include amoxicillin / clavulenic acid, piperacillin / tazobactam, ciprofloxacin and third generation cephalosporin[92].

5. Compartmental syndromes and fasciotomy[93]

   The appearance of an immobile, tensely- swollen, cold and apparently pulseless snake-bitten limb may suggest to surgeons the possibility of increase intracompartmental pressure, especially if the digital pulp spaces or the anterior tibial compartment are involved. Swelling of envenomed muscle within such tight fascial compartments could result in an increase in tissue pressure above the venous pressure, resulting in in ischemia. However, the classical signs of an intracompartmental pressure syndrome may be difficult to assess in snakebite victims and many unnecessary, dangerous and debilitating fasciotomies are performed, especially where surgeons rather than physicians have the primary responsibility for managing snakebite cases. Fasciotomy is generally falling out of favour for the treatment of snake-bitten limbs[94].

Clinical features of a compartmental syndrome:

- Disproportionately severe pain.
- Weakness of intracompartmental muscles.
- Pain on passive stretching of intracompartmental muscles.
- Hypoaesthesia of areas of skin supplied by nerves running through the compartment.
- Obvious tenseness of the compartment on palpation.

Detection of arterial pulses by palpation or doppler ultrasound probes, does not exclude intracompartmental ischaemia. The most reliable test is to measure intracompartmental pressure directly through a cannula introduced into the compartment and connected to a pressure traducer or manometer.

Fasciotomy should not be contemplated until haemostatic abnormalities have been corrected[95,96,97,98].

Criteria for fasciotomy in snake- bitten limbs

Haemostatic abnormalities have been corrected (antivenom with or without clotting factors)

- Clinical evidence of an intracompartmental syndrome.
- Intracompartmental pressure > 40 mmHg(in adults).

Management of cobra spit ophthalmia[99]

1. **First Aid:**

   Consists of urgent irrigating the affected eyes and other mucous membranes with liberal quantities of water, saline, Ringer's lactate, milk or any other available bland liquid (even urine has been used).

2. **Medical treatment:**

- Pain is intense. Topical vasoconstrictors with weak mydriatic activity [e.g. instillation of 0.5% epinephrine (adrenaline) drops] relieve pain and inflammation.
- Endophthalmitis or blinding corneal opacities must be prevented by application of prophylactic topical antibiotics (eg. Tetracycline, chloramphenicol, 0.5% framycetin, "Soframycin", ciprofloxacin, penicillin- streptomycin ointment, polymixin B sulphate, gatifloxacin and moxifloxacin)

METHODOLOGY

A) Source of data:- General Medicine department of Dr. Prabhakar Kore, charitable hospital, Belagavi.

B) Study design:- Cross sectional study.

C) Study period:- One year, from 1/1/2016 to 31/12/2016.

D) Study population:- Patients admitted in General Medicine department of Dr. Prabhakar Kore, charitable hospital, Belagavi.

E) Sample size:- 50.

Method of collection of data:-

A) **Inclusion** criteria:-

1) Patients' history suggesting toxic snake bite.

2) Patients having clinical evidence of toxic snake bite, eg. Fang marks, local cellulitis, local bleeding, ptosis, respiratory failure.

B) **Exclusion** criteria:-

1) Patients coming with bites other than toxic snake bite.

C) Procedure:-

1) **Identification of snake**:- snakes were identified by the killed snakes brought by the relatives of patient or any photos taken by them, or any description of the snakes given by them. Also the development of local or systemic envenomation signs and symptoms were used to identify the snakes.

2) **History**:- detailed history was taken about the site and time of bite, and focus was given on the development of local or systemic envenomation signs and symptoms.

3) **Past history**:- patients were inquired about any significant medical past history, eg. Bleeding tendencies, CNS, CVS, or renal disorders.

4) **Local examination**:- local skin discoloration, pain, swelling or spontaneous bleeding was examined.

5) **General examination**:- vitals were noted down, generalized edema, cyanosis, pallor, lymphadenopathy, purpura, petechiae were examined. Neuroparalytic and hematotoxic symptoms were examined.

- **Neuroparalytic** signs and symptoms like breathlessness, dysarthria, dysphagia, blurring of vision, cyanosis, clubbing and altered sensorium were observed for in suspected neurotoxic snake bite victims.
- **Hematotoxic** signs and symptoms like active bleeding from the local site of the bite or systemic bleeding like hemetemesis, gingival bleeding, hematuria and even fundoscopy was done to check for optic disc hemorrhage.

All the above data was entered on a proforma and relavant investigations were done, eg. Hemoglobin, total wbc count, differential wbc count, erythrocyte sedimentation rate, platelet count, bleeding time, clotting time, prothrombin time, international normalized ratio, activated partial thromboplastin time, random blood sugar, blood urea and creatinine levels and D-dimer levels.

Electrocardiogram was taken to look for myocarditis changes. Urine examination was done to look for hematuria or pus cells.

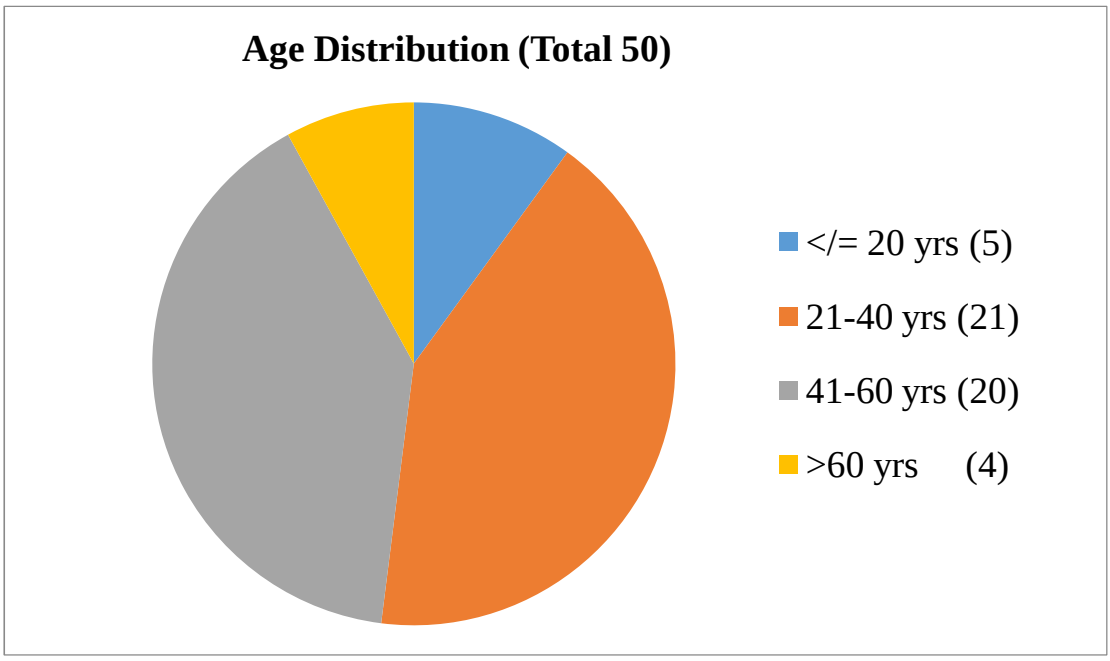
6) **Complications** that developed were noted.

7) **Final outcome** in terms of mortality was noted.

RESULT

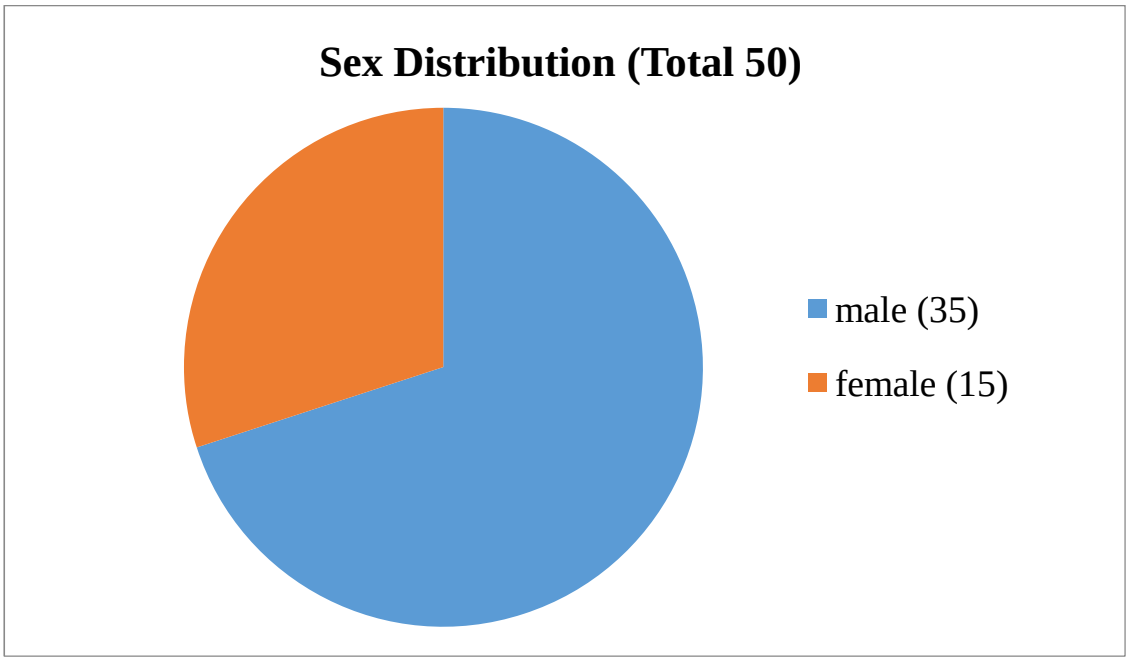
In an analysis of 50 cases of toxic snakebite admitted in Dr. Prabhakar Kore, charitable hospital, Belagavi, during January 1, 2016 to December 31, the following results were obtained.

A) AGE DISTRIBUTION:-



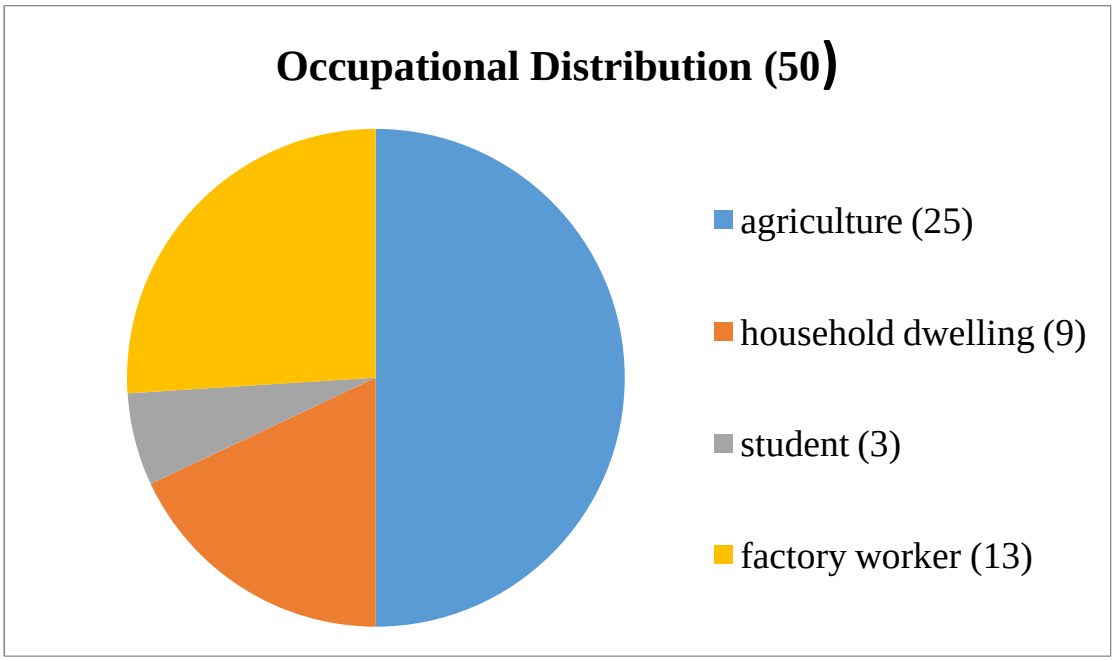
The age distribution from the present study shows the maximum number of victims in the age group between 21-40 yrs of age (42%).

B) SEX DISTRIBUTION:-



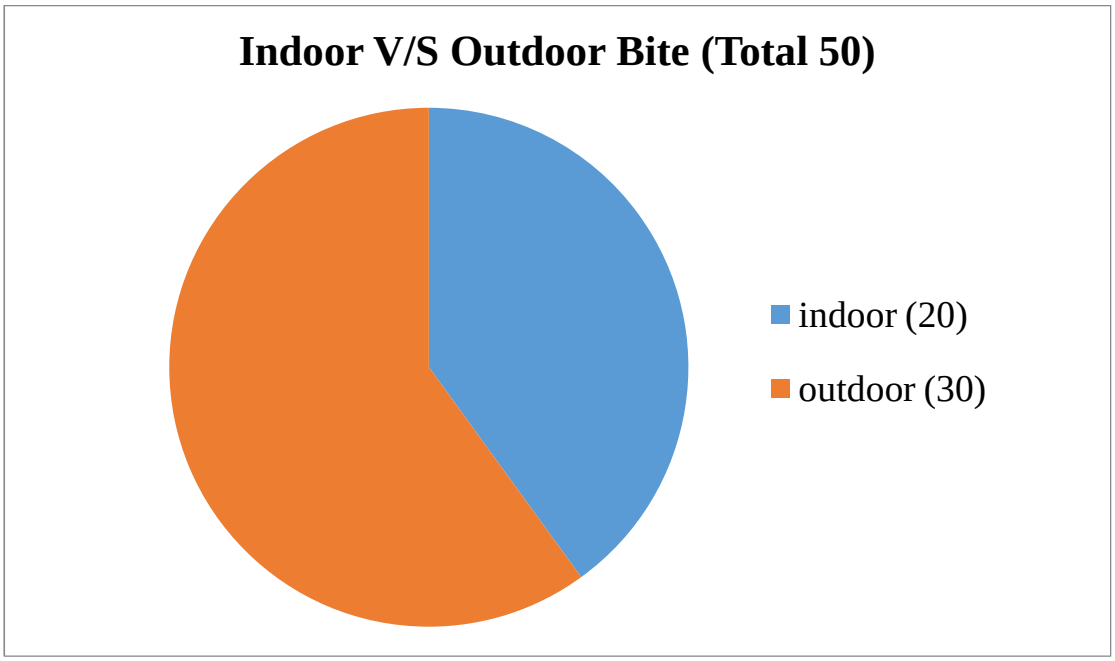
The sex distribution in the present study shows a male predominance of 35 patients (70%).

C) OCCUPATIONAL DISTRIBUTION:-



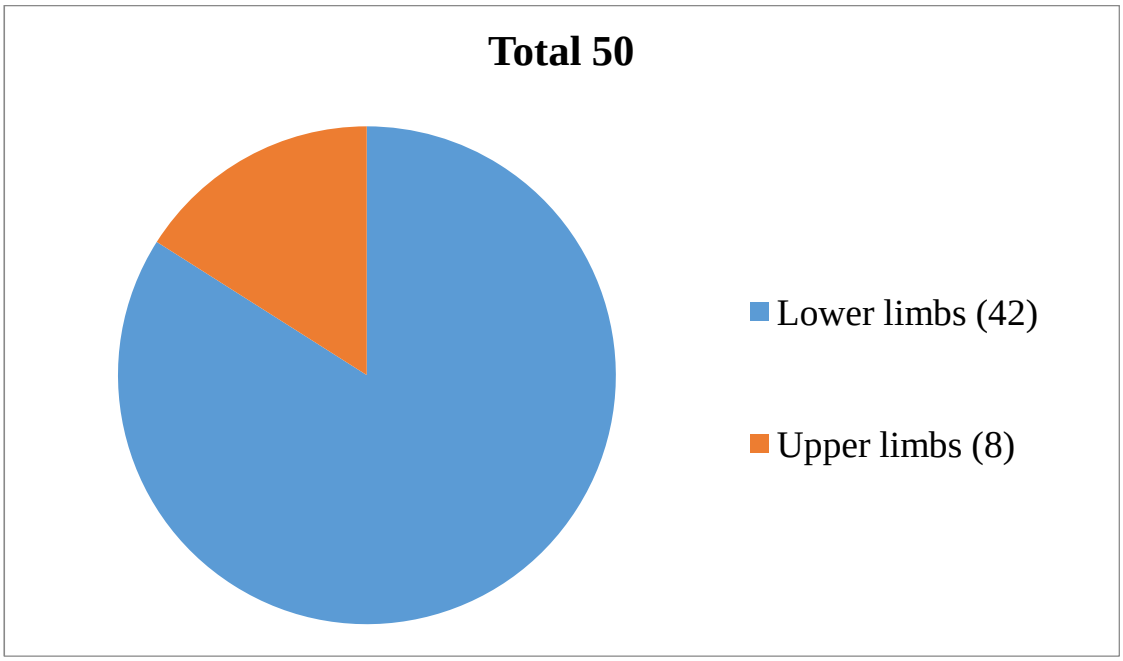
The present study shows an occupational distribution as above. It shows a majority of bites were reported in the agricultural community (50%), owing to their exposure in the open fields. This was followed by factory workers (26%), while working in various factory units. Other major groups of patients were the ones bitten in their respective households (18%), while doing various household chores. Also commonly seen among students (6%), usually while playing in the playgrounds of their respective schools.

D) INDOOR V/S OUTDOOR BITES:-



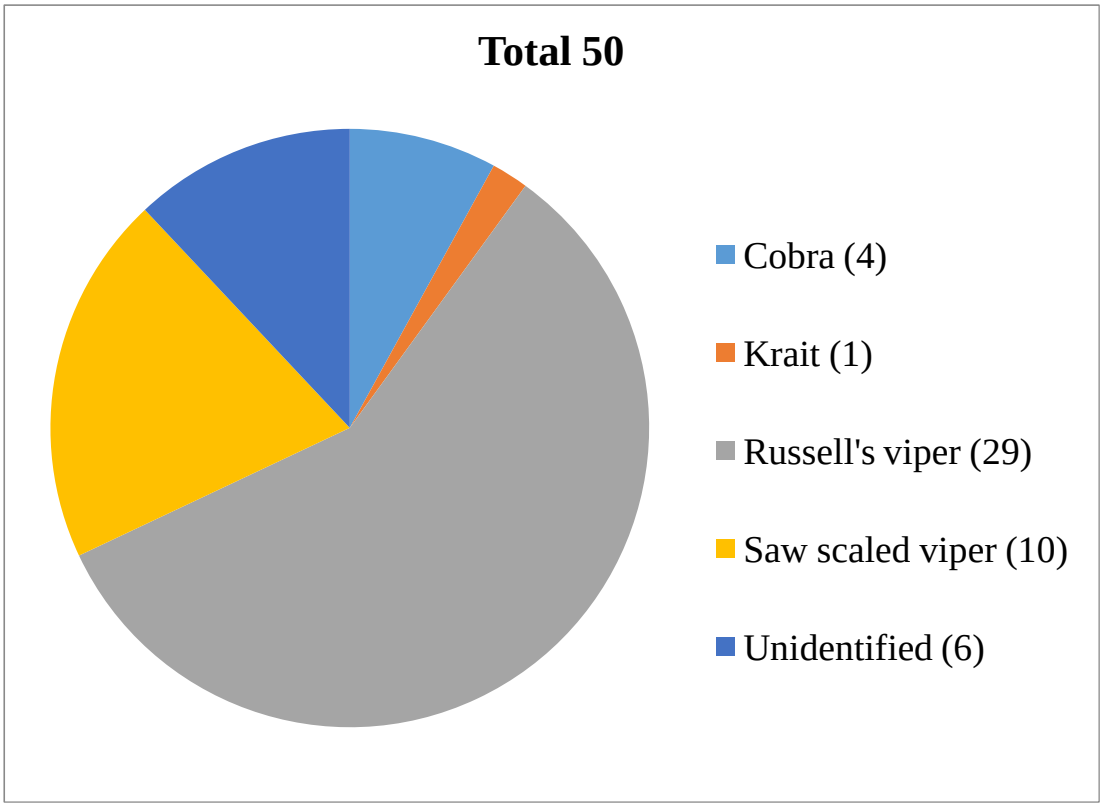
This chart clearly indicates that majority of snakebites occurred in the outdoors (60%), while comparatively less in the indoors (40%).

E) SITE OF THE BITE:-



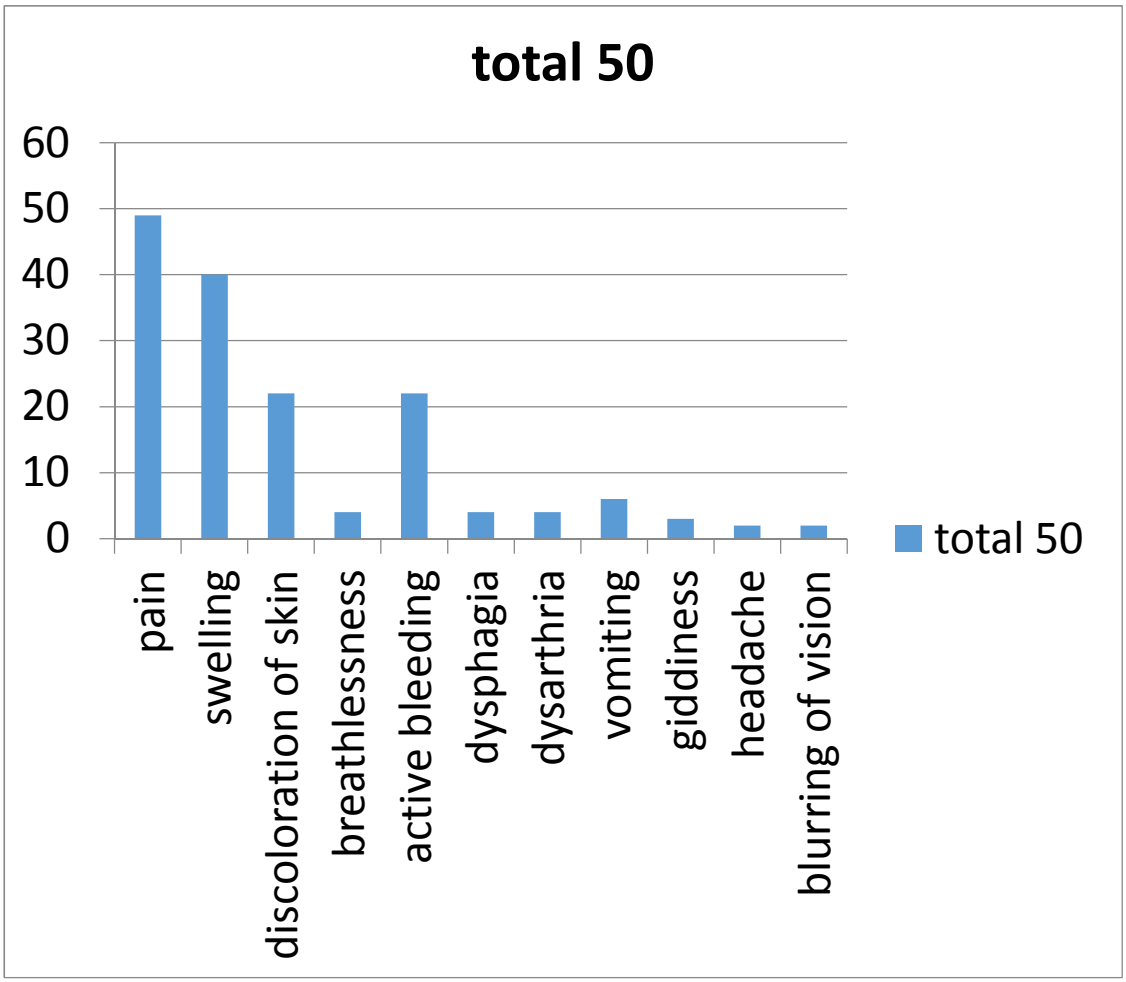
The above distribution shows that majority of bites occurred on the lower limbs (84%), which included the foot, toes, ankle and the calf region. Among the upper limbs (16%), most common involvement was the fingers, palm and forearm.

F) TYPE OF THE SNAKE (AS IDENTIFIED BY THE PATIENT OR THE ATTENDANTS:-



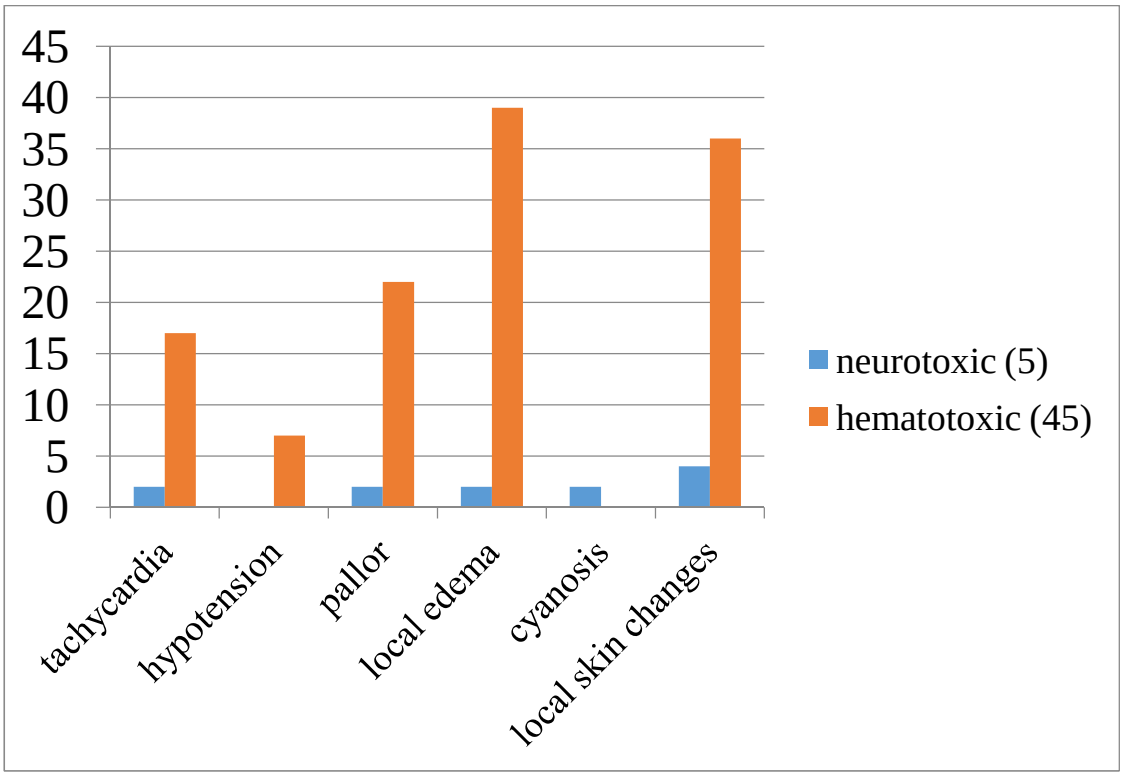
The present study shows a clear predominance of Russell's viper bites (58%), followed by Saw-scaled viper bites (20%) among the hematotoxic group commonly found in this region. Among the neurotoxic snakes, Cobra bites (8%) were commoner than Krait bites (2%). However, a significant number of bite victims were unable to identify the snakes (12%).

G) SYMPTOMS:-



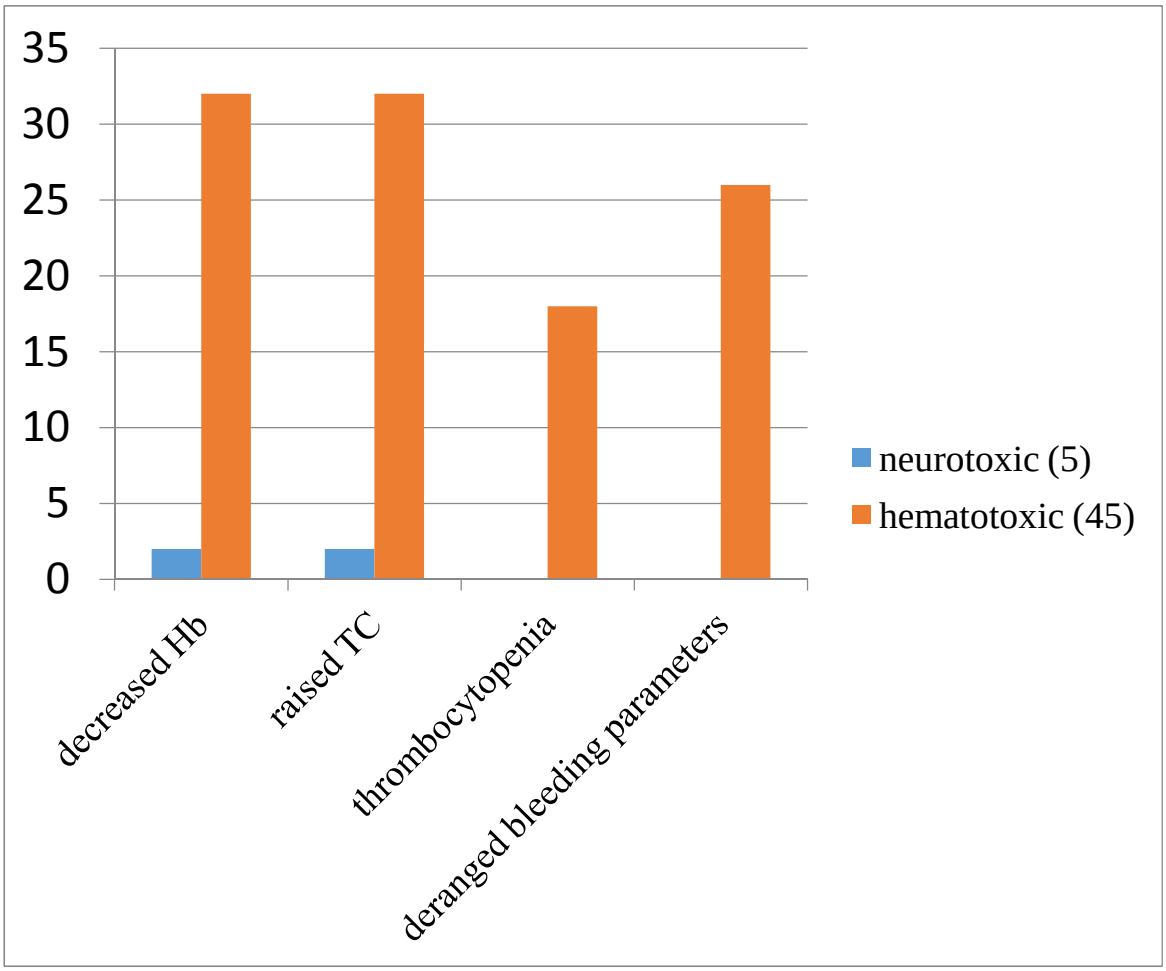
Among the symptoms with which the snakebite victims presented to the hospital, pain (98%) was clearly the most common. This was followed by local swelling (80%), discoloration of surrounding skin and active bleeding from the site of the bite (44% each), vomiting (12%), breathlessness (8%), dysphagia (8%), dysarthria (8%), giddiness (6%), headache (4%), blurring of vision (4%).

H) EXAMINATION FINDINGS:-



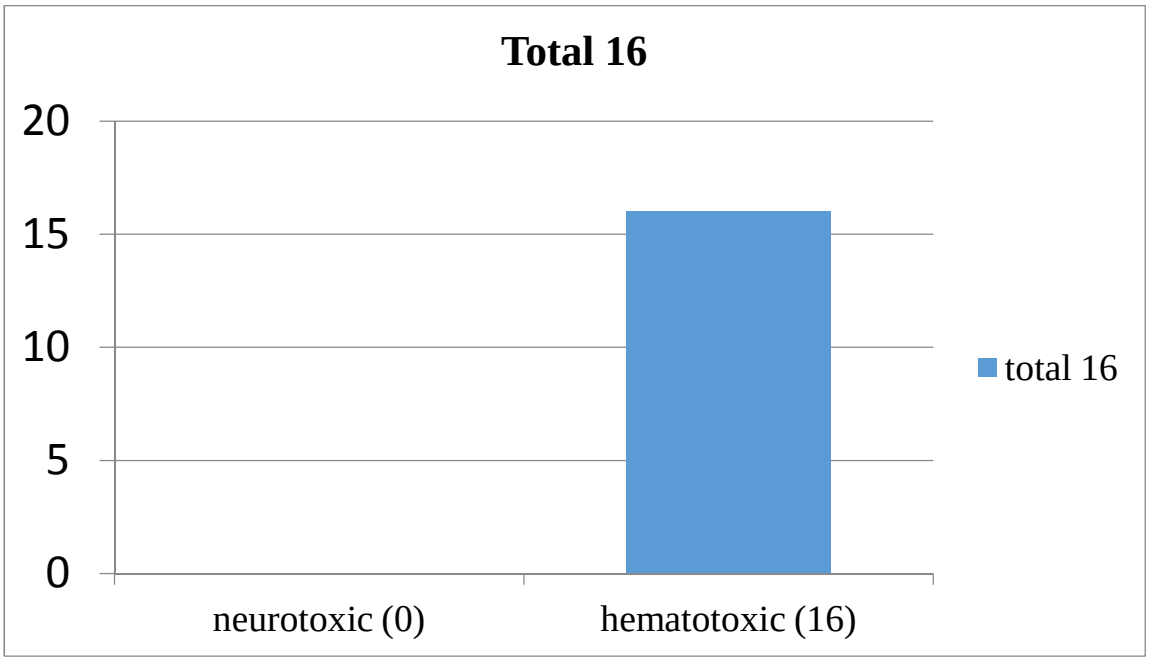
In the clinical examination done for these snakebite patients, the above chart shows a comparative analysis of neurotoxic with hematotoxic snakebite victims with reference to each of the findings. Total of 5 neurotoxic and 45 hematotoxic snakebites were reported. Tachycardia was seen in 37.7% (17/45) of hematotoxic and 40%(2/5) of neurotoxic victims. Hypotension was seen in 15.5% (7/45) of hematotoxic victims, while none of the neurotoxic victims had hypotension. Pallor was seen in 48.8% (22/45) of hematotoxic victims, while 40% (2/5) in the neurotoxic victims. Local edema was seen in 86.6% (39/45) of hematotoxic victims, while 40% (2/5) in the neurotoxic victims. Cyanosis was seen in 40% (2/5) of neurotoxic victims, while none of the hematotoxic victims had cyanosis. Local skin changes were seen in 80% (36/45) of hematotoxic as well as in neurotoxic victims [80% (4/5)].

I) DERANGED HEMATOLOGICAL PROFILE:-



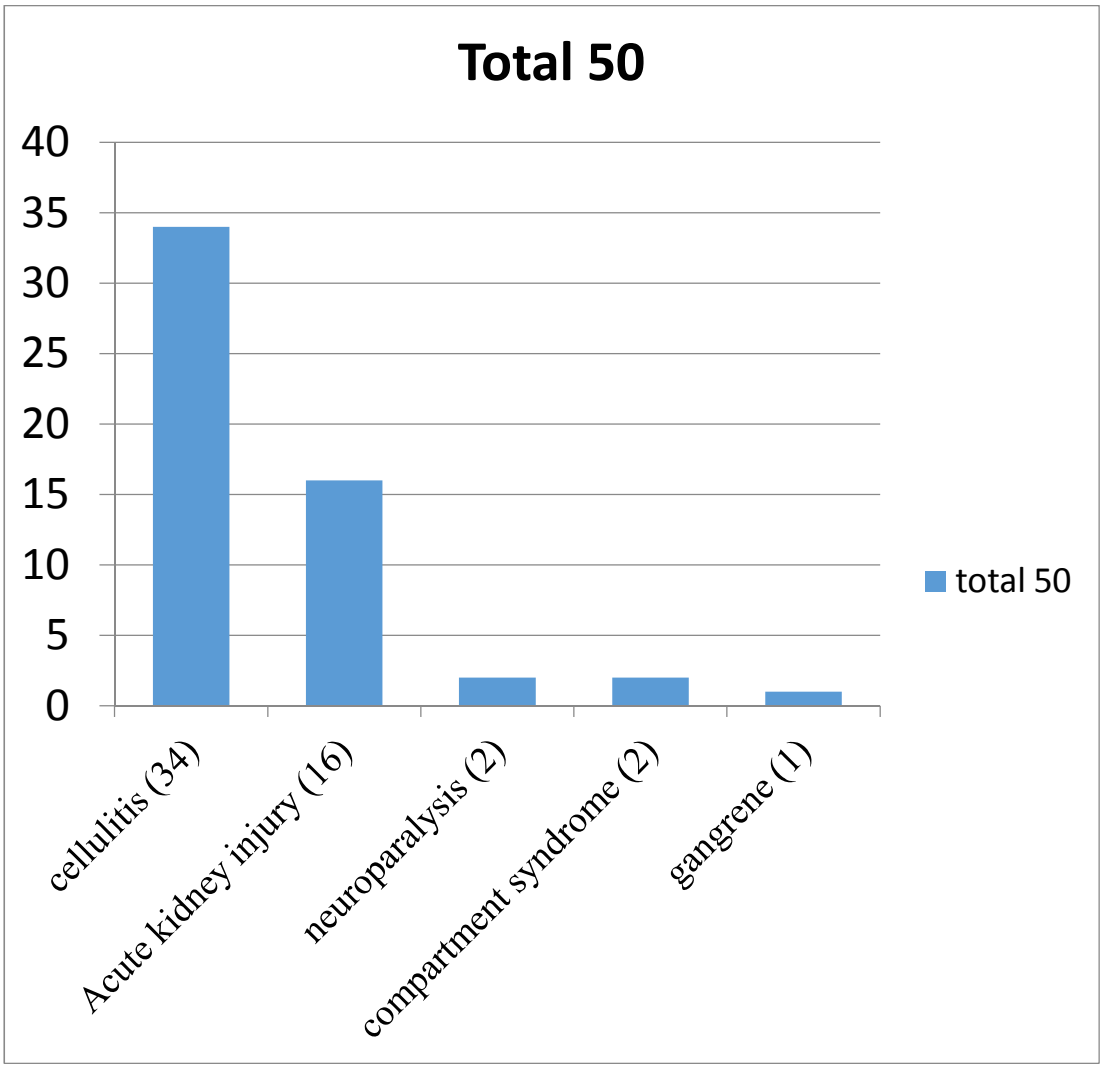
The above chart shows a comparative analysis of neurotoxic and hematotoxic victims with reference to their deranged of hematological profile. Decreased hemoglobin (Hb) was seen in 71.1% (32/45) of hematotoxic victims, while it was seen in 40% (2/5) of neurotoxic victims. Raised total wbc count (TC) was seen in 71.1% (32/45) of hematotoxic victims, while it was seen in 40% (2/5) of neurotoxic victims. Thrombocytopenia was seen in 40% (18/45) of hematotoxic victims, while none of the neurotoxic victims had thrombocytopenia. Deranged bleeding parameters i.e. raised Prothrombin time, raised INR, raised activated partial Thromboplastin time (aPTT), raised D-dimer values, were seen in 57.7% (26/45) of hematotoxic victims, while none of the neurotoxic victims had these deranged blood parameters.

J) DERANGED RENAL PROFILE:-



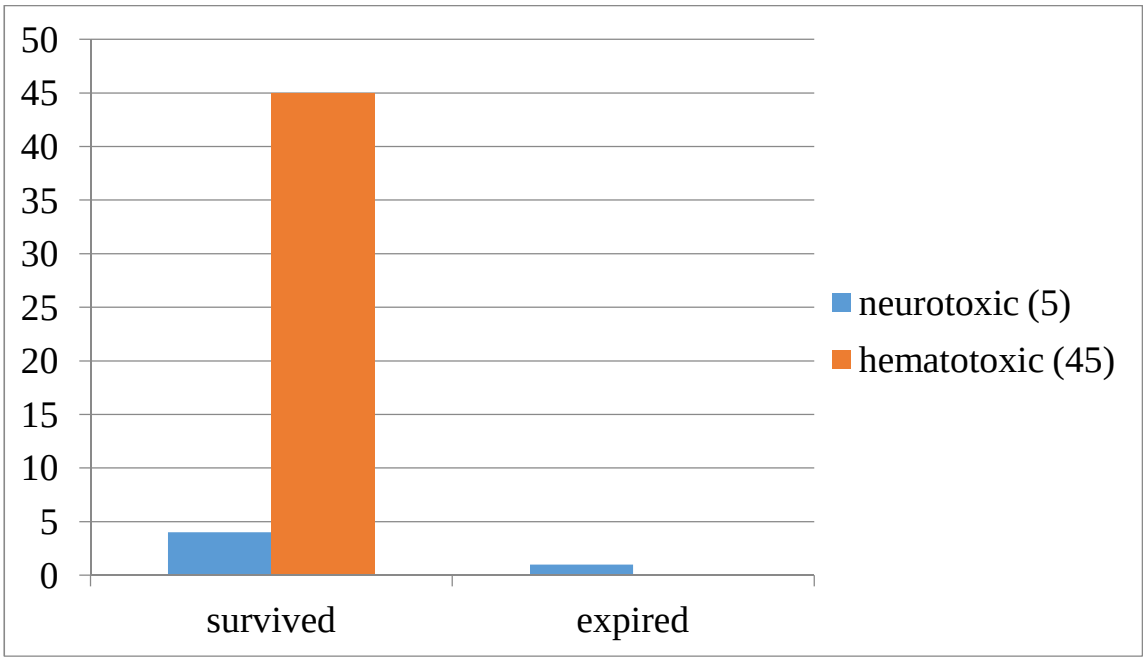
Out of the total 50 patients taken in this study, 16 (32%) had deranged renal profile which included raised blood urea and creatinine values. All of these 16 were hematotoxic victims. Hence, none of the neurotoxic victims had deranged renal profile.

K) COMPLICATIONS:-



This chart shows the complications that developed in the total of 50 cases of toxic snakebite. Cellulitis was seen in 68%, acute kidney injury was seen in 32%, neuroparalysis and compartment syndrome was seen in 4% each, while gangrene was seen in only 2% of the victims.

L) FINAL OUTCOME (MORTALITY):-



This graph shows the comparative analysis of the total 50 patients with reference to their respective final outcome in terms of mortality. All the hematotoxic victims survived (100%), while among the neurotoxic victims, 80% (4/5) survived, while 20% (1/5) expired.

DISCUSSION

In a predominantly agricultural country like India, snake bite poisoning is an important public health hazard.

Similar studies were done by Dr. V Dharma Rao et al, in Mamata General Hospital, Andhra Pradesh between June 2010 to May 2012. Another similar study was done in western Maharashtra by Dr. Gaurav et al, between May 2010 to May 2012.

Some other studies results were also compared with the present study.

Age (yr.)	Present study	Himmatrao et al
0-20	10%	28%
21-40	42%	46.2%
41-60	40%	21.2%
>60	8%	4.6%

A) AGE DISTRIBUTION:-

Even though snake bites have been observed in all age groups, the maximum number of bites have occured in the age group between 20-60 yrs. This age group is usually the more active age group involved in outdoor work or exposure, where they can come in contact with snakes' habitats.

Sex	Present study	Gaurav et al	Dharma Rao et al
Male	70%	80%	62%
Female	30%	20%	38%

B) SEX DISTRIBUTION:-

Male predominance was a common finding in all the studies, owing to the fact that males are more active section of population with reference to outdoor activities and exposure.

Occupation	Present study	Gaurav et al
Agriculture	50%	81.33%
Non-agricultural	50%	18.67%

C) OCCUPATIONAL DISTRIBUTION:-

Though in the present study there was similar incidence between agricultural and non-agricultural section of population, in majority of the other studies, agricultural population have had a clear predominance of snake bite owing to their exposure in the fields.

Site	Present study	Gaurav et al	Dharma Rao et al
Lower limb	84%	96%	82%
Other site	16%	4%	18%

D) SITE OF THE BITE:-

In all the studies, there was a clear predominance of lower limb bites. It suggests that the site of bite was predominantly determined by accidental contact of the snakes during activities, which is more likely in the lower limbs compared to any other part of the body.

Type	Present study	Himmatrao et al
Cobra	8%	23.87%
Krait	2%	21.1%
Russell's viper	58%	32.2%
Saw-scaled viper	20%	15.81%
Unidentified	12%	5.96%

E) TYPE OF SNAKE:-

Russell's viper's bite was found to be most common in the present study (58%) which was also observed by Himmatrao et al.

Place	Present study	Dharma Rao et al
Outdoor	60%	54%
Indoor	40%	36%

F) OUTDOOR V/S INDOOR BITES:-

Outdoor bites were found to be more common than indoor in all the studies. This is due to more exposure to the natural habitats of snakes in the outdoors as compared to household dwellings or other indoor units.

Symptoms	Present study	Gaurav et al	Dharma Rao et al
Pain	98%	69.7%	—
Active bleeding	44%	83.33%	23%
Dysphagia	8%	11.8%	—
Dysarthria	8%	—	38%
Vomiting	12%	—	21%

G) SYMPTOMATOLOGY:-

Pain was present in almost all the patients of snake bite in all the studies. It was seen in 98% of cases in the present study. Pain was relieved only after the administration of anti snake venom or pain killers. This was followed by local swelling (80%). Local swelling of varying degrees was observed in the present study.

Usually it was of a progressive nature, more commonly seen in viper bites than with neurotoxic snakes, which can be attributed to the relatively higher amount of proteinases and hyaluronidases present in the viper venom. Active bleeding from the bite site was seen in 44% of patients in present study, while 83.33% in study by Gaurav et al. In the present study, bleeding from any systemic sites other than the bite site was not observed, though bleeding from the bite site stopped only after the administration of the anti snake venom. Neuroparalytic symptoms like dysphagia and dysarthria were seen in 8% of the cases in the present study, all of which were neurotoxic victims. Similar findings were observed by Gaurav et al and Dharma Rao et al as mentioned in the table. Vomiting is an important sign of systemic envenomation, and was seen in 12% of the patients at the time of presentation in the present study, and 21% by Dharma Rao et al.

Other common findings in the present study were headache (4%), breathlessness (8%) and giddiness (6%).

Blurring of vision (4% in the present study) and diplopia was also a common finding in many of the studies. Cyanosis due to respiratory paralysis was seen in 4% of the cases.

Parameter	Present study	Dharma Rao et al
Prolonged prothrombin time, INR, a PTT	52%	23%
Raised total WBC count	68%	25.6%

H) DERANGED HEMATOLOGICAL PROFILE:-

Amongst the haematological profile, bleeding parameters like PT (prothrombin time), INR (International Normalized Ratio) and aPTT (activated partial thromboplastin time were closely monitored in most of the studies including the present study, where a majority of viper victims had these deranged. These victims also had other haematological abnormalities like thrombocytopenia (36%) and anaemia (68%), which is attributable either to consumption coagulopathy or active bleeding.

Other abnormalities like raised D-dimer levels was commonly seen in viper victims. Raised total count in view of local infection or sepsis was common. Frank hematuria was not observed in any of the patients, though microscopic hematuria was quite common in the viper victims.

Among the neurotoxic victims, only raised total count was observed in 2 cases. Bleeding parameters were all normal in neurotoxic victims.

Present study	Dharma Rao et al	Gaurav et al
32%	10%	26.31%

I) DERANGED RENAL PARAMETERS:-

Deranged renal parameters include raised blood urea and creatinine. This is common in viper bites as the viper venom has direct nephrotoxic property. Or it can be seen in victims who have developed sepsis or multi-organ dysfunction with acute kidney injury. In the present study no neurotoxic victim had deranged renal parameters.

Type of complication	Present study	Dharma Rao et al	Gaurav et al
Cellulitis	68%	—	42%
Acute kidney injury	24%	10%	26.3%
Respiratory paralysis	4%	10%	25%
Gangrene	2%	—	11.8%
Compartment syndrome	4%	—	—

J) COMPLICATIONS:-

Amongst the complications following toxic snake bite, local cellulitis is the most common finding seen in all the studies. Relatively more common with viper bites as they have higher amount of proteinases and hyaluronidases in their venom.

Acute kidney injury is also a common complication, more so with viper victims.

Respiratory paralysis was seen in only 4% of the cases in the present study which is significantly less as compared to other studies as the total neurotoxic cases were less in this study.

Gangrene and compartment syndrome are other complications seen for which amputations and fasciotomy was performed respectively.

	Present study	Dharma Rao et al	Gaurav et al
Mortality	2%	10%	9.2%

K) FINAL OUTCOME:-

In the present study, mortality was seen only for 1 patient who died due to respiratory failure following cobra bite.

CONCLUSION

1) The maximum number of snakebite cases (42%) are seen among the age group of 20-40 yrs.

2) Males are more frequently (70%) bitten as compared to females.

3) The agricultural section of the population is most vulnerable (50%) to snakebites.

4) A higher incidence (60%) of snakebites occured during outdoor activities as compared to indoor activities.

5) Lower limbs are more susceptible (84%) to snakebites as compared to any other body parts.

6) The type of snake (as identified by the patient or the attendants) which was most frequently encountered was Russell's viper (58%), followed by Saw-scaled viper (20%), Cobra (8%) and Krait (2%). 12% of the victims failed to adequately identify the snake.

7) Amongst the symptoms with which the victims presented to the hospital, the most common was local pain (98%), followed by local swelling (80%), local discolouration of skin and active bleeding from the bite site (44% each). Among the other less common symptoms were vomiting (12%), breathlessness (8%), dysphagia and dysarthria (8% each), giddiness (6%), headache and blurring of vision (4% each).

8) On initial examination, the most common finding was local edema (82%), followed by local skin changes (80%), pallor (48%), tachycardia (38%). The less common findings were hypotension (14%) and cyanosis (4%)

9) Amongst the laboratory investigations, anaemia and leucocytosis (68% each) was the most common finding, followed by deranged coagulation profile (52%) seen only in viper victims and thrombocytopenia (36%).

10) Cellulitis was the most common complication observed (68%), followed by acute kidney injury (32%) seen only with viper bites. Neuroparalysis (4%), compartment syndrome (4%) and gangrene (2%) were the other complications observed.

11) Mortality was seen for only 1 case (2%), who died due to respiratory failure following cobra bite.

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH

Mr. /Mrs._____ we are requesting you to enroll yourself in study titled "**CLINICAL PROFILE OF TOXIC SNAKE BITE CASES IN PATIENTS ADMITTED AT DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI. A ONE YEAR CROSS SECTIONAL STUDY.**" -A Study conducted by Dr._____, postgraduate student in MD GENERAL MEDICINE under the guidance of Dr. _____ at J.N.Medical College, Belagavi.

You have been requested to participate in research because your profile matches with the study group. All the patients admitted with toxic snake bite can become participants of study. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge.

Your participation in the research is absolutely voluntary. Your decision to participate in the study or otherwise will not affect your relationship with J.N.M.C. If you decide not participate you are free to withdraw at any time.

The purpose of research is to study the clinical profile of toxic snake bite cases admitted in Dr. Prabhakar Kore charitable hospital, Belagavi, and also to study its complications and outcome.

Procedure involved

A detailed history taking, clinical examination, and blood investigations.

Risks and benefits

There are no risks involved and benefits are many. The study helps to find out the most common clinical signs and symptoms that develop in victims of toxic snake bite. It also helps to monitor relevant laboratory investigations that are required to assess the in-hospital progress of the snakebite victim. The results deduced at the end of study will help all similar patients admitted in the hospital to assess their prognosis.

Alternatives

Even if you decline to participate, there will not be any change in the line of your management or the relationship with your doctor. You will be told about all the new information that may affect your decision to participate in the study.

Withdrawing/removal from study

You can withdraw any time from the study as you wish. You will not be penalized for such a decision.

Privacy and confidentiality

The only people to know that you are a research subject are the members of research team. No information about you or provided by you during the research will be disclosed to others without your written permission except:

In emergency to protect your rights and welfare.

If required by law.

Financial incentives for participation

You will not be paid any monetary benefits or free gifts for participation in the research. You will not be reimbursed for expenses.

Authorization to publish results

When the results of the research are published or discussed in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

CONSENT STATEMENT

I, the undersigned, have been explained in my own vernacular language about the study and my participation in the study is voluntary. If I want I can withdraw at any time. Also I have been given enough time to clear my doubts about the study and my rights as a study participant.

In case you have any questions related to the study you can contact Dr. _____, (_____).

In case you have any questions about your rights as a study participant you can contact Dr. _____ (_____).

Signature or the left thumb impression of the participant or legally authorized representative.

Participant's name: _____Signature: _____

Witness name: _____ Signature: _____

Experimenter's name: _____ Signature: _____

Guardian's name: _____ Signature: _____

Place: _____

Date: _____

ANNEXURE II – PROFORMA

"CLINICAL PROFILE OF TOXIC SNAKE BITE CASES IN PATIENTS ADMITTED AT DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI. A ONE YEAR CROSS SECTIONAL STUDY"

A) Preliminary data:

1. Case number:
2. Name:
3. Age:
4. Sex:
5. Address:
6. Occupation:
7. IP No:

B) Symptomatology:

1. Site of bite:
2. Time between bite and hospitalization:
3. Pain:
4. Swelling (Present / Absent):
5. Discolouration of skin:
6. Breathlessness:
7. Bleeding tendencies (from any site / presentation):
8. Dysphagia:
9. Dysarthria:
10. Nausea / vomiting:

11. Giddiness:

12. Headache:

13. Blurring of vision:

14. Altered sensations:

C) Past history (relevant and significant CNS, CVS, RS, GIT, RENAL, or Hematologic disorders that the patient may have before the bite incidence):-

D) Personal history:

1. Diet:
2. Appetite:
3. Sleep:
4. Bowel habits:
5. Bladder habits:
6. Addictions:

E) Family history (relevant disorders in family):-

F) General Examination:-

1. Pulse:
2. BP:
3. Pallor:
4. Edema (local / generalized):
5. Lymphadenopathy:

6. Cyanosis (central / peripheral):
7. Clubbing
8. Icterus:

G) Local Examination:

1. Bitemarks (number of fangs, active bleeding present through the bitemarks or not):
2. Skin changes (swelling, temp, color, blisters, gangrene)

H) Systemic Examination:

1. CNS:

2. CVS:

3. RS:

4. P/A:

I) Investigations:

1. Hb:
2. TC:
3. DC:
4. ESR:
5. Platelet:
6. BT:
7. CT:
8. PT:
9. INR:
10. APTT:
11. RBS:
12. Urea:
13. Creatinine:
14. D- Dimer:
15. ECG Changes:
16. Fundus examination findings:
17. Urine examination findings:

J) Management:

1. Injection TT:
2. Antibiotics:
3. Analgesics:

4. Other- anti-inflammatory agents used:
5. ASV:
6. Inj. Neostigmine:
7. Inj. Atropine:
8. Blood Transfusions:
9. Local applications (Glycerine, mgso4 etc.):
10. Mechanical Ventilation:

K) Complications developing:

L) Final Outcome:

1. Date of admission:
2. Date of discharge (or expiry):
3. No. of hospital days:

ANNEXURE III – KEY TO MASTER CHART

P — Present

A — Absent

M — Male

F — Female

S — Significant

NS — Not significant

V — Vegetarian

Mi — Mixed

N — Normal

Ab — Abnormal findings

L — Local

Ge — Generalised

R — Raised

r — Reduced

G — Given

NG — Not given

CL — Cellulitis

AKI — Acute kidney injury

P — Neuroparalysis

CS — Compartment syndrome

Ga — Gangrene

case.no.	age	sex	Ip.no.	site of bite	time to hospitalisation (in hours.)	pain P/A	swelling P/A	discoloration of skin P/A	breathlessness P/A	bleeding P/A	dysphagia P/A	dysarthria P/A	vomitting P/A	giddiness P/A	headache P/A	blurring of vision P/A	altered sensorium P/A	past hist. S/NS	diet V/Mi	apetite N/Ab	sleep N/Ab	bowel N/Ab	bladder N/Ab	addictions P/A	family hist. S/NS	pulse	BP
1	50	M	705510	left lateral malleolus	2	P	P	A	A	P	A	A	P	A	A	A	A	NS	Mi	N	N	N	N	A	NS	82	132/82
2	75	M	711415	Right calf	3	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	80	140/92
3	43	M	715357	left great toe	0.5	P	A	A	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	78	140/88
4	58	M	715512	Right toe	1	P	P	A	A	A	A	A	A	A	A	A	A	S	Mi	N	N	N	N	A	S	78	138/80
5	26	M	715934	Right hand	3	P	P	A	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	S	92	130/80
6	47	M	717330	Right great toe	6	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	88	110/72
7	19	F	717890	Right great toe	6	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	88	110/72
8	29	M	718940	Left lateral maiieolus	2	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	80	120/82
9	60	F	721021	Left wrist dorsal	3	P	P	P	A	P	A	A	A	A	A	A	A	NS	V	N	N	N	N	A	NS	100	100/80
10	45	M	723739	Right foot dorsal	8	P	P	P	A	P	A	A	A	A	A	A	A	NS	V	N	N	N	N	P	NS	92	120/70
11	26	F	723762	Left lateral malleous	6	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	92	110/70
12	55	M	725322	Right foot dorsum	3	P	P	A	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	80	138/80
13	19	F	728301	Right middle phalynx	3	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	88	118/70
14	56	M	729179	Right dorsum foot	6	P	P	A	A	A	A	A	A	A	A	A	A	NS	V	N	N	N	N	P	NS	90	96/50
15	27	F	732395	Left dorsum foot	3	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	110	96/60
16	30	M	733556	Right sole of feet	0.5	P	P	A	A	P	A	A	A	A	A	A	A	NS	V	N	N	N	N	A	NS	72	110/70
17	35	M	734658	Left ankle n heel	11	P	P	A	A	P	A	A	P	A	A	A	A	NS	Mi	N	N	N	Ab	A	NS	54	130/80
18	50	F	734825	Left leg malleous	8	P	P	P	A	P	A	A	A	A	A	A	A	NS	V	N	N	N	N	A	NS	120	90/60
19	19	M	736042	Right forearm	4	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	118	120/80
20	40	M	736249	Right calf	1	P	A	A	A	A	A	A	A	A	A	A	A	S	Mi	N	N	N	N	P	NS	90	140/80
21	42	M	737093	Left foot dorsum	2	P	P	P	A	P	A	A	A	A	A	A	A	NS	V	N	N	N	N	A	NS	80	108/70
22	26	F	738806	Right medial malleous	1	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	122	92/70
23	56	M	739314	Right foot planter	4	P	A	A	P	A	P	P	A	P	A	A	A	NS	Mi	N	N	N	N	P	NS	70	112/70
24	21	M	739323	left medial malleolus	3	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	110	110/70
25	55	M	740007	Left lateral malleolus	2	P	P	P	A	A	A	A	A	A	A	A	A	S	Mi	N	N	N	N	A	NS	84	138/84
26	22	M	740201	Right foot dorsum	2	P	A	A	A	A	A	A	P	A	A	A	A	NS	Mi	N	N	N	N	A	NS	90	120/68
27	45	F	740921	Left medial malleolus	3	P	P	A	P	A	P	P	A	P	A	P	P	NS	Mi	N	N	N	N	A	NS	110	120/70
28	52	M	742955	Left hand mid finger	2	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	74	122/80
29	36	M	744122	Left dorsum of foot	6	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	80	132/78
30	65	M	744686	eft palm thenar prominenc	7	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	110	100/72
31	32	M	745576	Right foot dorsum	3	P	P	A	A	P	A	A	P	A	P	A	A	NS	V	N	N	N	N	A	NS	104	122/72
32	25	F	745959	Right lateral malleolus	3	P	P	A	A	A	A	A	P	A	A	A	A	NS	V	N	N	N	N	A	NS	104	110/60
33	18	M	746531	Left leg medialy	4	P	A	A	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	122	90/60
34	55	M	748120	Left dorsum of foot	3	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	92	138/80
35	60	M	752176	Right dorsum of foot	3	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	90	120/72
36	70	F	752235	Left sole near heel	3	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	114	100/70
37	23	M	752700	Right thumb palmer	4	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	133	98/58
38	40	M	753562	Left dorsum of foot	6	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	90	140/80
39	70	F	756426	Right leg calf	7	P	P	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	80	150/70
40	30	M	758525	Left great toe planter	6	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	110	100/72
41	52	M	759057	Left dorsum of foot	4	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	P	NS	88	130/70
42	45	M	759769	Right medial malleolus	2	P	A	A	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	88	130/78
43	22	F	761591	Right wrist index finger	4	A	A	P	P	A	P	P	A	A	A	A	P	NS	Mi	N	N	N	N	A	NS	120	110/72
44	41	M	761901	Right sole of foot	4	P	A	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	92	140/80
45	28	F	762172	Left ankle lateraly	1	P	P	P	A	A	A	A	P	A	A	A	A	NS	Mi	N	N	N	N	A	NS	110	110/70
46	30	F	762290	Left foot dorsum	2	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	108	108/70
47	20	M	763190	Left lateral malleolus	1	P	A	A	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	118	100/62
48	40	M	764008	Right foot sole	4	P	P	P	A	P	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	90	92/60
49	32	F	764112	Left calf region	8	P	A	A	P	A	P	P	A	P	P	P	A	NS	Mi	N	N	N	N	A	NS	90	106/68
50	45	M	765091	Left medial malleolus	6	P	P	P	A	A	A	A	A	A	A	A	A	NS	Mi	N	N	N	N	A	NS	112	104/68

case.no.	pallor P/A	edema L/Ge	lymphadenopathy P/A	cyanosis P/A	clubbing P/A	icterus P/A	skin changes P/A	CNS N/Ab	CVS N/Ab	RS N/Ab	P/A N/Ab	Hb N/r	TC N/R	ESR N/R	PLT N/r	BT N/R	CT N/R	PT N/R	INR N/R	APTT N/R	Rbs N/R	Urea N/R	Creat N/R	D-Dimer N/R	ECG N/Ab	fundoscopy N/Ab	urine R/M N/Ab	inj.TT G/NG	antibiotics G/NG	analgesics G/NG	anti-inflammatory G/NG	ASV	neostigmine G/NG	atropine G/NG	Bld.Transfusions G/NG	L/A G/NG	Cx CL/AKI/P/CS/Ga	DOA	DOD/Exp.	hosp. stay
1	P	L	A	A	A	A	A	N	N	N	N	r	N	N	N	R	R	R	R	R	N	N	N	R	N	N	N	G	G	G	G	18	NG	NG	NG	G	CL	1/12/2015	12/1/2016	11
2	A	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	N	R	R	R	N	N	N	R	N	N	N	G	G	G	G	10	NG	NG	NG	NG	CL	3/1/2016	7/1/2016	4
3	P	Nil	A	A	A	A	A	N	N	N	N	r	N	R	N	N	N	N	N	N	N	N	N	R	N	N	N	G	G	G	G	10	NG	NG	NG	NG	CL	21/1/2016	30/1/2016	9
4	A	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	R	R	R	N	N	R	R	N	N	Ab	G	G	G	G	18	NG	NG	NG	G	CL/AKI	25/1/2016	8/2/2016	14
5	A	L	A	A	A	A	A	N	N	N	N	r	R	R	r	R	R	R	R	R	R	R	R	R	N	N	Ab	G	G	G	G	28	NG	NG	G	G	CL/AKI	27/1/2016	4/2/2016	8
6	P	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	N	N	N	N	N	N	R	N	N	N	G	G	G	G	14	NG	NG	NG	G	CL	4/2/2016	11/2/2016	8
7	P	L	A	A	A	A	P	N	N	N	N	r	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	G	10	NG	NG	NG	NG	CL	8/2/2016	13/2/2016	5
8	A	L	A	A	A	A	P	N	N	N	N	r	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	G	12	NG	NG	NG	NG	CL	13/2/2016	20/2/2016	7
9	A	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	R	R	R	R	N	N	Ab	G	G	G	G	28	NG	NG	G	G	CL/AKI	24/2/2016	7/3/2016	11
10	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	N	N	R	R	R	N	R	R	R	N	N	Ab	G	G	G	G	18	NG	NG	G	G	L/AKI/(	9/3/2016	19/3/2016	10
11	A	L	A	A	A	A	P	N	N	N	N	N	R	R	N	N	N	N	N	N	R	N	N	N	N	N	Ab	G	G	G	NG	10	NG	NG	NG	NG	CL	10/3/2016	18/3/2016	7
12	A	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	R	R	R	N	N	N	R	N	N	N	G	G	G	G	18	NG	NG	G	NG	CL	17/3/2016	27/3/2016	10
13	A	L	A	A	A	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	G	10	NG	NG	NG	NG	CL	3/4/2016	8/4/2016	5
14	P	L	A	A	A	A	P	N	N	N	N	r	N	R	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	G	16	NG	NG	NG	G	CL	7/4/2016	15/4/2016	8
15	A	L	A	A	A	A	P	N	N	N	N	N	R	R	N	N	N	N	N	N	N	N	N	N	N	N	Ab	G	G	G	G	28	NG	NG	NG	G	CL	25/4/2016	5/5/2016	10
16	P	P	A	A	A	A	P	N	N	N	N	N	N	N	N	N	N	R	R	N	R	N	N	R	N	N	N	G	G	G	NG	11	NG	NG	NG	NG	CL	30/4/2016	7/5/2016	8
17	P	P	A	A	A	A	P	N	N	N	N	r	R	R	N	R	R	R	R	N	R	R	R	R	N	N	Ab	G	G	G	G	28	NG	NG	G	G	AKI	6/5/2016	14/5/2016	8
18	P	L	P	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	N	R	R	R	N	N	Ab	G	G	G	G	30	NG	NG	G	G	CL/AKI	7/5/2016	19/5/2016	12
19	A	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	N	N	N	N	N	N	R	N	N	Ab	G	G	G	G	14	NG	NG	NG	G	CL	13/5/2016	23/5/2016	10
20	P	Nil	A	A	A	A	A	N	N	N	N	r	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	NG	10	NG	NG	NG	NG	Nil	14/5/2016	20/5/2016	6
21	A	L	A	A	A	A	P	N	N	N	N	N	R	R	r	R	R	R	R	R	N	N	R	R	N	N	Ab	G	G	G	G	20	NG	NG	G	NG	CL/AKI	18/5/2016	30/5/2016	12
22	P	L	A	A	A	A	P	N	Ab	N	N	r	R	R	r	R	R	R	R	R	N	R	R	R	N	N	Ab	G	G	G	G	30	NG	NG	G	G	CL/AKI	26/5/2016	8/6/2016	14
23	P	L	A	A	A	A	P	N	N	N	N	N	N	R	N	N	N	N	N	N	N	N	N	R	N	N	N	G	G	NG	NG	20	G	G	NG	NG	Nil	29/5/2016	4/6/2016	5
24	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	r	N	N	R	N	N	N	G	G	G	G	25	NG	NG	G	NG	CL	29/5/2016	6/6/2016	7
25	A	L	P	A	A	A	P	N	N	N	N	N	R	R	N	N	N	N	N	N	N	N	N	R	N	N	N	G	G	G	G	20	NG	NG	NG	G	CL	1/6/2016	15/6/2016	14
26	A	Nil	A	A	A	A	P	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Ab	G	G	G	NG	10	NG	NG	NG	NG	Nil	2/6/2016	7/6/2016	5
27	P	L	A	p	A	A	A	Ab	Ab	N	N	r	N	R	N	N	N	N	N	N	N	N	N	N	N	N	Ab	G	G	NG	NG	40	G	G	NG	NG	P	6/6/2016	9/6/2016	3
28	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	N	N	N	R	N	N	Ab	G	G	NG	NG	10	NG	NG	G	NG	CL	16/6/2016	26/6/2016	10
29	A	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	N	N	N	N	N	N	R	N	N	N	G	G	G	G	10	NG	NG	NG	G	CL	22/6/2016	2/7/2016	10
30	P	L	A	A	A	A	P	N	N	N	N	r	R	R	N	R	R	R	R	R	N	R	R	R	N	N	Ab	G	G	G	G	20	NG	NG	G	G	CL/AKI	24/6/2016	4/7/2016	10
31	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	N	N	N	R	N	N	N	G	G	G	G	20	NG	NG	G	G	Nil	28/6/2016	7/7/2016	9
32	A	L	A	A	A	A	P	N	N	N	N	N	R	R	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	NG	10	NG	NG	NG	NG	Nil	30/6/2016	8/7/2016	8
33	P	Nil	A	A	A	A	A	N	N	N	N	r	R	R	r	R	R	R	R	R	N	N	N	R	N	N	Ab	G	G	G	G	28	NG	NG	G	NG	Nil	4/7/2016	17/7/2016	13
34	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	N	R	R	R	N	N	Ab	G	G	G	G	16	NG	NG	G	G	CL/AKI	12/7/2016	20/7/2016	8
35	P	L	A	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	N	N	N	R	N	N	Ab	G	G	G	G	18	NG	NG	G	NG	CL	1/8/2016	9/8/2016	8
36	P	L	P	A	A	A	P	N	N	N	N	r	R	R	N	N	N	N	N	N	R	R	R	R	N	N	Ab	G	G	G	G	10	NG	NG	G	G	CL/AKI	1/8/2016	12/8/2016	11
37	A	L	A	A	A	A	P	N	N	N	N	N	R	R	r	R	R	R	R	R	R	N	N	R	N	N	N	G	G	G	G	10	NG	NG	G	G	CL	4/8/2016	13/8/2016	9
38	A	L	A	A	A	A	P	N	N	N	N	N	R	R	N	N	N	N	N	N	R	N	R	N	N	N	N	G	G	G	G	10	NG	NG	NG	G	AKI	8/8/2016	15/8/2016	7
39	P	L	A	A	A	A	P	N	N	N	N	r	N	N	N	N	N	R	R	R	N	N	N	R	N	N	N	G	G	G	G	10	NG	NG	NG	NG	Nil	22/8/2016	28/8/2016	6
40	A	L	A	A	A	A	P	N	N	N	N	N	R	R	r	R	R	R	R	R	R	R	R	R	N	N	Ab	G	G	G	G	20	NG	NG	G	G	CL/AKI	2/9/2016	14/9/2016	12
41	P	L	P	A	A	A	P	N	N	N	N	r	R	R	r	R	R	R	R	R	R	R	R	R	N	N	Ab	G	G	G	G	28	NG	NG	G	NG	CL/AKI	5/9/2016	15/9/2016	10
42	A	Nil	A	A	A	A	P	N	N	N	N	r	N	R	r	R	R	R	R	R	N	N	N	R	N	N	Ab	G	G	NG	NG	20	NG	NG	G	G	Nil	8/9/2016	16/9/2016	8
43	A	Nil	A	P	A	A	P	Ab	N	N	N	N	R	R	N	N	N	N	N	N	R	N	N	R	N	N	N	G	G	G	NG	40	G	G	NG	NG	P	18/9/2016	16/10/2016	28
44	A	Nil	A	A	A	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	R	N	N	N	N	N	N	G	G	G	G	10	NG	NG	NG	NG	Nil	19/9/2016	22/9/2016	3
45	A	L	A	A	A	A	A	N	N	N	N	N	N	R	N	R	R	R	R	R	R	N	N	R	N	N	Ab	G	G	G	G	15	NG	NG	G	G	CS	1/10/2016	6/10/2016	6
46	A	L	A	A	A	A	P	N	N	N	N	r	R	R	N	N	N	N	N	N	R	N	N	R	N	N	Ab	G	G	G	G	10	NG	NG	NG	G	CL	13/10/2016	22/10/2016	10
47	A	Nil	A	A	A	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	G	G	G	NG	10	NG	NG	NG	NG	Nil	15/10/2016	20/10/2016	5
48	P	L	A	A	A	A	P	N	N	N	N	r	R	R	N	R	R	R	R	R	R	R	R	R	N	N	Ab	G	G	G	G	28	NG	NG	G	G	CL/AKI	17/10/2016	30/10/2016	13
49	A	A	A	A	A	A	P	Ab	N	N	N	r	R	R	N	N	N	N	N	N	N	N	N	N	N	N	Ab	G	G	G	NG	20	G	G	NG	NG	Ga	26/10/2016	2/11/2016	7
50	A	L	P	A	A	A	P	N	N	N	N	r	R	R	r	N	N	N	N	N	N	R	R	R	N	N	Ab	G	G	G	G	10	NG	NG	NG	g	CL/AKI	1/12/2016	19/12/2016	18