"A CLINICAL STUDY OF TREATMENT OUTCOME IN COMPLICATED SNAKEBITES RECEIVING ASV AS PER INDIAN GUIDELINES AND PROTOCOL"

By

Dr HARISH BV

DISSERTATION SUBMITTED TO THE SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

In partial fulfilment of the requirements for the degree of

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IN

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Under the guidance of

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ABSTRACT

Background:

Snake bite is one of the common medical emergencies and an occupational hazard encountered in day to day practice in rural populations of India, where farming is a major source of employment. The morbidity and mortality rates of snake bite patients are high. In India, there are 216 species of snakes of which most important venomous snakes are Cobra, Common Krait, Russell's viper, and Saw scaled Viper.

There has been a lack of epidemiological studies on snakebites in our country. ASV is irrationally utilized due to poor experience and improper training. Many times it is administered in non-indicated cases and avoided in an indicated case due to fear of anaphylaxis or used in excess in a serious case without extra benefit. So this study is undertaken to study the clinical profile, treatment outcome and to determine the ASV requirement in treatment of complications of snakebite.

Objectives of the Study:

1. To study the clinical profile of complicated poisonous snakebite.
2. To assess the morbidity, recovery and mortality at time of discharge in complicated snakebite receiving ASV as per Indian Guidelines and Protocol.

Materials and Methods:

Patients aged 18 years and above with the history of snake bite and fulfilling the inclusion criteria were admitted. 20WBCT & other relevant investigations were done and divided the patients into hemotoxic, neurotoxic and only local envenomation group. They were started on ASV as per Indian Guidelines and Protocol given by Association of Physicians of India in 2013. They were reassessed clinically and outcome was recorded on the day of discharge. Complete Recovery, morbidity or mortality was the outcome measures.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Chi-square test of Fischer's exact test was used as test of significance for qualitative data. Yates correction was applied where ever chi-square rules were not fulfilled.

Results:

103 patients fulfilling the inclusion criteria were included in the study. 29.1% were in 3rd decade and 28.2% in 2nd decade. 68% were males and 32% were females. 67% were farmers. 43.7% bites occurred in Monsoon and 41.7% in winter season. 64.1% bites occurred in Lower limb and 35.9% in upper limb. 35.9% bites occurred in morning and 30.1% in evening. 74.8% presented within 6 hrs, 21.4% with in 6 to 24 hrs and 3.9% after 24 hrs of bite. 90.3% had tied tourniquet. 24.3% had hemotoxic envenomation, 22.3% had local features, 17.5% had neurotoxic envenomation and other subjects had combination of toxicity.

Mean ASV given in hemotoxic snake bites was 18.6 units, in neurotoxic snake bites was 14.2 units and in locally toxic snake bites 10 units were used. 32% subjects had reaction to ASV. 22.3 % of subjects had life threatening complications. Most common life threatening complication observed was ARF (10.7%), followed by Cellulitis in 8.7%, MODS in 1.9% and DIC in 1% of subjects. 17.5% of subjects required ventilator support. 82.5% of subjects had complete recovery, 9.7% underwent debridement, 3.9% underwent hemodialysis and 3.9% had mortality during the course of treatment.

Conclusion:

Snakebite is common in males of 2nd and 3rd decade. Farmers are more prone to snakebites especially in monsoon and winter season with lower limb more common site. Hemotoxic bites are more common than neurotoxic and local envenomation and average ASV used is 18.6, 14.2 and 10 units respectively. Life threatening complications and mortality was high in subjects who presented late. So early presentation and early initiation of ASV according to protocol helps reducing the morbidity and mortality and also reduces the amount of ASV used thus reducing the financial burden on the patients.

LIST OF ABBREVATIONS

WHO	**World Health Organisation**
API	**Association of Physicians of India**
NTD	**Neglected Tropical Disease**
ASV	**Anti Snake Venom**
20 WBCT	**20 Minute Whole Blood Clotting Test**
ASV	**Anti Snake Venom**
ESR	**Erythrocyte Sedimentation Rate**
ECG	**Electrocardiogram**
SPSS	**Statistical Package for Social Sciences**
ARF	**Acute Renal Failure**
MODS	**Multi Organ Dysfunction Syndrome**
DIC	**Disseminated Intravascular Coagulation**

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INTRODUCTION

Our environment hosts a vast diversity of venomous and poisonous animals and plants. This wild extravagance of toxicity is fascinating from the evolutionary point of view but, as well as threatening human and animal health.[1] It is estimated that globally 5 million snakebite cases occur annually resulting in about 1,25,000 deaths. More than 2,00,000 cases of snakebites are reported in India each year out of which 35,000-50,000 turn out to be fatal, the most snakebite deaths for any country.[2] Hence, snakebite is emerging as a serious public health problem in India.[3]

Out of more than 2000 snakes in the world only 216 are in India of which only 52 are poisonous. Since majority of the snakes are non-venomous, it is important to know the anatomical differences which will help obviate needless administration of potentially harmful antivenom in every case of snakebite, especially in those cases where the snakes have been killed and brought along with them.[4] Snake bites affects millions of people annually creating one of the most neglected health problems of the tropics due to a lack of availability of antivenoms. Contributing to this in developing nations, there is also a deficiency in the reporting of cases, management of complications, transportation, hospital equipments and public knowledge of appropriate first-aid, which results in a mortality rate 100 fold higher than in developed countries.[5]

Snakebite is a common acute medical emergency faced by rural populations in tropical and sub-tropical countries with heavy rainfall and humid climate. Snakes enter human dwellings during the night in search of prey such as rats, mice and lizards[6] and accidentally bite humans. Increase in deforestation trends, migration and as the number of week end camps in the forest areas rises, an encounter with a venomous reptile becomes more likely.[7] Adding on to this problem, the major burden of human suffering caused remains

unrecognized and unheard by the global public health community. The problem is so underrated that it was only recently added to the WHO's list of neglected tropical diseases in April, 2009.[8] The peak incidence of snakebite cases is reported during the paddy sowing and harvesting periods.[6] In India, a significant proportion of medico-legal autopsies comprise cases of alleged snakebite, which are cover-ups for death caused by foul play,[4] thereby making them of medico-legal importance.

Although there is availability of ASV in all population centres[2,3], during the past few years there seems to have been little improvement in reducing the fatalities, mainly because of administration of antivenom in non-therapeutic doses resulting in wastage of precious drugs and also increasing the risk of reactions in addition to wastage of time. Delay in getting antivenom combined with use of ineffective first-aid leads to systemic envenoming by the time they seek medical treatment.[9] A lot of faith is put in traditional healers, snake charmers and other alternative system of medicine, as they are often the earliest and easiest help available especially in semiurban and rural areas.[10] The paucity of available data hampers the understanding of venom chemistry for the development of clinical management guidelines and syndromic diagnosis.[11]

There has been a lack of epidemiological studies on snakebites in our country. ASV is irrationally utilized due to poor experience and improper training. Many times it is administered in non-indicated cases and avoided in an indicated case due to fear of anaphylaxis or used in excess in a serious case without extra benefit.[12] So this study is undertaken to study the clinical profile, treatment outcome and to determine the ASV requirement in treatment of complications of snakebite.

OBJECTIVES

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1. To study the clinical profile of complicated poisonous snakebite.
2. To assess the morbidity, recovery and mortality at time of discharge in complicated snakebite receiving ASV as per Indian Guidelines and Protocol.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The universal philosophy taught by every civilization to humans, is that animals communicate with them as messengers of god. Every human belonging to this world has had some experience with animals, some having wonderful and some painful. Man has had a natural fear of venomous animals mainly because of painful experiences. The words "venom" and "poison" are almost similar, but commonly the term venom is used to describe a poison which is injected either by stinging or biting.[13]

Snakes play an important part in maintaining ecological balance by controlling the rodent population, thus preventing destruction of grains and minimizing the spread of diseases found among rodents to humans.[13] The scientific study of snake bite is part of clinical toxinology, the subspecialty of toxicology that deals with the effects of natural toxins of microbial, animal and plant origin on human beings and domestic animals, particularly their epidemiology, patho-physiology, prevention and treatment.[14]

MYTHOLOGY

Snakes have been described as various mythological characters and been used symbolically by many civilizations, cultures, religions and societies.

Greek Mythology :

Apollo, the son of Leto killed the python which was sent by Hera. To celebrate this victory, Apollo took the name Pythius and organized the Pythian games. Our medical symbol of two snakes wrapped around a staff comes from the ancient Greek mythology. According to the myth, the mythical figure Asclepius (son of Apollo) discovered medicine by watching a snake that used herbs to bring another snake back to life. Medusa is a lady with thousands of snakes on her head instead of hair and had the power to turn anyone who looked directly at her into a stone.[13]

Egyptian Mythology :

Nehebka was a falcon winged cobra goddess of magic, was believed to protect the Pharoah and the Egyptian royal family. She is said to have swallowed seven serpents in a mystical rite that made her completely immune to any spells cast upon her.

African Mythology :

African people regard snake as immortal, as it sheds its skin and still continues to live. In many African art works there is a symbol of snake depicted with its tail in its mouth,

as a symbol of eternity. Some African cultures worshiped rock pythons and considered it a serious crime to kill one.

Indian Mythology :

Kundalini yoga also centers on the imaginery of serpent. Goddess Kundalini is described as a sleeping serpent coiled three and a half times around the first chakra at the base of the spine. Snakes are considered sacred animals, outside Hindu temples in South India, small sculptures in various forms of serpents are set up at the foot of sacred trees. These images are worshipped by couples who wish for children. These snake stones consists of pictures of five headed, seven headed snakes or two copulating snakes.

Naga (cobra) is worshiped in India on two days each year, "Nag Panchami" and "Anant Chaturdasi". The word Naga means serpent in Sanskrit. All over India snake charmers carry live cobra snakes during Nag Panchami to each house, where people offer milk and coins to the Naga. In South India, termite mounds are believed to be the living places of the Naga and are specially worshipped. Killing a Cobra is said to be a sin and associated with severe consequences even in the future generations.

Common beliefs about Cobra in Hindu mythology :

Lord Vishnu is depicted as resting on the seven headed serpent, Vasuki in an ocean of milk – Ksheera-sagara. Lord Shiva is depicted wearing a cobra around his neck and Lord Ganesha around his belly.

Biblical symbolism :

In the book of Genesis, snake symbolized temptation of Adam and Eve where the snake is said to have persuaded them to eat the forbidden fruit. The creator is said in turn to have punished the couple by sending them to lower levels of creation and the snake by making it crawl on its belly in the dust. God also has known to said enemity would always exist between the snake and the woman. Thus, the enemity between snakes and humans.

Staff of Asclepius :

Asclepian snake is the common name for a harmless snake that symbolizes Greek god of medicine, Asclepius. The staff that Asclepius used to carry features only one snake and has no wings and is considered the true symbol of medicine.

Figure 1: The Staff of Asclepius[13]

Caduceus Symbol:

The Caduceus is a wing topped staff with two snakes winding around it. Hermes, messenger of the gods, carried it as a symbol of peace. It has largely replaced the one snake symbol of Asclepius, as a symbol of medicine.

Figure 2: The Caduceus symbol[13]

The staff of Asclepius and Caduceus is both derived from Greek mythology. Caduceus usually stands for peace and also serves as a symbol of trade and communication, while the staff of Asclepius stands for healing.[13]

Morphology and biology of snakes :

Snakes are classified based on the arrangement of their scales, dentition, osteology, myology, sensory organs and more recently by immunological studies of their venoms and serum proteins.[15] Snakes are predatory carnivores, also are preyed upon by other animals, so they tend to be secretive and have evolved many survival strategies [16]. Snakes are the most

linear of vertebrates, having only a skull and extended spinal column with no appendages for locomotion. The whole body of the snake is covered with scales which are periodically shed during the process of moulting. Snakes will be blind and lethargic during this period.[17] Most legless lizards can be distinguished from snakes by their closable eyes, friable tails or lack of enlarged ventricles.[15]

They use 4 patterns of movement: lateral undulation, concertina movement, rectilinear movement and side winding (used by desert vipers). At rest, their bodies are always coiled and never remain stretched out.[13] Snakes locate their prey by their senses of vision, smell or thermo sensitivity. The remarkable vision helps them to locate their prey, they smell by using their forked tongue which collects airborne particles and then passes them to the Jacobson's organ or the vomero-nasal organ in the mouth for examination. The body of the snakes is also very sensitive to vibration, enabling them to sense approaching animals by the vibrations on the ground. Some snakes have infrared sensitive receptors near the nostrils or eyes, which allows them to see the radiated heat from their preys and there by easily locate their prey.[17]

Snakes prefer not to confront large animals such as humans so give them the chance to slither away.[16] Almost all snakes will bite when provoked, although there is a lot of difference what constitutes provocation to different animals. In a confrontation, an animal can kill or get killed, so they prefer to retreat. For the same reason venomous animals are seen forced to fight if they are unable to slip away unseen. Snakes have got a reputation for attacking on sight.

Distribution of snakes in the environment :

Snakes lack an effecting way of creating and maintaining body heat; thus they are referred to as cold blooded animals, hence their distribution is most common in tropical and warm desert environments. In the tropics, because of presence of high temperatures throughout the year, at night as well as during day, snakes can be active with little concern for the weather. In temperate regions they retreat to hibernation and their body temperature drops so low that vital body functions become impossible.[13] Venomous snakes are found on all continents except Antarctica, and in tropical waters from East Africa to the Pacific coast of Americas.[18] More than 2,700 species of snakes are currently recognized, placed in about 420 genera and 18 families.

MAGNITUDE OF THE PROBLEM

Venomous snakebites are said to be the single most important global cause of human injury from venomous and poisonous animals of all types.[18] Precise estimates on snake bite morbidity and mortality is available from industrialized countries like USA and Australia, but in tropical countries where snake bite is a serious problem, reliable data are missing.[15] Apart from venomous bites, large pythons in Indonesia, have been reported to attack and even ingest humans, usually farmers.[16]

World -

Snake bite envenoming is a serious health problem in rural areas of tropical and sub-tropical countries situated in Africa, Asia, Oceania and Latin America. It is estimated that at

least 421,000 envenomings and 20,000 deaths occur worldwide from snake bite each year, even may be as high as 1,841,000 envenomings and 94,000 deaths.[20] In sub-Saharan Africa annual snake bite are close to 1,000,000 with annual fatalities ranging from 3,500 to 32,000.[21] It has been estimated that, four million snake bites occur in Asia annually of which approximately 50% are venomous bites resulting in 100,000 annual deaths.[22] A fundamental problem throughout much of the Asia-Pacific Region is that snake-bite treatment has remained in the domain of traditional or herbal practitioners, so that the majority of snake-bite victims are not seen or recorded in western-style hospitals or dispensaries.[16]

India -

India has remained notorious for its venomous snakes and the effects of their bites. Alexander the Great when invaded India in 326 BC, was said to be impressed by the skill of Indian physicians in the treatment of snake bites. Joseph Fayrer of the Indian Medical Service first quantified, 11,416 human snakebite deaths in 1869 for about half of British India. Subsequent estimates of human deaths from snake bite prior to Indian Independence ranged from 7,400 to 20,000 per year.[23] Venomous snakebites have constituted a major medical concern in India for the past 100 years. India is said to have the highest estimated annual envenomings and deaths of 81,000 and 11,000 respectively.[20]

A WHO survey conducted in the mid- 20th century estimated about 200,000 bites with an annual mortality of 15,000. By the end of the century the mortality rate raised to 25,000.[24] Government of India hospitals from all but six states reported only 1,364 snakebite deaths in 2008 but was believed to be an under-report as many victims of snake bite choose village-based traditional therapists and most die outside government hospitals. Uncertainties in mortality rates among states have resulted in indirect estimates of annual snakebite

mortality in India that varied from approximately 1,300 to 50,000.[23] The estimated total of 45,900 national snakebite deaths in 2005 was said to constitute about 5% of all injury deaths and nearly 0.5% of all deaths in India. It is more than 30-fold higher than the number declared from official hospital returns.[23]

In India, victims of snakebite are said to have a high risk of dying even when they reach the hospital because the snake venom contains variety of enzymes capable of affecting multiple organs and most of the rural hospitals in India lack the intensive care facilities needed for managing patients with multi-organ dysfunction.[25] Snake bite remains an underestimated cause of accidental death in India, causing about one death for every two HIV-related deaths.[23] The Indian snake bite statistics are alarming as the figures are the highest in the world, even though it does not host the largest number of snakes in the world.[17]

Karnataka –

Our state is one amongst the 13 states in India with the highest snakebite mortality. States with a high-prevalence of snakebite deaths are defined as those with more than 10 million people where the annual snakebite death rate exceeds 3 per 100,000 population. According to the National representative mortality survey conducted in 2001-03, death rates due to snake bites in Karnataka were 4.2 per lakh population higher than the national rate of 4.1. Snake bite was responsible for 41 out of the total 6961 deaths with 32 cases having died outside the health facility.[23]

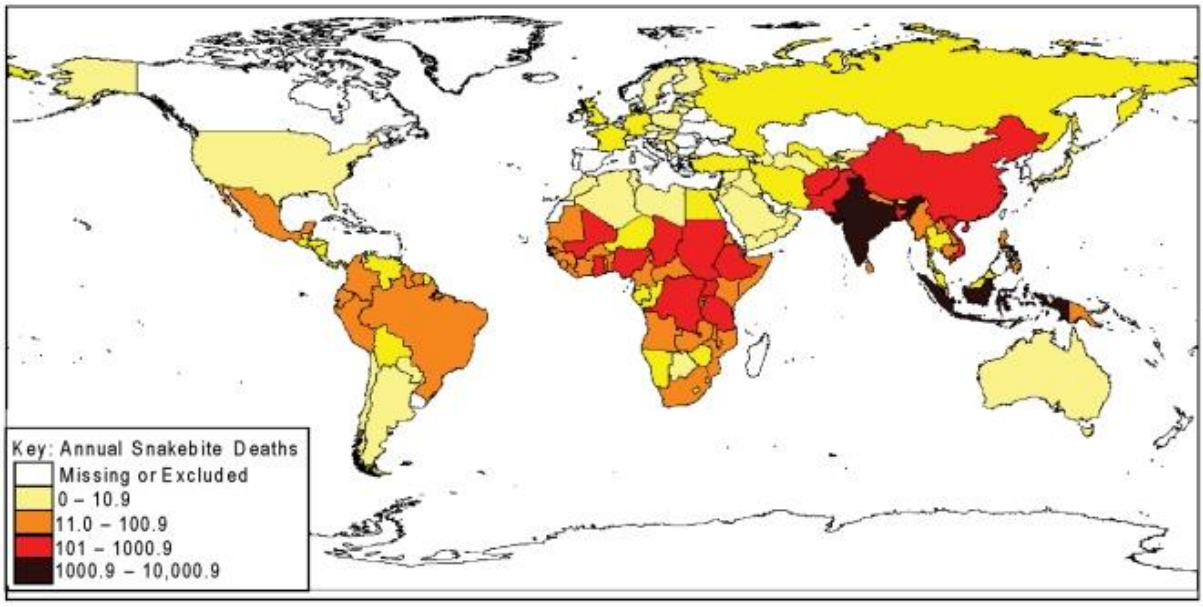

Figure 3: Global estimates of annual snakebite deaths[26]

The above figure clearly represents the actual burden of the problem in our country. Almost every state in our country, has got annual mortality rates due to snake bites exceeding one thousand, in spite of availability of an effective anti-venom. Annual snakebite deaths were greatest in the states of Uttar Pradesh (8,700), Andhra Pradesh (5,200) and Bihar (4,500). Because a large proportion of global totals of snake bites arise from India, global snake bite totals might also be underestimated. Snake bite remains an important cause of accidental death in modern India, and its public health importance has been systematically under estimated.[23]

<u>Snakebite – a neglected tropical disease</u> :

Every year snake envenoming kills more people in the tropics than some of the world's recognised neglected tropical diseases (NTDs), although it lacks the epidemic potential of an infectious/vector-borne disease. Highest toll is especially in the rural tropics, accounting for 10% of all hospital admissions.[18] The recent categorisation of snake

envenoming as an NTD by WHO is an important advance that hopefully is said to result in the wider recognition and allocation of resources, particularly since death from snake envenoming is preventable; antivenom is very effective when correctly administered.

Snake envenoming urgently requires international support to instigate the epidemiological, health education, and effective treatment initiatives that proved to be so effective in addressing the medical burden of other NTDs such as Leprosy and Dracunculosis. Snake bites probably cause more deaths in the region than do Entamoeba histolytica infections but not even a small fraction of the research investment in Amoebiasis is spent on snake bites.[16] All the global estimates of snake envenoming and deaths from snakebite indicate that mortality is highest in the world's tropical countries.[26]

Medico-legal significance :

Snakes can sometimes be used with intent to cause harm, easily mimicking an accident. Venomous snakes can be used to commit a murder by throwing it over the bed of a sleeping person. It can also be rarely used with the intention of committing suicide. Queen Cleopatra is said to have committed suicide by getting herself bitten by a venomous snake.[27] So snake bite cases are commonly registered as medico-legal cases.

SNAKES

Snakes belong to the **Class -** Reptiles.

Order – Squamata

Sub order – Serpents (Ophidia)

There are about 2500 species of snakes in the world. In India there are 236 species of snakes of which 52 are poisonous and four species are dangerously venomous.[28]

There are five main families of poisonous snakes (Biggam and Wright)[29] i.e.

1. Colubridae (tree snakes).

2. Elapidae (Cobra and Kraits).

3. Hydrophidae (Poisonous sea snakes).

4. Viperidae (Russell's viper) and

5. Crotalidae (Pit viper).

Of these, Elapidae is most common type of family of poisonous snakes inhabiting India, especially the cobra and kraits. Crotalidae and Colubridae are not seen in India. Four medically important venomous land snakes in our country are – the Indian Krait (Bungarus caeruleus), the common cobra (Naja naja), the saw scaled viper (Echis carinatus) and Russell's viper (Viper russelii). These four dangerously venomous snakes live in cohabitation with men. The common non-poisonous snakes are natux piscator, rat snake, common whip snake, wolf snake, cat snake and Indian python.

General Characters:

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

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

Snakes are heterosexual and most (cobras-kraits) are oviparous-laying eggs which hatch in around 3 months. Vipers and sea snakes are viviparous. Snakes regularly cast of their skin every 2 months at which time they are lethargic. Snakes are poikilothermic (cold blooded) and thus hibernate in winter, maximal activity is seen in the rainy months and late summers.[30]

Morphology of poisonous snakes:

The snakes have modified teeth called fangs, usually two in number. The fangs have channels for pouring venom either in the form of a gutter as in cobra or hallow with a tiny opening at the pointed end like a hypodermic needle as in Russel's Viper. At the base of fangs are the ducts connected to the poison glands. Poison glands are modified salivary glands situated on either side of upper jaw.[31] Snakes have an elongated body. The body is divided into head, trunk and tail. The horny dry skin is covered by epidermal scales which vary in form, number and arrangement.

Identification of poisonous snakes:

In poisonous marine snakes the tail is laterally compressed. In terrestrial snakes if the ventral scales are incomplete then it is a non poisonous snake. If ventral scales are large transverse plates extending fully across the belly, the snake may be poisonous or non poisonous depending upon the following features.

Features	Poisonous snakes	Non-poisonous snakes
Belly scales	Large, covers entire breadth	Small scales, sometimes large but do not cover entire breadth
Head scales	Small(Viper) Large with a. Conspicuous pit between eye and nostril (PitViper) b. Third labial touches the eye (Cobra, King cobra, Coral) c. Central row of scales on back and with only four infralabials (Krait)	Large (except Cobra, Pit Viper and Krait)
Fangs	Long and grooved	Short and solid
Tail	Compressed	Not much compressed
Habits	Usually nocturnal	Not so
Teeth	Two long fangs	Several small tooth

TABLE 1: Differentiation between Poisonous and Non Poisonous snakes

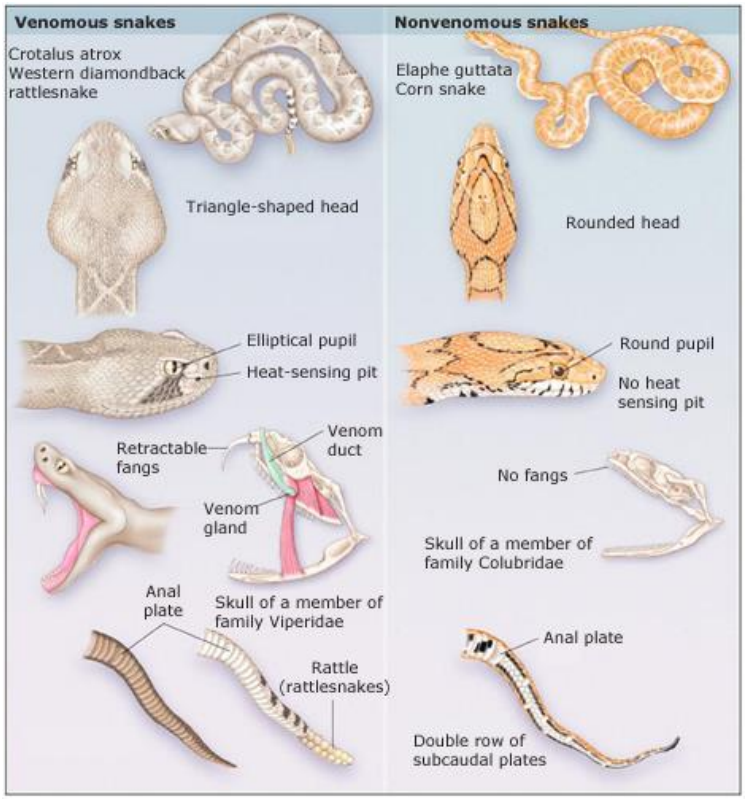

Figure 4: Comparison of Venomous Snakes and Non-venomous snakes

Poisonous:

1. If all the dorsal scales of head are small then it is a viper.

2. If 'loreal pit' between nostril and eye is present then it is a pit viper.

3. If the sub caudals are double and there is loreal pit then it is russel's viper.

4. If dorsal side of head has both small and large shields and the third supralabial shield touches the nostril and eye then it could be cobra, coral snake or king cobra.

5. If upper side of head has both small scales and large shields, no loreal pit, third supra labial shield does not touch eye, middle row of scales on back are larger than others and ventral side of lower jaw has fourth infralabial shield then it is a krait.[32]

DESCRIPTION OF COMMON POISONOUS SNAKES IN INDIA

Naja Naja:

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

Size: 1-2 meters.

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

Head: Oblong shape, has a truncated frontal shield. 3 distinct small post ocular scales and 7 supra labials of which 3rd is the largest and touching eye and the nasal scale.[33]

Eye: Has rounded pupils.

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

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

Tail: elongated.

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

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

Habitat and Habit: Cobra are remarkably adaptable snakes and found in all type of country; plains; jungles, open fields and even in the regions heavily populated by man. Their favourite hunts are the holes in embarkments, hollows of trees, old termite mounds, ruined

buildings, rock piles and dens of small mammals. They are fond of water and prefer late afternoon and early evening hours for moving around and seeking food.

Cobras are not aggressive and tend to escape when encountered in wild. They strike only when accidentally stepped on or under extreme provocation. They feed on rats, mice, food and frogs but birds, eggs and other small snakes are also eaten.

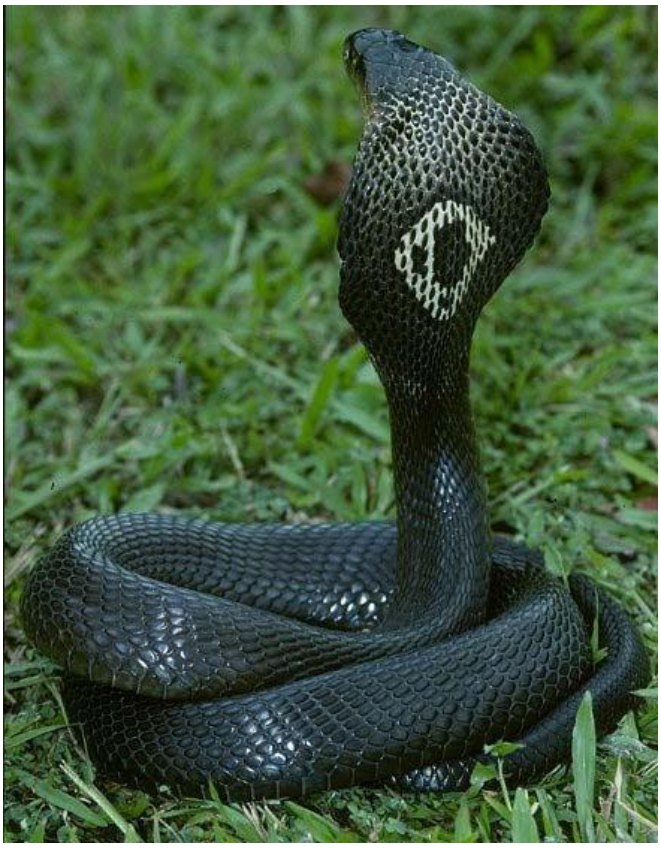

Figure 5: Common Cobra (Naja Naja)

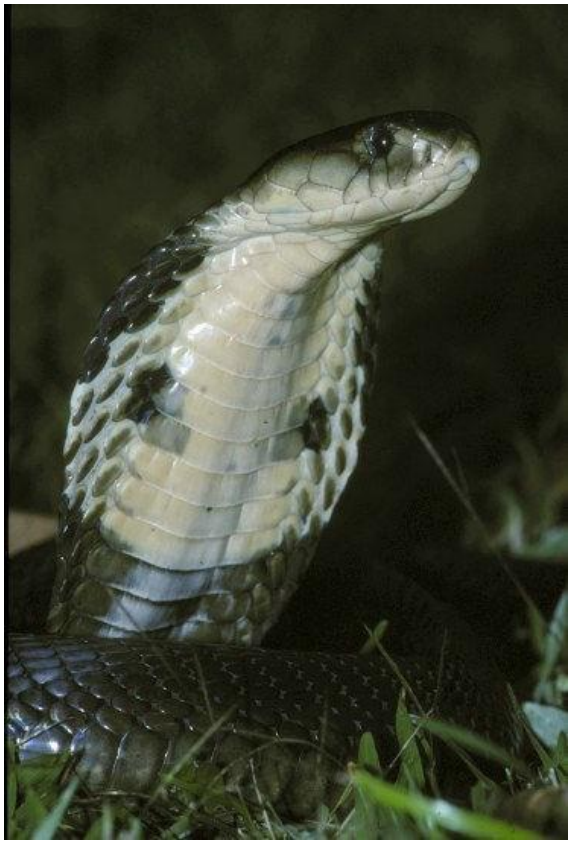

Figure 6: Naja Naja showing the 3 largest supralabia touching Eye and Nasal Scale

Figure 7: Naja Naja

Bungarus Caeruleus:

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

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

Size: 1 to 1.75 meter.

Head: Flat head. Head shields are normal, 4 shields along the margin of lower lips 3rd and 4th supra oculars touching the eye33.

Eye: Small with rounded pupils.

Fangs: Short.

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

Tail: Short and round.

Approximate yield of dry venom: 8-20 mg.

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

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

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

Figure 8: Common Indian Krait (Bungarus Caeruleus)

Figure 9: Common Indian Krait (Bungarus Caeruleus)

Viper Russelii:

Name: English – Russell's Viper

Kannada – Mandalada havu.

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

Size: 1 to 1.85 meter.

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

Eye: Large with vertical pupil.

Fangs: Fangs are big erectile and canaliculated.

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

Tail: Short.

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

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

Habitat and Habit: The Russell's viper is found both in plains and hills even at elevations upto 3000 meters. In the plains it is found in the bushy areas, grasslands, farmlands, cultivated fields and rocky areas. It is a sluggish and quiet snake during most of the day although it remains alert always.

It becomes active in the evening and at night when it wanders about in a slow, crawling motion. When disturbed, it does not move away quickly but holds the ground and

emits a lucid hiss to indicate its annoyance. It can bite with force if injured or provoked. It has a highly efficient biting mechanism with large fangs.

Figure 10: Russell's Viper (Viper Russelli)

Figure 11: Russell's Viper (Viper Russelli)

Echis Carinatus:

Name: English – Saw Scaled Viper

Kannada – Kallu havu.

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

Size: 30 to 809 cms.

Head: Triangular and very distinct from necks.

Eyes: Has a vertical pupil.

Fangs: Long and canaliculate.

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

Tail: Short and stubby.

Approximate yield of dry venom: 20-35 mg.

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

Habitat and Habit: The saw-scaled viper prefers the sandy soil, sans jungles or thick vegetations. Its favorite haunts are small hills and scrub jungles. It seems to be fond of basking in the scorching heat of mid day sun. When alarmed, it throws itself into a double coil somewhat like a figure of 8 and rubs the sides of body, producing violent rustling sound.

It is very nervous snake and quick to strike at slightest provocation. It flings in about 30 cm in the air to deliver the bite. Despite small size, this viper's habit of lying in the sand with only the head exposed poses a threat to the inhabitants of the desert area.

Figure 12: Saw Scaled Viper (Echis Carinatus)

Figure 13: Saw Scaled Viper (Echis Carinatus)

SNAKE VENOM

It is essential to understand the pharmacological actions of snake venom in order to devise a rational treatment for snakebite. The biochemical nature of the venom is very diverse and complicated. A single snake may contain several varieties of poison, for example there may be 515 enzymes, 3-13 non-enzymatic proteins and peptides and half-a-dozen or more of other substances which have a poisonous actions.[34] The more lethal fraction of snake venom appears to be peptide and perhaps-certain non-enzymatic proteins and most important effects are produced on heart, nervous system, blood vessels, kidneys and respiratory system.

The biochemical constituents of snake venom can be broadly grouped into (1) the enzymes and (2) non-enzymatic protein and polypeptide.

ENZYMES:

1. Proteinases: It is a proteolytic enzyme that digests tissue proteins and peptide leading to marked tissue changes and destruction. The anticoagulant effect of several snakes venom may be attributable in part to the proteolytic disintegration of fibrinogen. Proteinases are abundantly present in viperidae venom, while elapidae have either very little or no proteolytic activity.[29]

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

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

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

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

6. α-Amino Acid Oxidase: It is found in the venom of all snakes. It is most active of the known amino acid oxidases. This enzyme is responsible for the yellow colour of the snake venom.[35]

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

8. Enzymes Affecting Coagulation Cascade: The venom can act as both procoagulant and anti-coagulant. It was Fontanna who first described certain interactions between snake venom and blood coagulation system. Subsequently, Mitchell and Riechert demonstrated that the altered coagulation was associated with a particular venom component the globulin fraction.[35]

There are number of different mechanisms that cause snake venom proteins to act either as procoagulant or anticoagulant.[36]

Procoagulant activities are:

a) Factor X-Activators: Found in venom of Russell's viper and activates factor X in the presence of calcium.

b) Factor IX Activators: The same factor, which activates the factor X also activates, factor IX.

c) Indirect prothrombin activator: Viper Russelii venom also contains an indirect prothrombin activator that along with activated factor X converts prothrombin into thrombin.[37]

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

e) Thrombin like enzymes: The venom of viperidae appear to contain significant amounts of thrombin like enzymes. These are glycoproteins and not inhibited by thrombin inhibitors or protease inhibitors. There is a formation of fibrinogen clot. There is little direct effect on other clotting factors and no activation of plasminogen. They also do not appear to affect any cellular constituents.[38]

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

f) Factor V Activator: There are isolated reports that V.Russelii venom contains a component that increases the activity of the clotting factor V.

Anticoagulant Activities:

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

• Inhibit one or more of the blood clotting factors or prevent activation of one of the clotting factors.

• Fibrinolytic or fibrinogenolytic action by direct action on fibrin or fibrinogen.

• Activate fibrinolytic mechanism by direct action on plasminogen or activation of a plasma proactivators of plasminogen.

• Inhibit clotting by direct action of the venom anticoagulant with phospholipids.

These venom activities appear to affect both extrinsic and intrinsic clotting system. The anticoagulant activity is noted predominantly with viper and elapid venom. Viper venom is fibrinolytic, whereas cobra venom are fibrinogenolytic. The fibrinogenolysis sometimes observed following envenomation by viper might be attributable to primary pathological fibrinolysis as a result of direct activator. Enzyme phospholipase probably does not hydrolyze the phospholipids necessary for blood coagulation, but rather it forms complex with the phospholipids making interaction with clotting protein difficult.

NON-ENZYMATIC:

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

1. Hemorrhagins

2. Cardiotoxins

3. Neurotoxins.

Hemorrhagins:

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

Pharmacological studies have shown that the hemorrhagic principles induce the release of certain auto-pharmacological mediators such as histamine and 5-HT from various

tissues which open up the endothelial cell junctions and disrupt the basement membrane thereby causing vascular damage and hemorrhage.[39]

Cardiotoxin:

Cobra venom contains a cardiotoxin, which is extremely toxic for the mammalian heart. It acts directly on the cell membranes, causing many effects on the skeletal, cardiac and smooth muscles, nerve and the neuromuscular junction, thus contributing to muscle paralysis, circulatory and respiratory failure and cardiac asystole. The pharmacological action of cardiotoxin has been shown to be due to an irreversible depolarization of the cell membrane transport mechanism and a systolic cardiac arrest possibly due to release of calcium from the surface membrane of the myocardium.[40]

Neurotoxin:

These toxins are found in the elapid venom. Neurotoxins of elapid venom cause neuromuscular block of non-depolarizing type similar to that of curare. However, the action differs from that of curare in that the onset of action is slower and are bound much more strongly to the receptors than curare and they are also more potent.[41]

According to the mechanism by which they block the neuromuscular transmission neurotoxins in the elapid venoms fall into two groups:-

The first group comprising of cobratoxin, alpha-bungarotoxin and probably neurotoxin in most other elapid and sea snake venom. They produce antidepolarizing neuromuscular block by acting on the post-junctional membrane of the motor end plate similar to d-tubocurarine. They depress the end plate potential without affecting the terminal nerve spike, resting membrane potential and action potential of the muscle. The neuromuscular blockade caused by this group can be reversed by neostigmine. The blockade caused by the short

chain neurotoxin cobratoxin is more readily reversible than that with long chain toxins like alpha bungarotoxin.

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

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

CLINICAL FEATURES

Snake envenomation is a complex phenomenon manifesting as hematological, renal, cardiac and neurological features. The symptoms, signs and gravity of snake venom poisoning are dependent upon a number of factors[42]:

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

2. Nature, Location, Depth and Number of Bites: Deeper the bite and more the number of bites, more lethal it is likely to be. Bite through clothing is less dangerous than bite on a bare limb.

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

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

5. Victim's Sensitivity to Venom: It will vary from person to person. Based on this desensitization has been suggested as a form of protection against snakebite.

6. Pathogens present in the Snake's Mouth: Snake's mouth contains usually anaerobic and gram negative organisms. They are responsible for the secondary infection of the wound following snakebite.

7. Degree and Kind of First-aid Treatment and the subsequent Medical Care: Delay in the first aid measures or wrongly and over enthusiastically applied first aid measure by untrained persons, contribute substantially to morbidity and mortality, so also the delay in seeking medical help.

GENERAL SYMPTOMS

Fright: Most common symptom following snakebite whether poisonous or nonpoisonous is fright, particularly the fear of rapid and unpleasant death.[43] It is an emotional response occurring within minutes and present to varying degree in all victims.

May manifest as sudden onset of weakness, difficulty in breathing or swallowing (non-paralytic), fainting attacks, or semi-consciousness.

On examination victim may have cold clammy skin, feeble pulse and rapid shallow breathing. These symptoms usually resolve dramatically after a placebo therapy, but has to be properly differentiated from that due to envenomation.

LOCAL SYMPTOMS

1. Pain: After the bite there is some pain, which for most part is confined to the area of bite. The pain is extremely variable in severity and duration depending on the species of snake and amount of venom injected. The pain is most severe with viper bite, which usually appears within 5-10 minutes of bite. Following a cobra bite patient often complain of burning sensation at the site within 15 to 30 minutes. The pain may last for several days.

Most of the non-poisonous snakebites cause mild to moderate pain within few minutes of bite and subside within few hours after taking a mild analgesic. There are exceptions to this, like rat snake and fresh water snake, which cause severe pain after the bite and may require strong analgesics.

2. Local Swelling: Most viper venom in man act predominantly on the haemostatic system, particularly on capillary endothelium. Locally this causes swelling, which starts within minutes of the bite. Massive swelling of whole limb may develop in the ensuing 48-72 hours and is often misinterpreted as resulting from venous thrombosis or bacterial infection from the mouth of the snake.

Swelling with viper bites usually resolve completely in 2-3 weeks, occasionally it can take 2-3 months, and in exceptional cases limb may remain permanently swollen. A fair estimate of the dose of venom received can be made from the amount of local swelling i.e. the larger swelling of the limb the greater the quantity of venom injected.

Swelling after cobra bite usually starts from 1 to 3 hours and reaches a maximum in 24-48 hours, which is usually localized. The swollen part is painful and tender to palpation.

Poisoning by Kraits or non-poisonous snakebites cause little or no swelling, unless it is secondarily infected. If occurrence of edema (swelling) has not manifested within 4 hours after snakebite, it is generally safe to assume that the patient does not have pit viper envenomation.

Figure 14: Localised Swelling Following Snakebite

3. Ecchymosis and Erythema: They appear within few hours of the bite. Ecchymosis may occur along with edema and without bleb formation, depending on the amount of venom injected and species involved.

In bites by the vipers, spontaneous systemic bleeding is rare whereas discoloration of the bitten limb is typical, the reverse is the case with E.carinatus envenoming. In viper bites extravasation of red blood cells as well as plasma into the subcutaneous tissue results in discoloration, which may not be appreciated in dark skin. Usually the discoloration is only around the bite, but in severe poisoning it may extend up the whole limb. It will be particularly evident in any area, where the skin rubs against itself such as between fingers or toes.

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

Figure 15: Ecchymosis following Snakebite

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

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

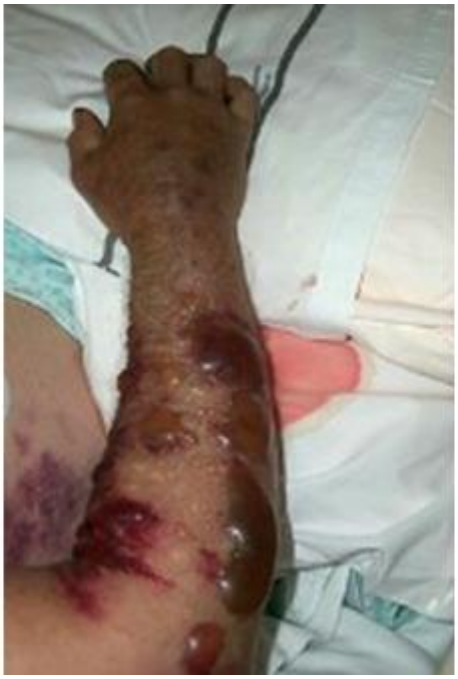

Figure 16: Hemorrhagic Bullae following Snakebite

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

Local effects of cobra bites are different: Swelling does not usually appear until 2-3 hours after the bite, but necrosis develops rapidly presenting like wet gangrene within a few days with a putrid smell. Presumably it is caused mainly by a direct cytolytic venom effect. As with burns, the dead tissue provides ideal culture for secondary growth of anerobes, hence the importance of early excision. Healing of local necrotic lesions requires at least a month and may take over 6 months, even with expert surgical attention.

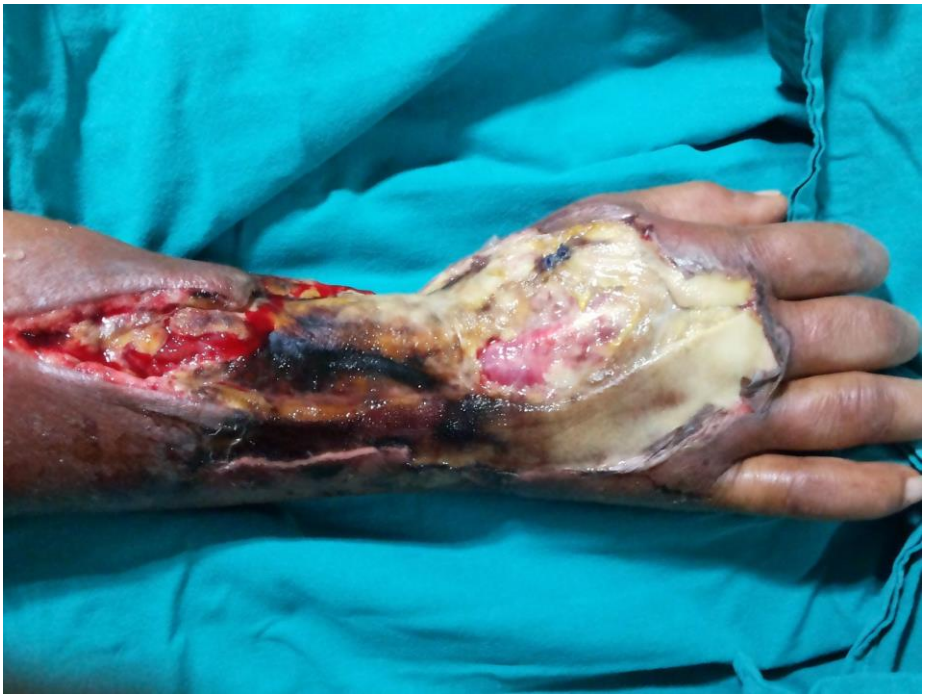

Figure 17: Necrosis following Snakebite

6. Bleeding from the Bite Site: Minimal bleeding from the wound is common following all snakebites whether poisonous or non-poisonous. Continuos oozing from the bite site are common following viper bites.

7. Fang Marks: The absence of discernible fang marks does not exclude snakebite, but the discovery of two discrete puncture marks does suggest a bite of venomous snake. As a rule, two lacerated punctures, about 1.25 cm deep in the case of colubrids and about 2.5 cm deep in the case of vipers.[44] An inverted 'U' shaped bite mark is caused by the teeth of a non-poisonous snake. Presence of marks by accessory fangs, other teeth and sometimes multiple bites makes it difficult to identify the type of snake. The distance between the fang marks is proportional in the size of the snake.

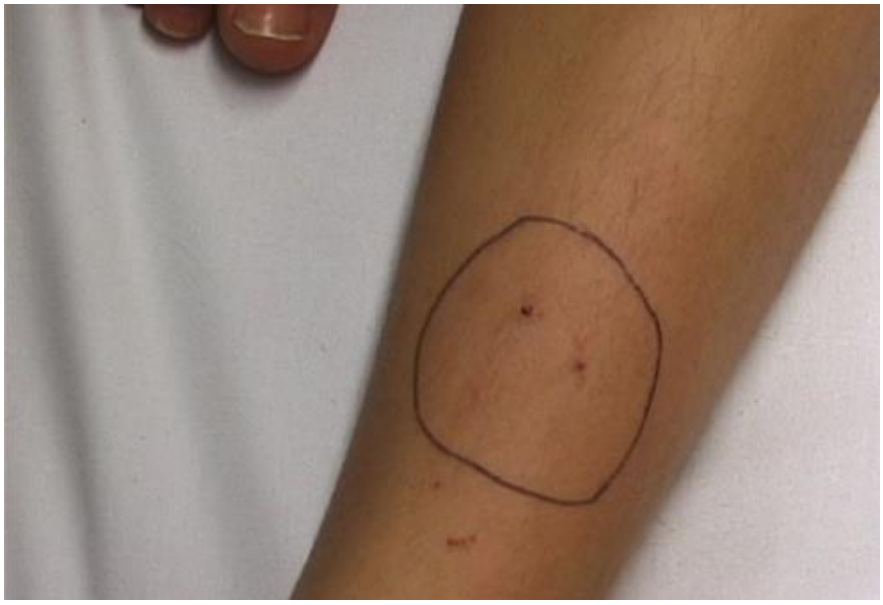

Figure 18: Fang Marks following Snakebite

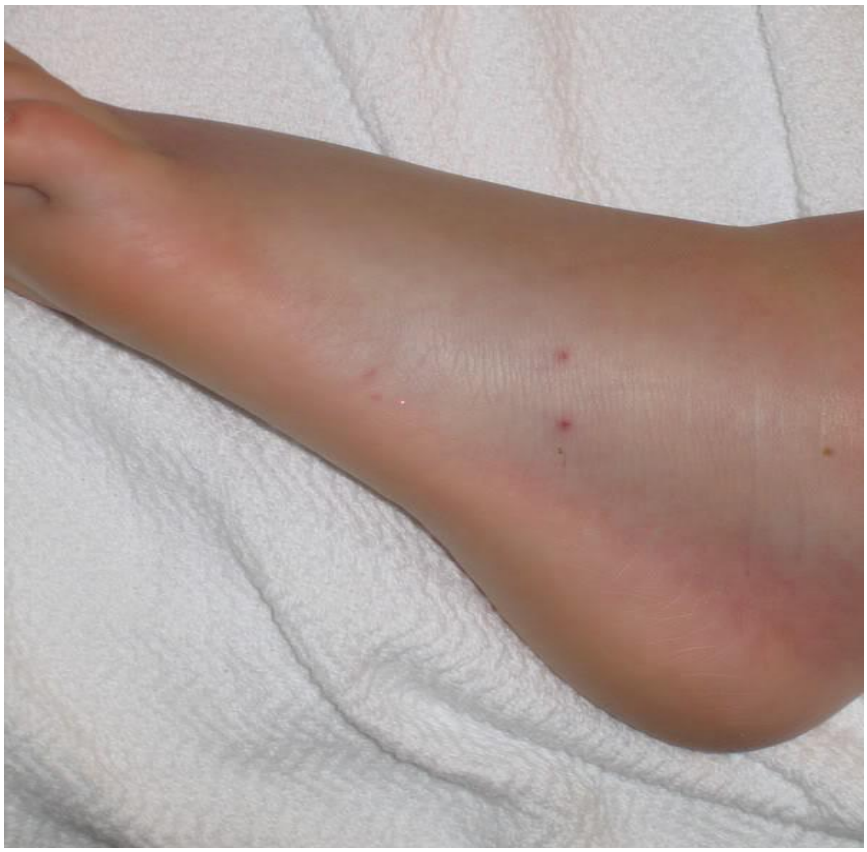

Figure 19: Fang Marks following Snakebite

SYSTEMIC SYMPTOMS

Viper Envenomation:

Non-specific early systemic symptoms:

Within a few minutes of the bite, vomiting, headache, abdominal pain, explosive diarrhea, and collapse with unrecordable blood pressure can occur. These features usually resolve spontaneously within 30-60 minutes, suggesting activation of the kinin system followed by inhibition of brady-kinin, rather than a direct venom effect.[43]

Shock:

Patients show varying degrees of signs of peripheral failure with or without signs of impending coma, hypotension, renal failure, dehydration and electrolyte disturbance. Shock starting later, as effect of envenomation is the main cause of death in viper bite.

Hypovolaemia from loss of blood and plasma into the swollen limb is one causal factor. Further important factors in pathogenesis of shock are pulmonary intravascular clotting, pulmonary edema and cardiac effects as evidenced by abnormal ECG and serum enzyme levels.[43]

The shock usually develops after 30 minutes, most often seen between 624 hours. But may occur as late as 3 or 4 days. Generally resolve within a week in patients surviving without antivenom.

Hemorrhagic Symptoms:

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

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

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

Figure 20: Hematuria following Snakebite

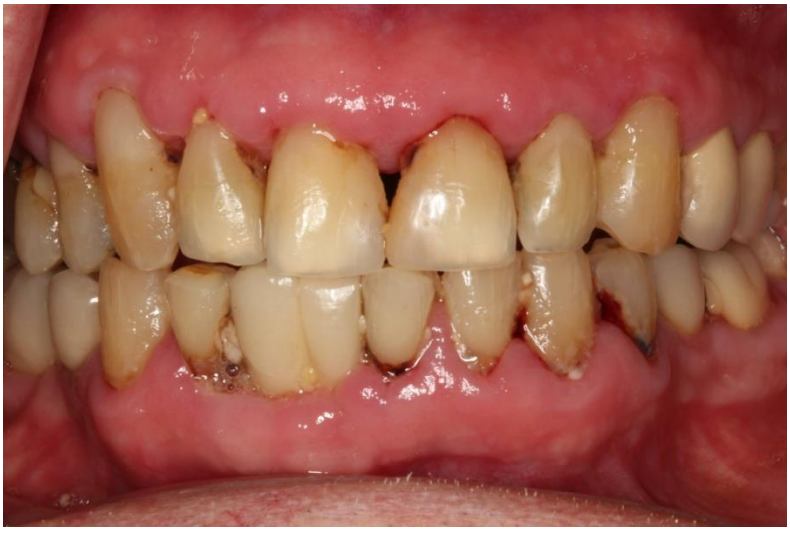

Figure 21: Bleeding Gums following Snakebite

Systemic Elapid Envenomation:

Presents with neurotoxic and cardiotoxic manifestation.

Neurotoxic Manifestation:

The earliest symptom of systemic elapid envenomation is a feeling of drowsiness or intoxication that starts from 15 minutes to 3 hours. There is selective neuromuscular block affecting mainly the muscles of eyes, tongue, pharynx, chest and finally limbs.[43] The symptoms and signs usually develop within 1 to 4 hours of bite.

Bilateral ptosis is the earliest and commonest manifestation. Eyelids may remain completely closed despite normal ability to wrinkle the forehead. The eye movements may be impaired both in vertical and lateral direction, when the patient may have blurring of vision or double vision, or the eye may be central and fixed (immobile). The pupils are usually dilated but react normally to light except in the terminal stage. With small doses of venom, these eye signs may be the only evidence of muscle paralysis.

Following the onset of ocular symptoms, the patient may develop difficulty in speech, which may become nasal because of palatal palsy, difficulty in opening the mouth and moving the lips and difficulty in swallowing.

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

may go into deepening coma, non-reactive dilated pupils, twitching and convulsions and ultimately leading to death.

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

Figure 22: Ptosis following Snakebite

Cardiotoxic Symptoms:

The symptoms due to direct acting cardiotoxin are usually of sudden onset appearing within 30 minutes to 20 hours of bite. Usually present with cardiovascular depression manifesting as sweating, cold extremities, tachycardia, hypotension and ECG changes usually in the ST segment or T-wave. These could often be followed by sudden hypotension, cardiac arrhythmia and cardiac arrest.[45]

COMPLICATIONS

Renal Failure:

Acute renal failure may follow serious poisoning by all three types of venomous snake – viper, elapid and sea snake – and appears to be unusually common after V. russelii bites. Acute renal failure complicates the course in 5-30% of victims of severe viper poisoning.[46] It usually becomes clinically evident towards the end of the first week after the bite.

No consensus exists on the single mechanism causing acute renal failure after viper bite. The alterations that contribute to renal failure include a varying degree of bleeding, hypotension, circulatory collapse, intravascular hemolysis and disseminated intravascular coagulation with or without microangiopathy.[47] A direct cytotoxic action of snake venom on the kidney is suspected, but convincing evidence is still lacking. Hypersensitivity to venomous or antivenomous protein occasionally causes acute renal failure.

The renal lesions of clinical significance in envenomed patients are acute tubular and patchy or diffuse cortical necrosis.[48] Glomerulonephritis, interstitial nephritis, and papillary necrosis have been reported in rare patients. Clinical presentation is similar to the acute renal failure of any other cause manifesting with oliguria, associated fluid and electrolyte imbalances.

Respiratory Paralysis:

A complication of severe envenomation by cobra and krait, it is principle cause of mortality from these two species[49]. Snake neurotoxins that bind to acetylcholine receptor sites on the motor end plates produce effects similar to those of curare and myasthenia gravis.[50] Initially only intercostals are involved. Later it also involves diaphragm.

The presentation in early stages will be with tachycardia, tachypnea and reduced tidal volume, which can progress to cyanosis, confusion, stuporousness, eventually leading on (if untreated) to coma, respiratory arrest and death. The respiratory failure in neurotoxic snakebites is acute type-II respiratory failure. In various degrees of presentations, the respiratory insufficiency and paralysis reported in 40-80% patients with elapid envenomation.

Gangrene:

Neglected local necrosis can result in gangrene of the limb. So the wound should be examined frequently for evidence of necrosis.[35] Early signs of necrosis include blistering, blackening or blanching of the skin, loss of sensation and a characteristic smell of putrefaction.[35] There is high risk of secondary infection and so the necrotic tissue should not be allowed to slough spontaneously but should be debrided under local or general anesthesia. Cobra envenomation tends to produce a wet gangrene, whereas viper envenomation produces superficial dry gangrene.

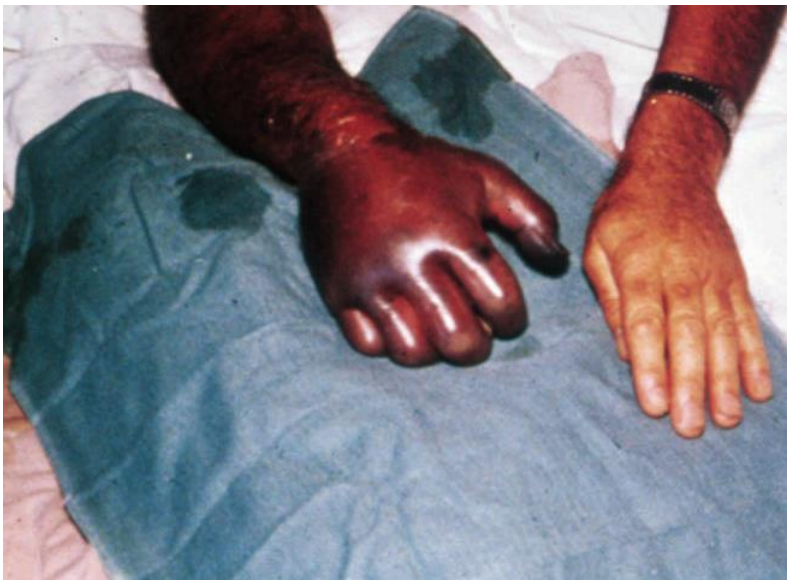

Figure 23: Gangrene following Snakebite

Non-bacterial Thrombotic Endocarditis (NBTE):

Commonly occurs in patients with wasting disease (e.g., malignancy) or with valves damaged following trauma due to intracardiac foreign body, scarring or marked turbulence. DIC is well documented following viperine bite and the underlying mechanism of NBTE is not fully understood.[51]

Guillain-Barre Syndrome:

Guillian-Barre Syndrome has been reported as an unusual complication after snake bite mainly due to krait bite. The patient presented with symmetric paresis and sensory signs in the upper and lower limbs, autonomic dysfunction, facial nerve involvement and mild elevated CSF protein at about 4 weeks after the bite. Electrodiagnostic studies, revealed profound sensory and motor polyneuropathy. Repeated electrophysiologic findings confirmed nerve regeneration. The patient reached satisfactory functional outcome after a short term intensive rehabilitation program despite severe axonal degeneration.[52]

Compartment Syndrome:

Hand compartment syndrome is a rare but potential complication of untreated crotala envenomations. It is due to direct intramuscular envenomation (compartment pressure greater than 30 mm of Hg).[53]

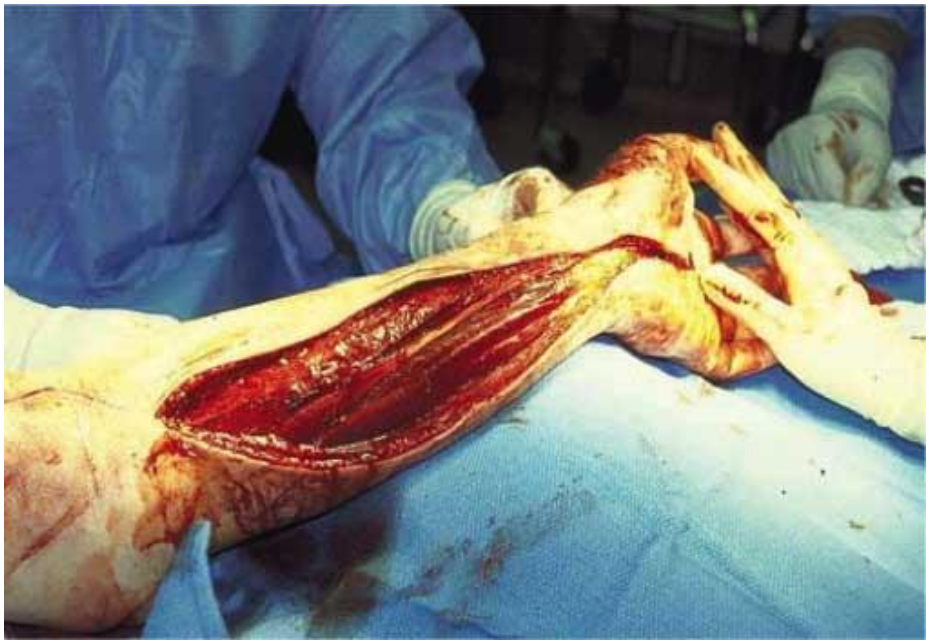

Figure 24: Compartment Syndrome following Snakebite

Rare Systemic Complications:

• Subarcahnoid hemorrhage

• Hysterical paralysis

• Second degree heart block

• New dyselectrocytemic acute MI

• Hypo-pituitarism

• Bilateral thalamic hematoma.[54]

INVESTIGATIONS

I. Blood Investigations:

A. Total Leucocyte count: Neutrophil count above 20,000 cells/μL indicate severe poisoning.[45]

B. RBC Count and haemoglobin and packed cells volume: In systemic Viperine poisoning there is usually no abnormal hemolysis, but anaemia caused by internal loss of Red Blood cells into the bitten limb and from external bleeding may result in fall of haemoglobin and RBC count. Hemolysis is more commonly seen with bites of Australian land snakes and cobra bites.[55]

C. Platelet Count: Platelet count may be normal but often reduced during the first few days after the bite although the bleeding time is normal.

D. Bleeding Time: Usually normal in Viper bites. Prolonged if bleeding diathesis develops.

E. Coagulation Profile: Prolonged if coagulation defect is present.[56]

F. 20 Minute Whole Blood Clotting Test: Non clotting of the blood indicates severe hemotoxic envenomation.

G. Plasma Fibrinogen: It is severely depleted in Viper poisoning.

H. Fibrin degradation products: Diagnostic of DIC.

I. Reticulocyte count: Increased in haemolysis (Cobra)

J. Red Cell Morphology: Spherocyte formation, acanthocytosis, Heinz body formation and Blurring of erythrocytes are readily demonstrated.

K. Grouping and cross matching: This is considered whenever there are bleeding manifestations.

L. Blood urea, serum creatinine: For assessment of renal function.

M. Serum electrolytes: To assess the electrolyte balance of the patient. Serum potassium may be raised in sea snake poisoning due to muscle damage.

N. Blood Lactate: To determine the lacltic acidosis in presence of Hypotension.

O. Liver Function Test: Haemolysis produces raise of unconjugated Bilurubin levels.

P. Serum Enzymes:

Raised CPK-MM-indicates skeletal muscle damage.

Raise of CPK-MB indicate Cardiac muscle damage.

Increased SGOT levels indicate Cardiac muscle damage.

Increased SGPT levels indicate damage to the liver.

II. <u>Urine Examination:</u>

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

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

C. Microscopic Hematuria: Common with Viper bites.

D. Hemoglobinuria: Associated with severe hemolysis.

E. Myoglobinuria: Seen in sea snake poisoning.

F. Specific gravity: reduced in renal failure.

III. <u>Stool Examination</u>: Malena and occult blood may be seen in case of Viper Bites

IV. <u>Other Investigations:</u>

1. Immunodiagnosis:

A. Demonstration of sites of Venom localization by immuno fluorescence Technique: By this method the localization of venom and probably of its action can be demonstrated.[57]

B. Micro Elisa: (Enzyme linked Immunosorbant Assay) By this technique quantification of the envenomation can be assessed. Snake venom levels upto 1-5 ng/ml can be detected. The assay is specific and further the specific anti body to the venom can also be demonstrated and can be carried out with serum, urine and other body tissues.

The important application of this being- to make an accurate retrospective diagnosis so as to compile distinctive clinical patterns in bites of various poisonous snakes, in epidemiological study and in assessing the effectiveness of various antivenoms.[58]

2. **Lumbar Puncture:** C.S.F. is examined for any evidence of cerebral haemorrhage or sub archnoid haemorrhage.

3. **X –ray chest:** This may show pulmonary oedema or evidence of Haemorrhage into the lungs.

4. **ECG:** ECG changes are unusual. Sinus bradycardia, ST-T changes, Various degrees of AV block Can occur due to cardiotoxicity.[59]

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

MANAGEMENT OF SNAKEBITE

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

First Aid Treatment Protocol

Much of the first aid currently carried out is ineffective and dangerous.[60]

The first aid being currently recommended is based around the mnemonic.

"CARRY NO R.I.G.H.T."[61]

It consists of the following:

CARRY = Do not allow victim to walk even for a short distance; just carry him in any form, especially when bite is at leg.

No- Tourniquate

No- Electrotherapy

No- Cutting

No- Pressure immobilization Nitric oxide donor (Nitrogesic ointment/ Nitrate Spray)

R = Reassure the patient. 70% of all snakebites are from non venomous species. Only 50% of bites by venomous species actually envenomate the patient

I = Immobilize in the same way as a fractured limb. Use bandages or cloth to hold the splints, not to block the blood supply or apply pressure. Do not apply any compression in the form of tight ligatures, they don't work and can be dangerous

GH= Get to Hospital Immediately.

Traditional remedies have NO PROVEN benefit in treating snakebite.

T= Tell the Doctor of any systemic symptoms that manifest on the way of hospital. Do not waste time for doing the first aid management. This method will get the victim to the hospital quickly, without recourse to traditional medical approaches which can dangerously delay effective treatment and will supply the doctor with the best possible information on arrival. Traditional Methods to Be Discarded.

Management of Snake bite in general

Pain:

Snakebite can often cause severe pain at the bite site. This can be treated with painkillers such as paracetamol.

Handling Tourniquets:

Care must be taken when removing tight tourniquets which most of the time used. Sudden removal can lead to a massive surge of venom leading to neurological paralysis, hypotension due to vasodilatation etc.

• Before removal of the tourniquet, test for the presence of a pulse distal to the tourniquet. If the pulse is absent ensure a doctor is present before removal.

• Be prepared to handle the complications such as sudden respiratory distress or hypotension. If the tourniquet has occluded the distal pulse, then a blood pressure cuff can be applied to reduce the pressure slowly. Anti Snake Venom (ASV) After assessing patient whenever decision is taken for giving ASV, start ASV whatever dose is available in hand, do not wait for full dose to be available.

ASV ADMINISTRATION CRITERIA

ASV is a scarce, costly commodity and should only be administered when there are definite signs of envenomation. Unbound, free flowing venom, can only be neutralised when it is in the bloodstream or tissue fluid. In addition, Anti-Snake Venom carries risks of anaphylactic reactions and should not therefore be used unnecessarily.

Systemic Envenoming:

• **Evidence of coagulopathy:** Primarily detected by 20WBCT or visible spontaneous systemic bleeding.

• **Evidence of neurotoxicity:** Ptosis, external ophthalmoplegia, muscle paralysis, inability to lift the head etc.

• **Cardiovascular abnormalities:** hypotension, shock,cardiac arrhythmia, abnormal ECG.

• **Persistent and severe vomiting or abdominal pain.**

Severe Current Local envenoming:

• Severe current, local swelling involving more than half of the bitten limb (in the absence of a tourniquet). In the case of severe swelling after bites on the digits (toes and especially fingers) after a bite from a known necrotic species.

• Rapid extension of swelling (for example beyond the waist or ankle within a few hours of bites on the hands or feet). Swelling a number of hours old is not grounds for giving ASV.

No ASV test dose must be administered

Test doses have been shown to have no predictive value in detecting anaphylactic or late serum reactions and should not be used .These reactions are not IgE mediated but Complement activated, They may also presensitize the patient and thereby create greater risk.

ASV DOSAGE

Initial Dosage:

Hemotoxic/ Neurotoxic Envenomation- 10 Vials

Local Envenomation- 10 Vials

Mode of Administration-

ASV can be administered in two ways:

1. Intravenous Injection: reconstituted or liquid ASV is administered by slow intravenous injection. (2ml/minute). Each vial is 1Oml of reconstituted ASV.

2. lnfusion: liquid or reconstituted ASV is diluted in 5-10ml/kg body weight of isotonic saline or glucose.

ASV to be administered over 1 hour at constant speed.

Neurotoxic Envenomation:

Neostigmine is an anticholinesterase that prolongs the life of acetylcholine and can therefore reverse respiratory failure and neurotoxic symptoms. It is particularly effective for post synaptic neurotoxins such as those of the Cobra. In the case of neurotoxic envenomation, Neostigmine Test can be done. The neostigmine dose is 0.04 mg/kg IV and atropine 0.6 mg/hr may be given by continuous infusion. The patient should be closely observed for l hour to determine if the neostigmine is effective.

Repeat Doses:

Hemotoxic Envenomation: In case of hemotoxic envenomation, the ASV strategy will be based around a six hour time period. When the initial blood test reveals a coagulation abnormality, the initial ASV amount will be given over 1 hour. No additional ASV will be given until the next Clotting Test is carried out. This is due to the inability of the liver to replace clotting factors in under 6 hrs. After 6 hours a further coagulation test should be performed and a further dose should be administered in the event of continued coagulation defect and in that case ASV to be given over 1 hr.

CT tests and repeat doses of ASV should continue on a 6 hourly pattern until coagulation is restored or unless a species is identified as one against which polyvalent ASV is not effective. The repeat dose should be 10 vials of ASV i.e. one full dose of the original amount.

Neurotoxic Envenomation: If the initial dose has been unsuccessful in reducing the symptoms or if the symptoms have worsened or if the patient has gone into respiratory failure then a further dose should be administered, after 2 hours. At this point the patient should be re-assessed. If the symptoms have worsened or have not improved, a second dose of ASV should be given. Second dose should be same as first dose (10 Vials).

MAXIMUM DOSAGE OF ASV

Hemotoxic Envenomation

The normal guidelines are to administer ASV every 6 hours until coagulation has been restored. However, once 30 vials have been administered and the coagulation abnormality persists, the use of Fresh Frozen Plasma (FFP) or factors can be considered.

This is based on evidence that suggests that the maximum venom yield from say a Russells Viper is 147 mg, which will reduce the moment the venom enters the system and starts binding to tissues. If 30 vials of ASV have been administered that represents 180 mg of neutrailsing capacity. This should certainly be enough to neutralise free flowing venom.

Neurotoxic Envenomation

Once the patient is in respiratory failure, has received 20 vials of ASV and is supported on a ventilator, ASV therapy should be stopped. This recommendation is due to the assumption that all circulating venom would have been neutralised by this point. Therefore further ASV serves no useful purpose.

Snakebite in Pregnancy

Pregnant women are treated in exactly the same way as other victims. The same dosage of ASV is given. The victim should be referred to a gynecologist for assessment of any impact on the foetus.

ASV Reactions

Anaphylaxis with ASV may be life-threatening. It can be of rapid onset and can deteriorate into a life-threatening emergency very rapidly. Adrenaline should always be immediately available.The patient should be monitored closely for urticaria, itching, fever, shaking chills, nausea, vomiting, diarrhoea, abdominal cramps, tachycardia, hypotension, bronchospasm and angio-oedema.

If anaphylaxis is evident, then:

- ASV should be discontinued.
- 0.5mg of 1:1000 Adrenaline should be given IM for adults.
- In addition, to provide long term protection against anaphylactoid reaction, 100mg

Of hydrocortisone and an H1 antihistamine, such as 10mg Chlorpheniramine Maleate should be administered IV.

If after 10 to 15 minutes the patient's condition has not improved or is worsening, a second dose of 0.5 mg of adrenalin 1:1000 IM is given. This can be repeated for a third and final occasion but in the vast majority of reactions, 2 doses of adrenaline will be sufficient. If there is hypotension or hemodynamic instabiiity, I.V. fluids should be given.

Once the patient has recovered, the ASV can be restarted slowly for 10-15 minutes, keeping the patient under close observation. Then the normal drip rate should be resumed.

TREATMENT OF COMPLICATIONS

Hypotension

Hypotension can have a number of causes, particularly loss of circulating volume due to haemorrhage, vasodilation due to the action of the venom or direct effects on the heart. Usually crystalloids are used for volume expansion. In cases where increased generalised capiliary permeability has been established a vasoconstrictor such as dopamine can be used. Dose being is 5- 10 mcg/kg/minute in normal saline or glucose solutions as I.V. infusion. The flow rate may be adjusted to maintain blood pressure adequately.

Persistent or severe bleeding

In the majority of cases the timely use of ASV will stop systemic bleeding. However in some cases the bleeding may continue to a point when further appropriate treatment should be considered. The major point to note is that clotting must be re-established before additional measures are taken. Adding clotting factors, fresh frozen plasma (FFP), cryopreclpitate or whole blood in the presence of un-neutralised venom will increase the amount of degradation products with the accompanying risk to the renal function.

Renal Failure

Renal failure is a common complication of Russell's viper and Hump-nosed pit viper bites. The contributory factors are intravascular haemolyiis, DIC, direct nephrotoxicity, and hypotension and rhabdomyolysis. Renal damage can develop very early in cases of Russells viper bite and even when the patient arrives at hospital soon after-the bite, the damage may already have been done. Studies have shown that even when ASV is administered within 1-2 hours after the bite, it is incapable of preventing ARF.

The following are indications of renal failure:

- Declining or no urine output although not all cases of renal failure exhibits oliguria
- Blood Bio-Chemistry

  Serum Creatinine: > 5mgldl or rise of > lmg I day or

  Urea: > 200mgldl or

  Potassium: > 5.6 mmol/l

- Evidence of Uraemia or metabolic acidosis.

Declining renal parameters require referral to a nephrologist with access to dialysis equipment and emergency hemodialysis.

Cardiac Complications

Studies reveal rare manifestations of cardiac toxicity. The rhythm abnormalities include, bradycardia, tachycardia, sinus arrhythmia, gallop rhythm and rarely pulmonary oedema and cardiomegaly. Apart from showing the rhythm abnormalities, ECG may also rarely show tall T waves, pattern suggesting myocardial ischemia and atrio-ventricular block. Bradycardia and tachycardia may be a feature of disturbed autonomic nervous system and most often due to anxiety rather than direct injury to the cell membrane. A cardiologist needs to be consulted if the rhyhm abnormalitils or other ECG findings persist.

Surgical Issues

The surgical issues observed in snake bite cases are:

- Ulcer following snakebite
- Necrosis of the skin and underlying tissues
- Gangrene of the toes and fingers
- Compartment syndrome and others

Emergency debridement and care of wound is required in these cases.

MATERIALS & METHODS

METHODOLOGY

SOURCE OF DATA

One hundred and three patients admitted in R L Jalappa Hospital with history of snakebite satisfying the aforementioned criteria were included in the study. The study was undertaken from November 2014 to October 2016 over the duration of two years.

Sample size has been estimated based on the expected recovery of 97.61% by the study done by Gosavi PA et al in similar settings of India.[63]

$$n = \frac{(1.96)^2 pq}{d^2}$$

p = 97.61

q = 100-p= 2.39

d (absolute error) at 5

alpha at 0.01 level (99% confidence level)

METHOD OF COLLECTION OF DATA:

Patients aged 18 years or more with snakebite were admitted and closely monitored from the time of admission till discharge. Patients were clinically assessed and required investigations were done and those fulfilling the inclusion criteria were enrolled in the study.

Detailed history including name, age, gender, occupation, time of snake bite, place of occurrence of incident, treatment in other hospitals was noted.

Snake bite Characteristics like Bite mark; Assessment of bite mark, Site, Tissue condition, Time of bite was noted.

Fang marks- Two close-set puncture marks would indicate that snake has fangs and is venomous. By contrast, a ragged bite mark means the snake lacks fangs, indicating non poisonous snakebite. Photographs and specimens were shown to identify the snake.

20 minute WBCT along with all other required investigations were done on admission and divided into hemotoxic, neurotoxic or only local envenomation patients and started on ASV. ASV treatment was based on Indian Guidelines and Protocol of Snake Bite 2013 given by Association of Physicians of India.[64]

20 WBCT: 3 ml of fresh venous blood is placed in a new, clean and dry glass test tube and left at ambient temperature for 20 minutes. The glass vessel was left undisturbed for 20 minutes and then gently tilted. If the blood did not clot then the patient has incoagulable blood suggestive of hemotoxicity. Then the 6 hourly cycles were adopted to test for the requirement for repeat doses of Anti Snake Venom. If the blood clots, the repeat test was carried out every 30 minutes from admission for three hours and then hourly after that to establish if envenomation is present for total of 6 hours.

- **Initial Dose**

Local Envenomation - 10 vials

Systemic Envenomation - 10 vials

- **Repeat Dose**

Hematological complication: WBCT is repeated after 6 hrs. If prolonged, 10 vials are given and same procedure is repeated every 6^{th} hourly till coagulation is restored.

Neurotoxic envenomation: Patient should be reassessed after 2 hours and if symptoms have worsened or have not improved - 10 vials should be given and then discontinued and supportive care should be given.

Time of administration of ASV, Frequency, Side-effects and total dose of ASV given per patient were recorded.

The patients were closely monitored and treated. All the life threatening complications like ARF, MODS, Cellulitis, DIC were recorded and managed accordingly. They were reassessed clinically and outcome was recorded on the day of discharge. Complete Recovery, morbidity or mortality was the outcome measures.

INCLUSION CRITERIA:

1. Poisonous snakebite patients developing local or systemic complications.
2. Patients with alleged history of snake bite but with presence of definite fang marks and developing complications.

INVESTIGATIONS DONE:

1. Complete Blood Counts ESR
2. Urine Routine and microscopy
3. Renal Function tests (B.Urea, S.Creatinine)
4. Bleeding time, Clotting time
5. 20 Minute Whole Blood Clotting Test
6. ECG
7. Chest X ray

STUDY DESIGN:

It is a Hospital-based observational study.

STUDY DURATION

November 2014 to October 2016

STATISTICAL METHODS

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation.

Chi-square test of Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. **Yates correction** was applied where ever chi-square rules were not fulfilled (for 2x2 tables only).

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data. EPI Info (CDC Atlanta), Open Epi, Med calc and Medley's desktop were used to estimate sample size, odds ratio and reference management in the study.

RESULTS

RESULTS

During the study period from November 2014 to October 2016, 256 patients were admitted in RL Jalappa Hospital with Snakebite. Out of this, 103 patients fulfilling the inclusion criteria were included in the study. Following are the observations made in those 103 patients.

AGE DISTRIBUTION

Table 2: Age distribution of subjects

		Count	%
Age	18-20 years	9	8.7%
	21 to 30 years	29	28.2%
	31 to 40 years	30	29.1%
	41 to 50 years	21	20.4%
	>50 years	14	13.6%
	Total	103	100.0%

Majority of subjects (29.1%) in the study were in the age group 31 to 40 years, followed by it was 21 to 30 years (28.2%), lowest snake bite were seen among 18-20 years age group.

This shows that snake bite is common among middle aged individuals i.e., 57.3% are between 21-40 years of age. Mean age of subjects with snake bite was 37.83 ± 13.58 years.

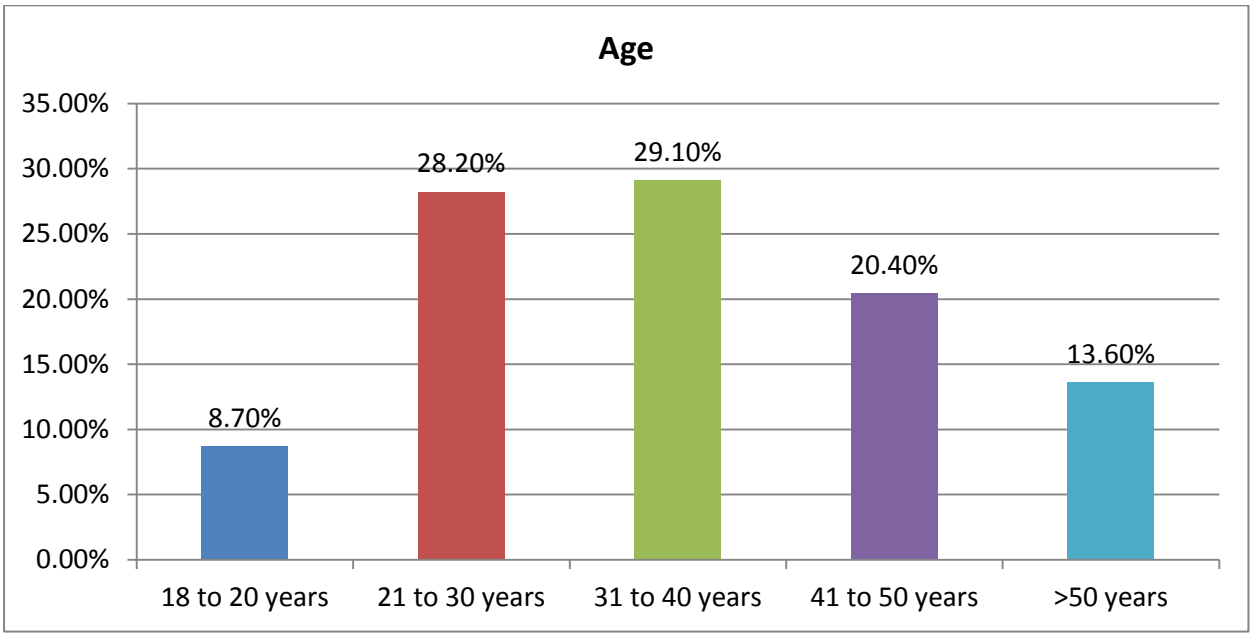

Chart 1: Bar Diagram showing Age distribution of subjects with snake bite

GENDER DISTRIBUTION

Table 3: Gender distribution of subjects

		Count	%
Gender	Female	33	32.0%
	Male	70	68.0%
	Total	103	100.0%

Majority of subjects with snake bite were males (68%) followed by females (32%).

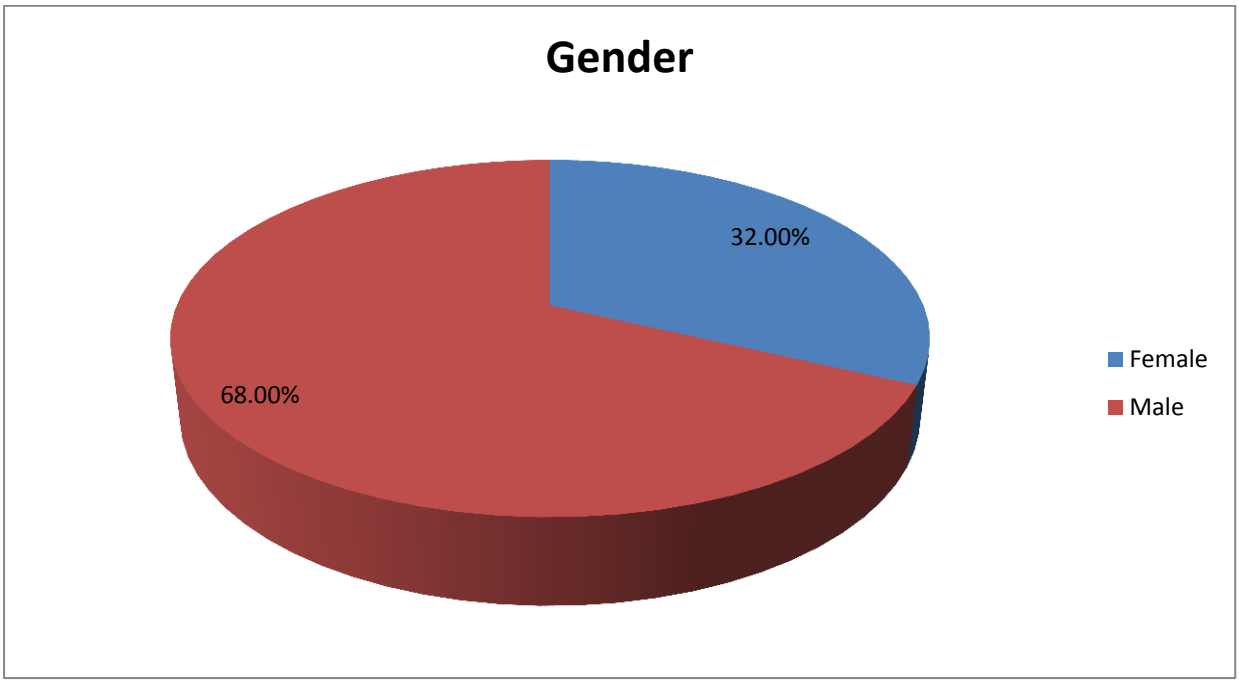

Chart 2: Pie diagram showing Gender distribution of subjects

OCCUPATION OF SUBJECTS

Table 4: Occupation distribution of subjects

		Count	%
Occupation	Agriculture	69	67.0%
	Business	11	10.7%
	House Wife	13	12.6%
	Student	10	9.7%
	Total	103	100.0%

Majority of the subjects with snake bite were among the farmers (67%), 12.6% were housewives, 10.7% were doing business and 9.7% were students.

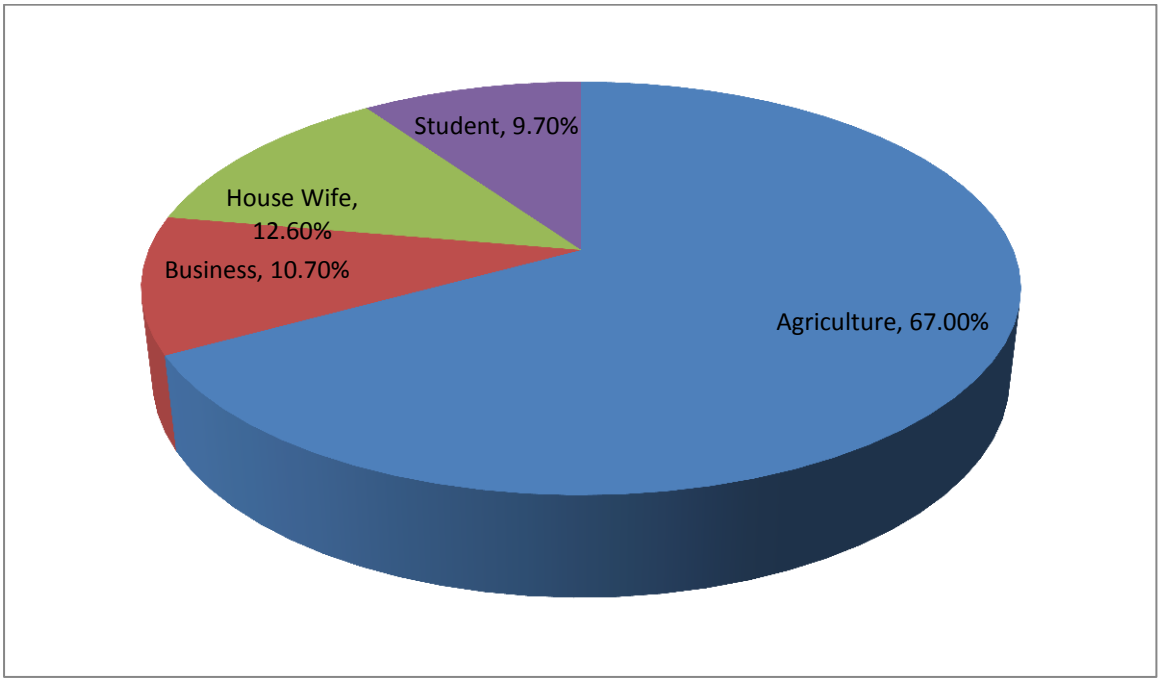

Chart 3: Pie diagram showing Occupation distribution of subjects

MONTH OF BITE

Table 5: Month of bite among the subjects

		Count	%
Month of Bite	January	5	4.9%
	February	7	6.8%
	March	5	4.9%
	April	5	4.9%
	May	5	4.9%
	June	15	14.6%
	July	14	13.6%
	August	9	8.7%
	September	9	8.7%
	October	14	13.6%
	November	7	6.8%
	December	8	7.8%

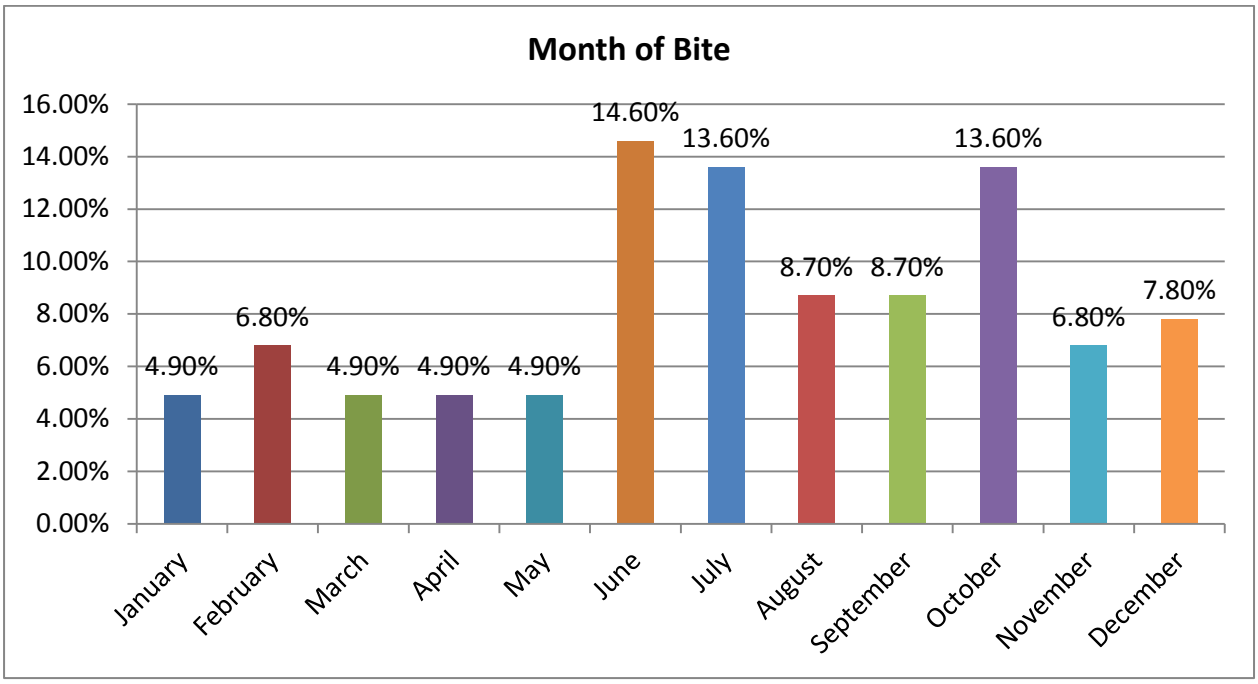

Chart 4: Bar diagram showing Month of Bite among the subjects

SEASON OF BITE

Table 6: Season of Bite

Season	Count	%
Summer	15	14.6%
Monsoon	45	43.7%
Winter	43	41.7%

Snake bite was highest during the Monsoon and winter season compared to summer. Monsoon season had the highest rate of snake bites (43.7%), followed by winter (41.7%) and summer had least snake bites (14.6%).

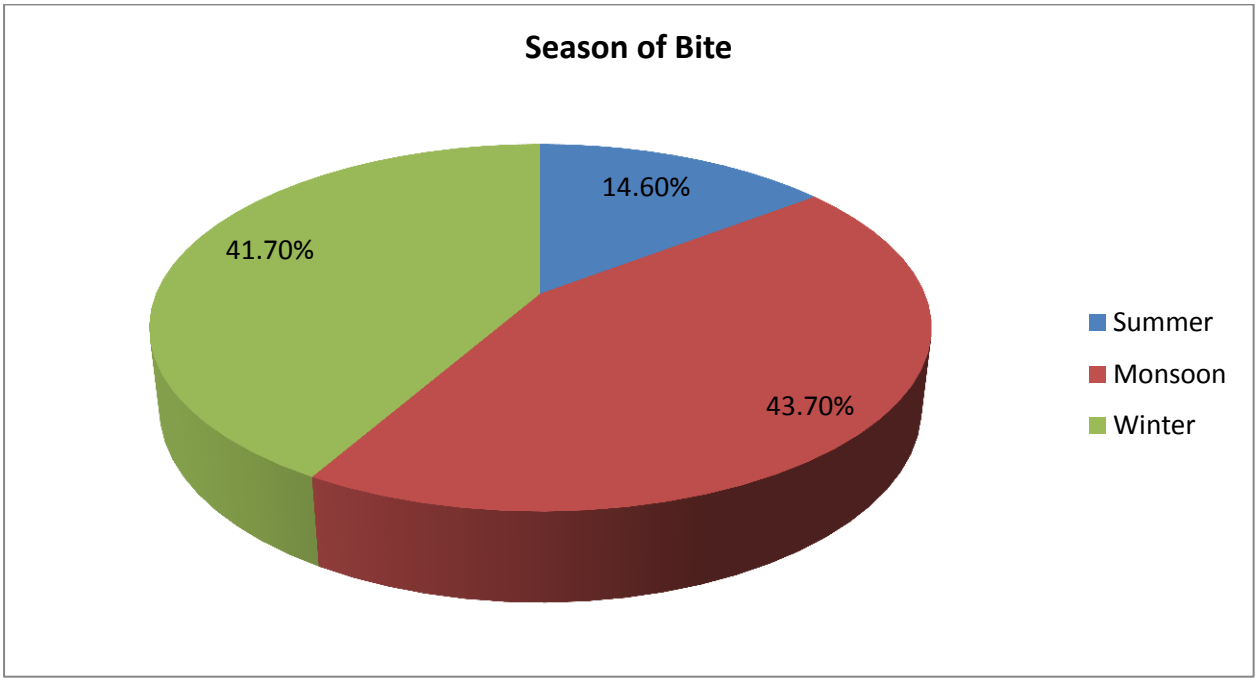

Chart 5: Pie diagram showing Season of Bite

SITE OF BITE

Table 7: Site of Bite

Site	Count	%
Lower limb	66	64.1%
Upper limb	37	35.9%

Snake bites were common on Lower limb (64.1%) followed by upper limb (35.9%).

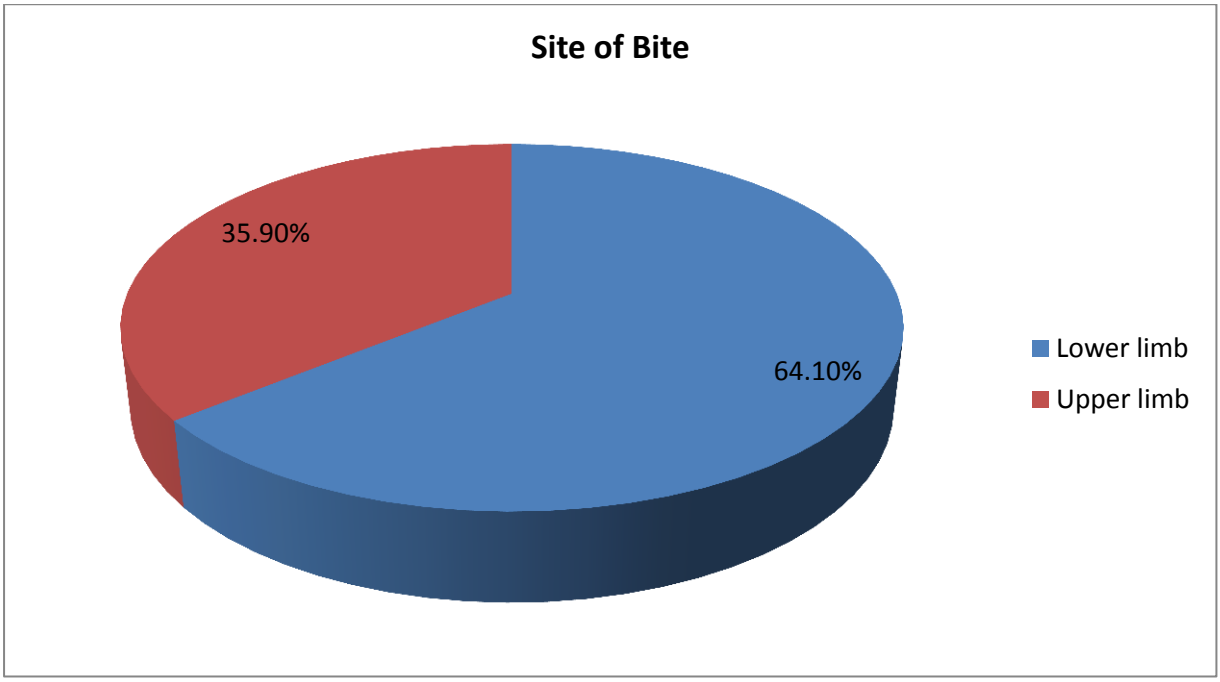

Chart 6: Pie diagram showing Site of Bite

TIME OF BITE

Table 8: Time of Bite

Time	Count	%
Morning	37	35.9%
Afternoon	20	19.4%
Evening	31	30.1%
Night	15	14.6%

Snake bites were more common in morning (35.9%) followed by evening (30.1%), afternoon (19.4) and night (14.6%).

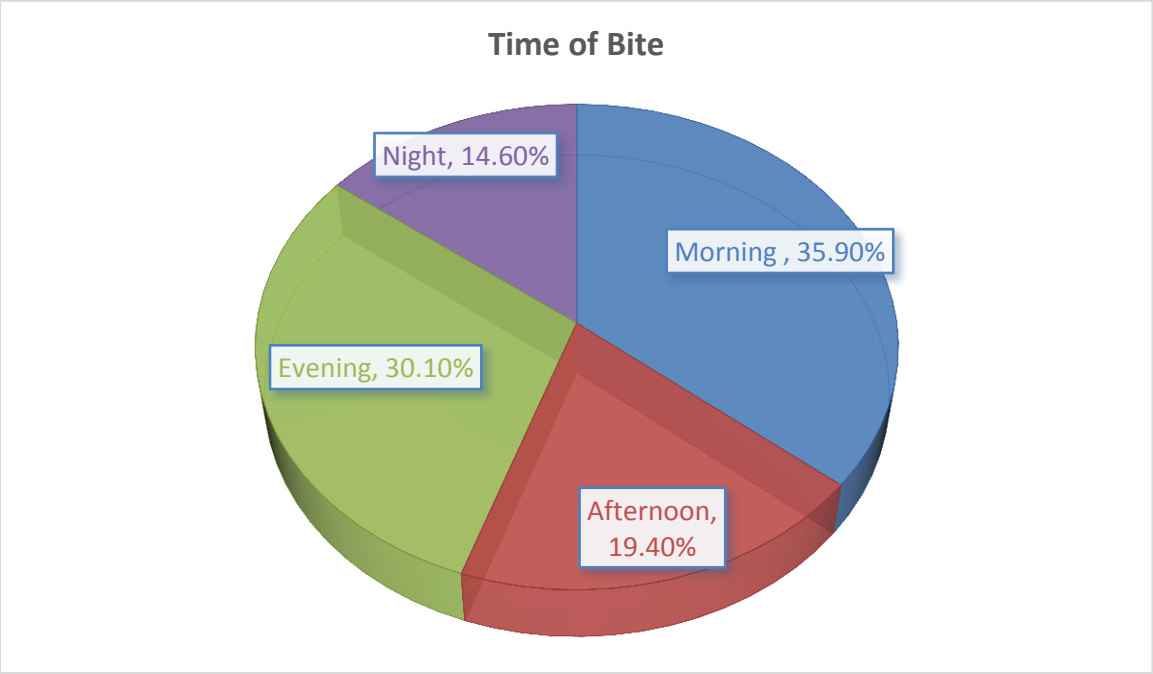

Chart 7: Pie diagram showing Time of Snake bite among subjects

TIME OF PRESENTATION

Table 9: Time of Presentation among subjects in the study

		Count	%
Time of Presentation	<6 hrs	77	74.8%
	6 to 24 hrs	22	21.4%
	>24 hrs	4	3.9%
	Total	103	100.0%

Majority of subjects in the study presented within 6 hrs (74.8%), 21.4% presented with in 6 to 24 hrs and 3.9% presented after 24 hrs.

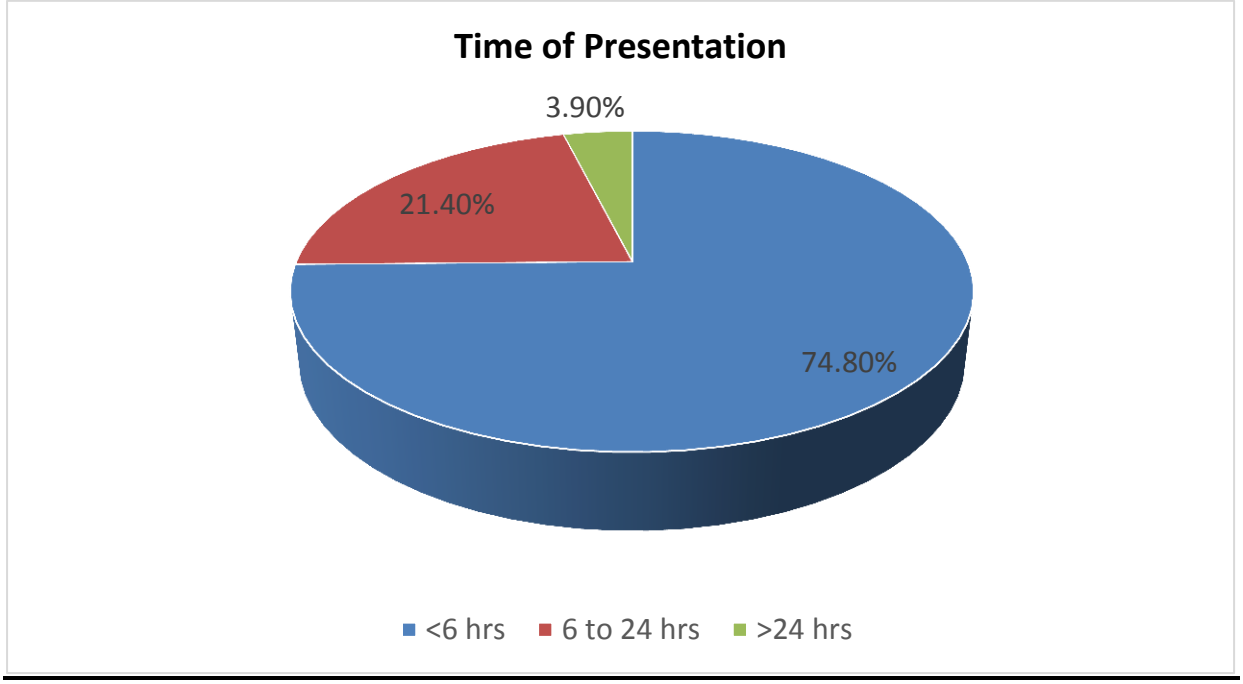

Chart 8: Pie diagram showing Time of Presentation among subjects in the study

TOURNIQUET USE

Table 10: Tourniquet usage among subjects in the study

		Count	%
Tourniquet	Tourniquet not used	10	9.7%
	Tourniquet Used	93	90.3%

In the study among 90.3% of subjects tourniquet was used and in 9.7% of subjects tourniquet was not used.

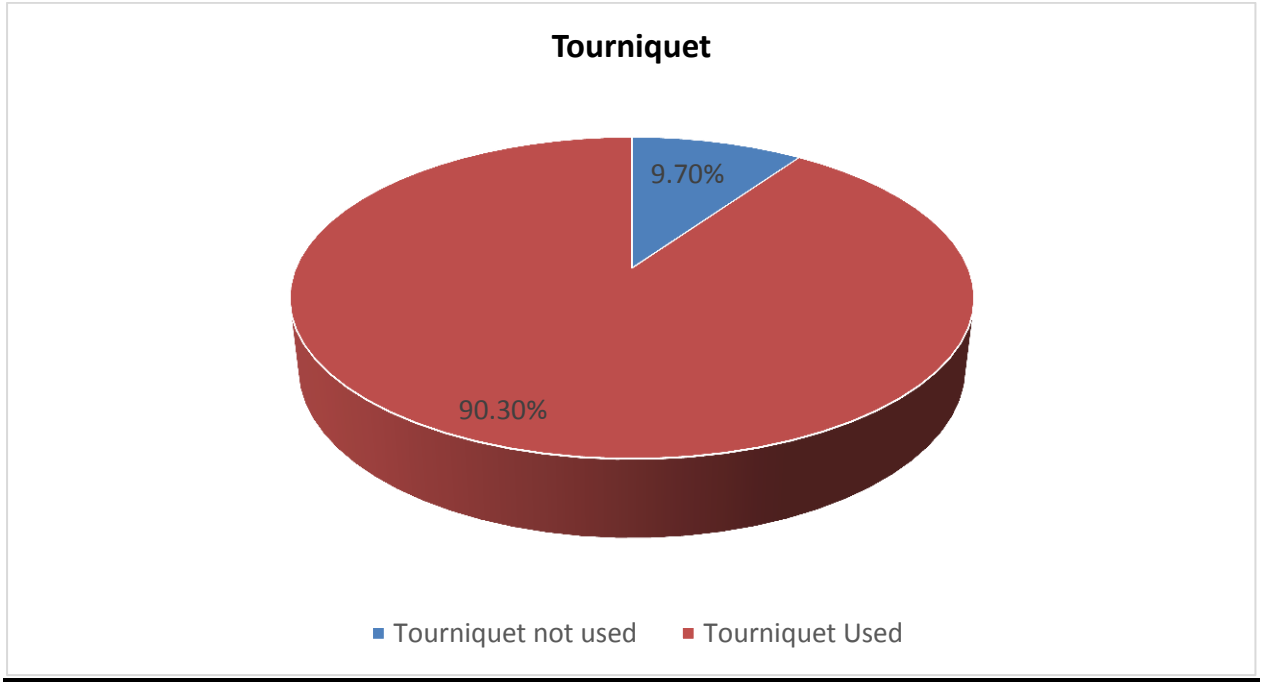

Chart 9: Pie diagram showing Tourniquet usage among subjects in the study

TYPE OF SNAKE

Table 11: Type of Snake identified among subjects

		Count	%
Type of Snake	Not Known	71	68.9%
	Cobra	12	11.7%
	Krait	7	6.8%
	Viper	13	12.6%
	Total	103	100.0%

In majority of the bites, type of snake was not known (68.9%). 11.7% were cobra bites, 12.6% had viper bites and 6.8% had krait bites in this study.

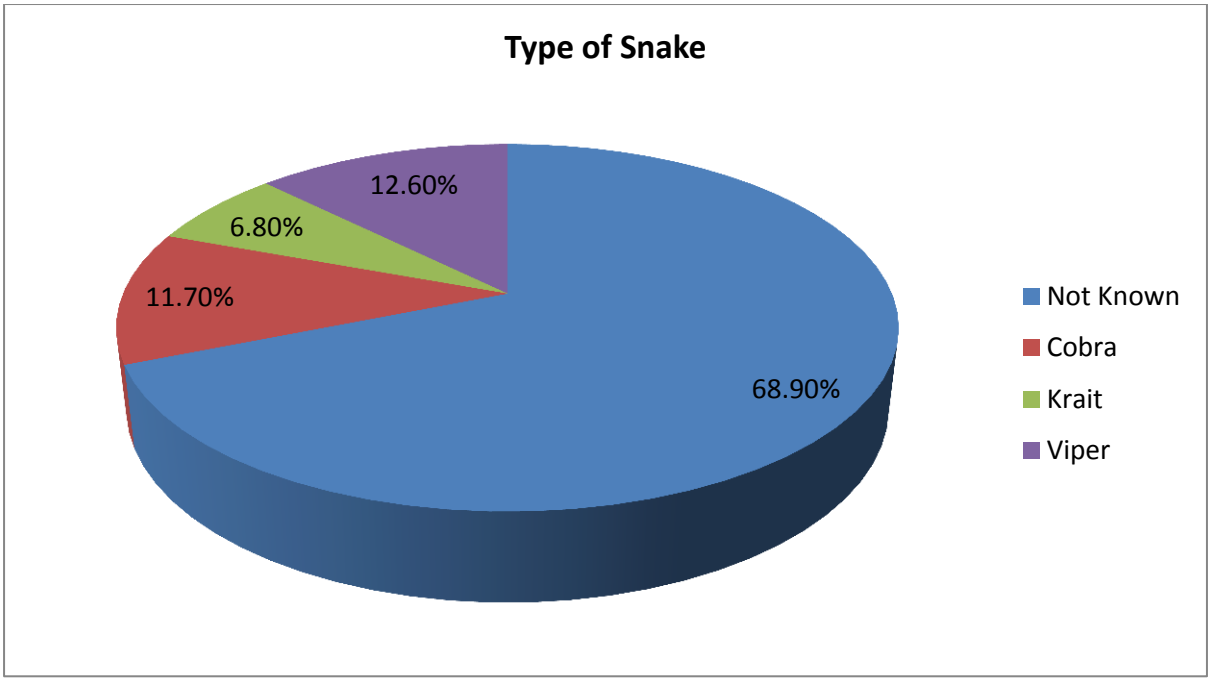

Chart 10: Pie diagram showing Type of Snake identified among subjects

LOCAL ENVENOMATION SYMPTOMS

Table 12: Local Envenomation symptoms among subjects with snake bite

Symptoms	Count	%
Pain	45	43.7%
Local Bleed	17	16.5%
Swelling	49	47.6%
Gangrene	10	9.7%
Combination of Symptoms	45	43.7%

In the study most common local envenomation symptom was swelling (47.6%), followed by it was pain in 43.7%, local bleeding 16.5% and gangrene in 9.7%. 43.7% patients had combination of two or more local symptoms.

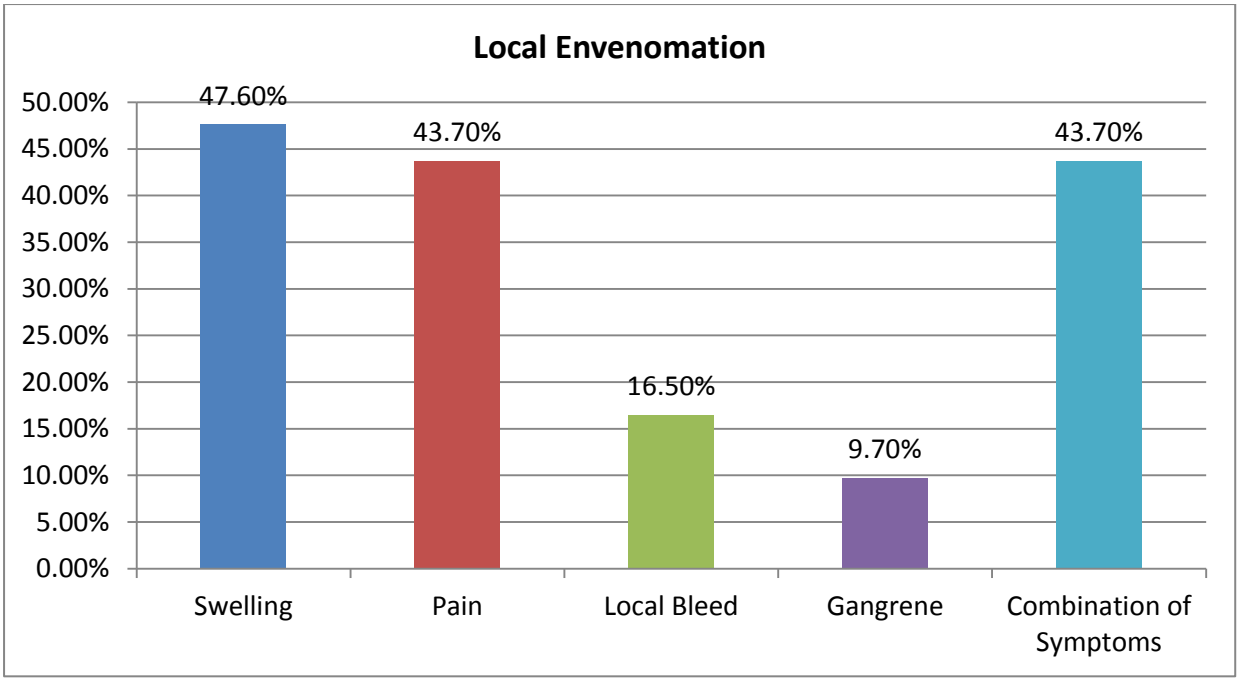

Chart 11: Bar diagram showing Local Envenomation symptoms among subjects

HEMOTOXIC ENVENOMATION SYMPTOMS

Table 13: Hemotoxic Envenomation symptoms among subjects

Symptoms	Count	%
Local bleed	19	18.4%
Gum bleed	12	11.7%
Hemoptysis	3	2.9%
Epistaxis	16	15.5%
Hematemesis	6	5.8%
Hematuria	24	23.3%
Combination of Symptoms	23	22.3%

Most common hematological manifestation was hematuria in 23.3%, followed by local bleed in 18.4%, epistaxis in 15.5%, gum bleeding in 11.7%, hematemesis in 5.8%, hemoptysis in 2.9%. 22.3% had more than one site of bleeding.

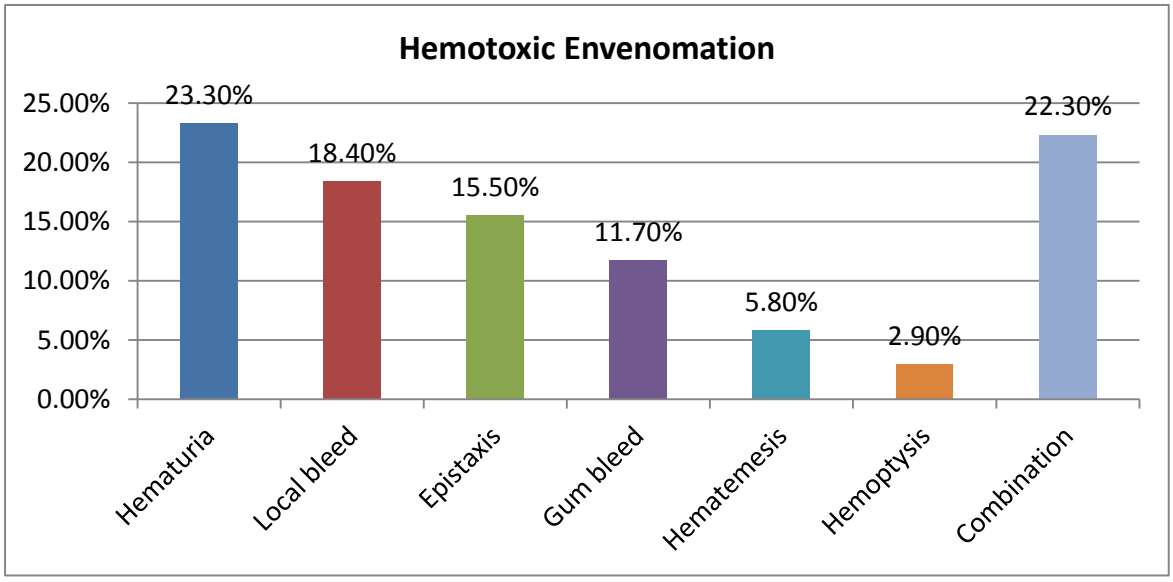

Chart 12: Bar diagram showing Hemotoxic Envenomation symptoms among subjects

NEUROTOXIC ENVENOMATION SYMPTOMS

Table 14: Neurotoxic Envenomation symptoms of subjects in the study

Symptoms	Count	%
Ptosis	35	34.0%
Blurred vision	16	15.5%
Ophthalmoplegia	9	8.7%
Flaccid limb paralysis	2	1.9%
Unconsciousness	8	7.8%
Respiratory paralysis	15	14.6%
Combination of Symptoms	21	20.3%

Most common neurological manifestation is Ptosis (34%) followed by Blurring of vision (15.5%), Respiratory paralysis (14.6%), Ophthalmoplegia (8.7%), Unconsciousness (7.8%) and Flaccid limb paralysis (1.9%). 20.3% patients had more than one neurotoxic envenomation symptoms.

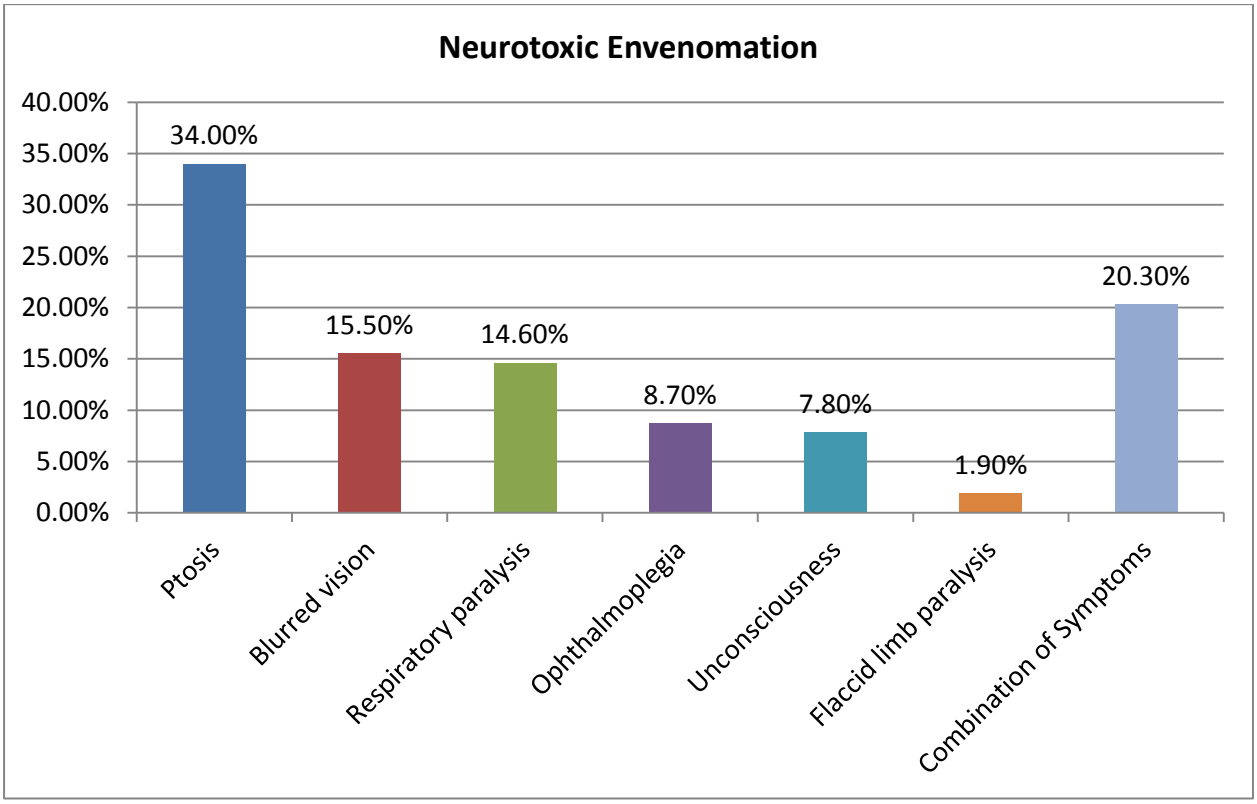

Chart 13: Bar diagram showing Neurotoxic Envenomation symptoms in subjects

TYPE OF ENVENOMATION

Table 15: Type of Envenomation among subjects

		Count	%
Type of Envenomation	Hematotoxic	25	24.3%
	Hematotoxic +Local	20	19.4%
	Hematotoxic +Neurotoxic	10	9.7%
	Hematotoxic +Neurotoxic + Local	1	1.0%
	Local	23	22.3%
	Neurotoxic	18	17.5%
	Neurotoxic +Local	6	5.8%
	Total	103	100.0%

In the study 24.3% had hemotoxic envenomation, 22.3% had local features, 17.5% had neurotoxic envenomation. Other subjects had combination of toxicity as shown in the above table.

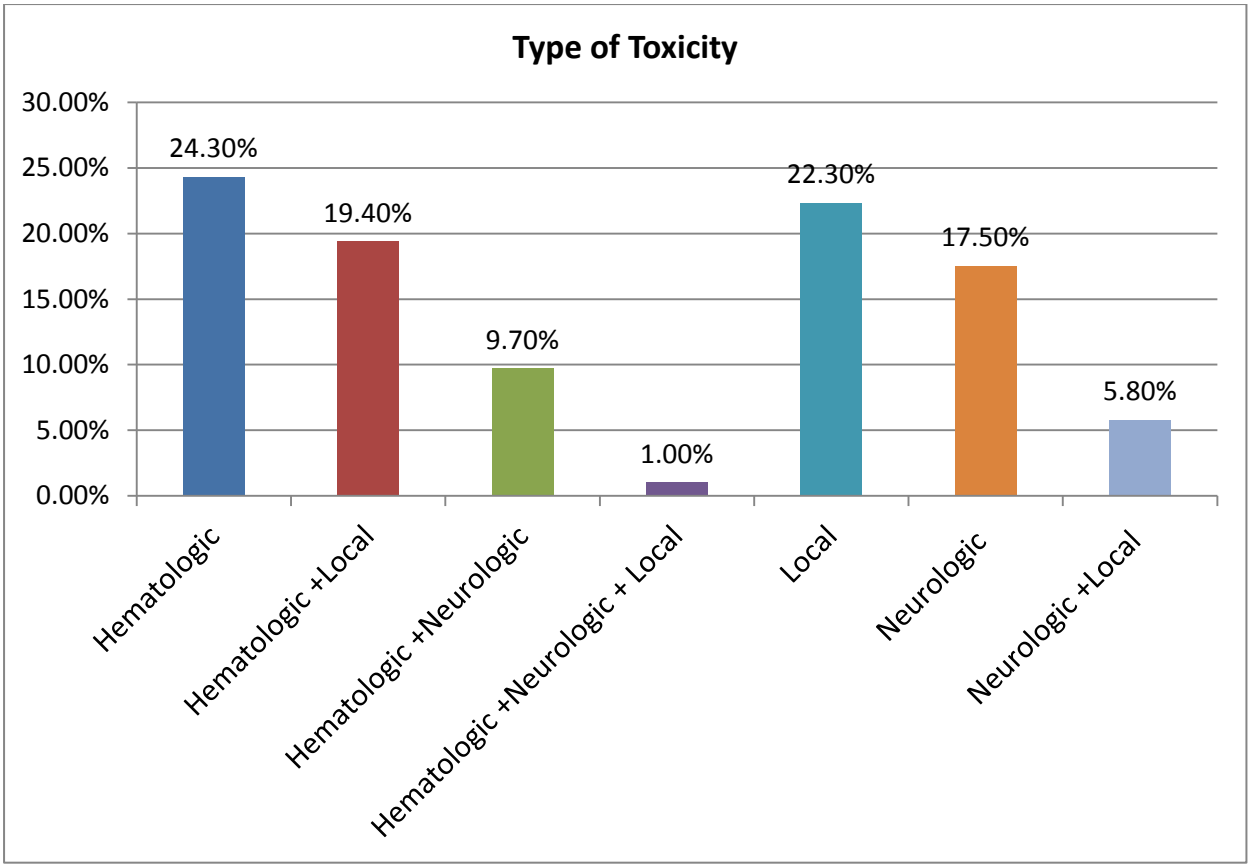

Chart 14: Bar diagram showing Type of Toxicity among subjects

20 MIN WHOLE BLOOD CLOTTING TIME

Table 16: 20 min Whole Blood Clotting Time among subjects

		Count	%
20 WBCT	Clotted	47	45.6%
	Not Clotted	56	54.4%
	Total	103	100.0%

In 54.4% of subjects 20 WBCT showed no clotting and in 45.6% showed clotting. All the 54.4 % where blood was clotted belonged to Hemotoxic envenomation and 45.6 % where blood had not clotted belonged to either Neurotoxic or Local envenomation category.

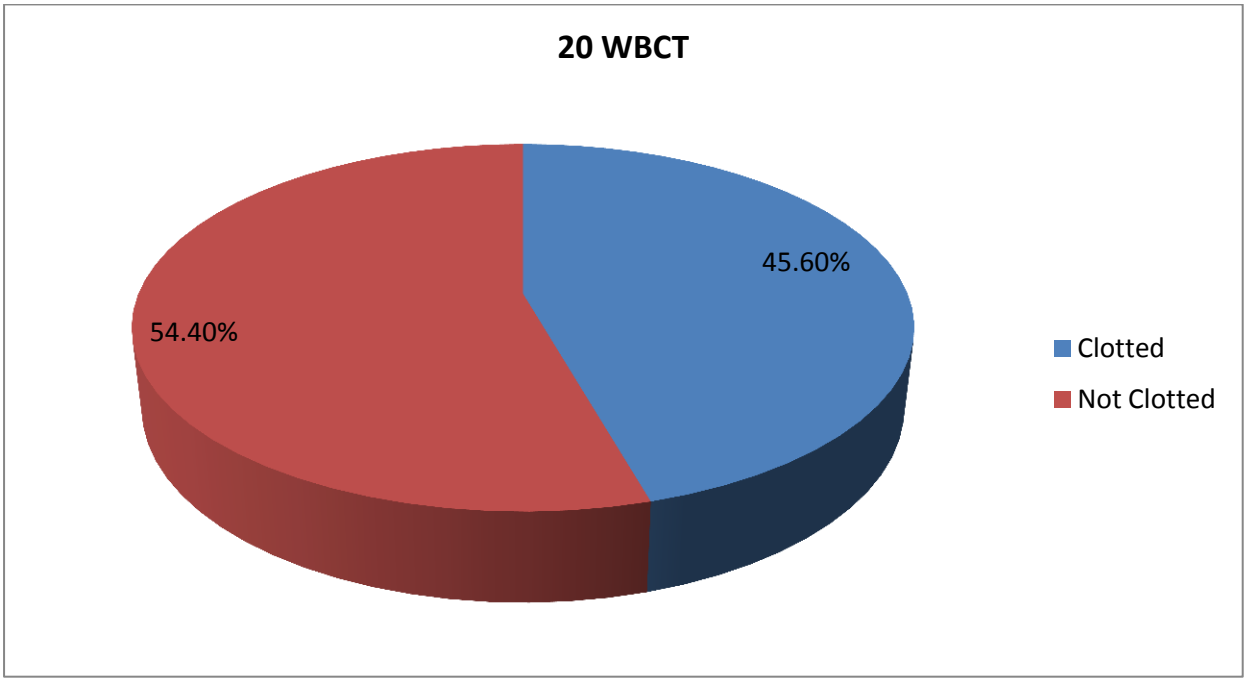

Chart 15: Pie diagram showing 20 min Whole Blood Clotting Time among subjects

TYPE OF TOXICITY VERSUS 20 MIN WHOLE BLOOD CLOTTING TIME

Table 17: Type of Toxicity versus 20 min Whole blood Clotting time

		Type of Toxicity					
		Hemotoxic		Neurotoxic		Local	
		Count	%	Count	%	Count	%
20 WBCT	Clotted	0	0.0%	24	100.0%	23	100.0%
	Not Clotted	56	100.0%	0	0.0%	0	0.0%

χ 2 = 103, df = 2, p <0.001*

In 56 subjects with hemotoxicity, 100% of them had their blood not clotted at 20 min. whereas in 24 subjects with neurotoxicity and local toxicity, 100% of them had their blood clotted at 20 min respectively.

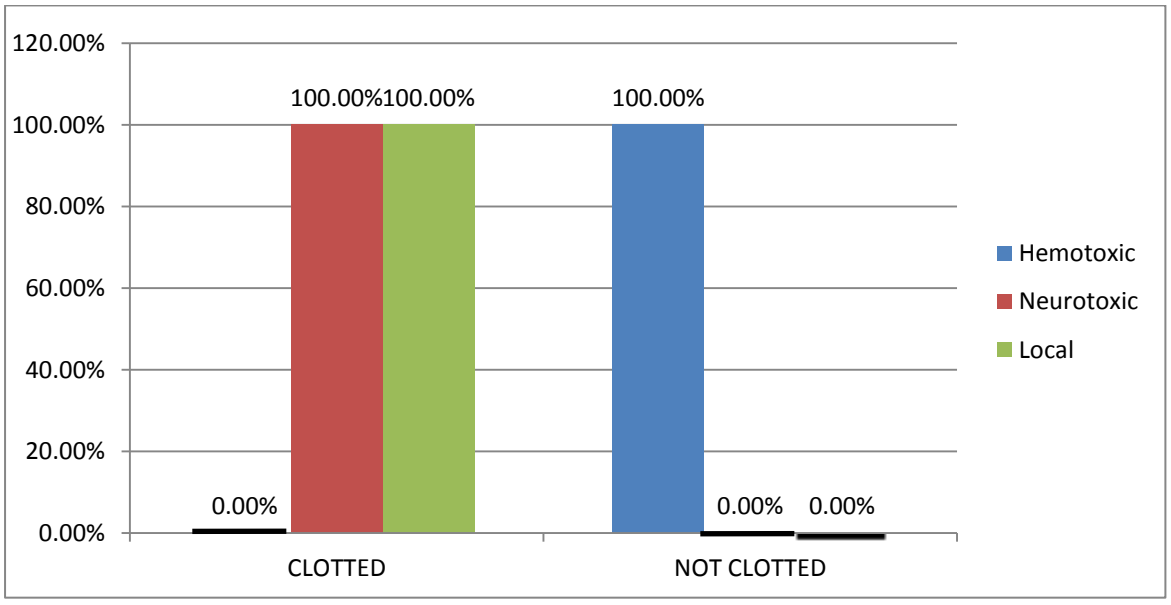

Chart 16: Bar diagram showing Type of Toxicity versus 20 min Whole blood Clotting time

ASV USAGE

Table 18: ASV Usage among subjects

		Frequency	Percent
ASV	10	54	52.4
	20	40	38.8
	30	9	8.7
	Total	103	100.0

Mean ASV given among subjects was 15.63 ± 6.51 units. 52.4% of subjects received 10 units of ASV, 38.8% received 20 units of ASV and 8.7% received 30 units of ASV.

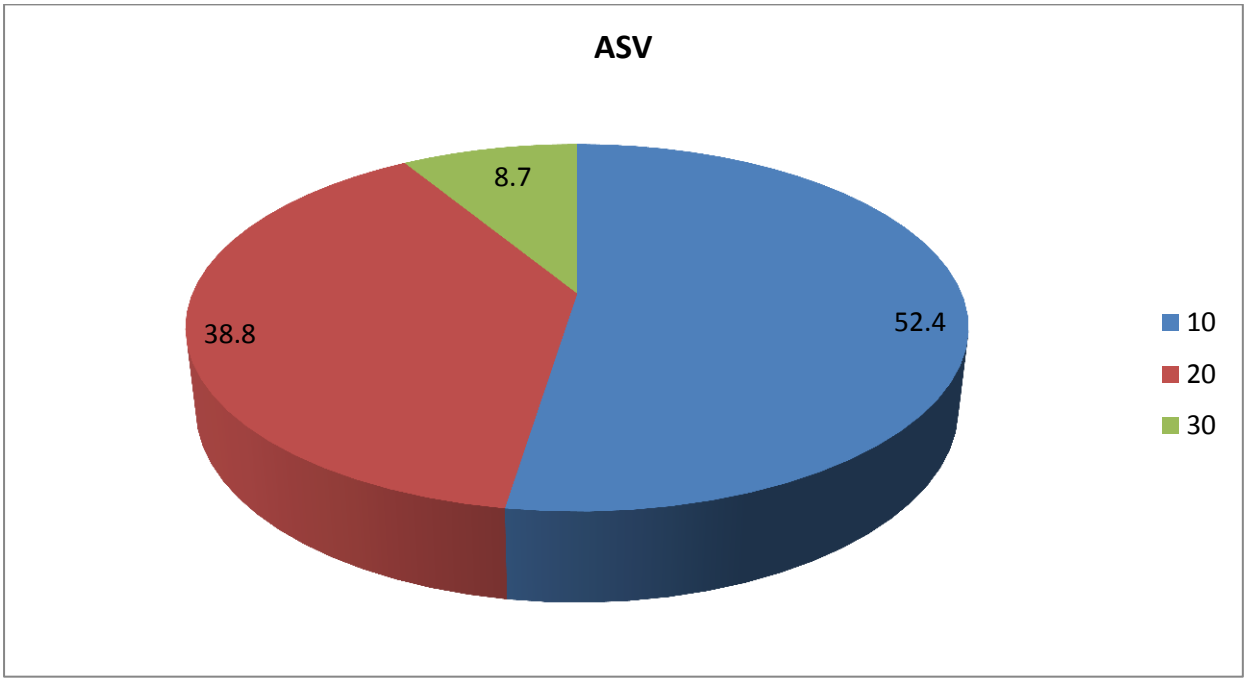

Chart 17: Pie diagram showing ASV Usage among subjects

TYPE OF TOXICITY VERSUS ASV RECEIVED

Table 19: Type of Toxicity versus ASV received

		Type of Toxicity					
		Hemotoxic		Neurotoxic		Local	
		Count	%	Count	%	Count	%
ASV	10	17	30.4%	14	58.3%	23	100.0%
	20	30	53.6%	10	41.7%	0	0.0%
	30	9	16.1%	0	0.0%	0	0.0%

$\chi 2 = 34.95$, df = 4, p <0.001*

In this study, among subjects with hemotoxicity, 30.4% received 10 units of ASV, 53.6% received 20 units and 16.1% received 30 units of ASV. Among subjects with Neurotoxicity, 58.3% received ASV of 10 units and 41.7% received 20 units of ASV, where as in subjects with local toxicity, 100% of them received only 10 units of ASV. This difference in use of ASV between different toxicity was statistically significant.

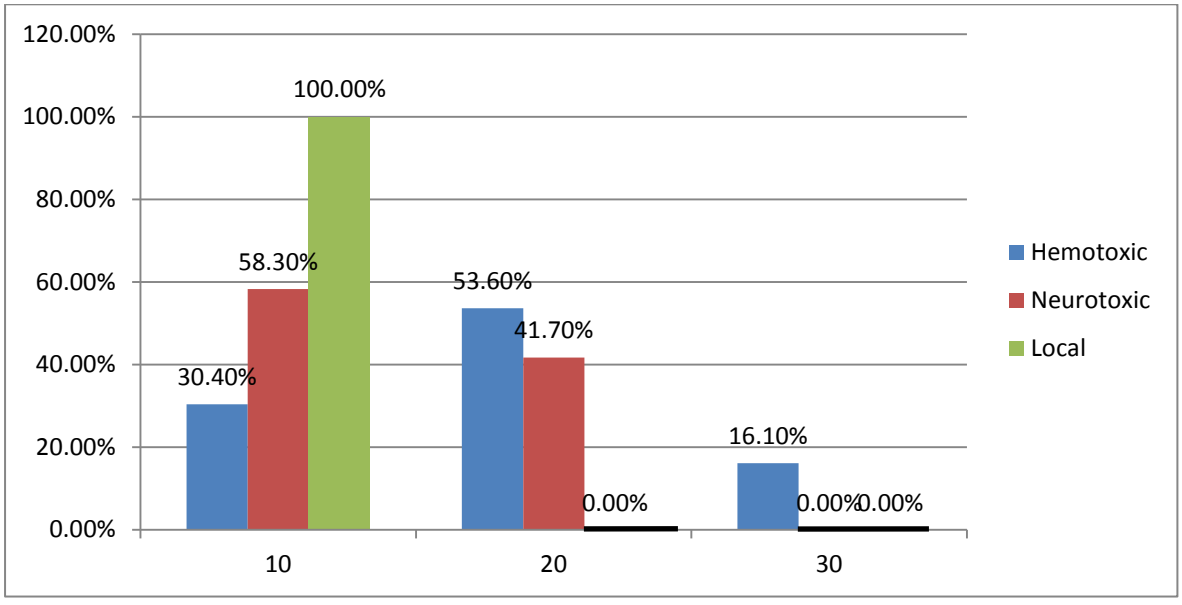

Chart 18: Bar diagram showing Type of Toxicity versus ASV received

MEAN ASV USAGE

Table 20: Mean ASV used in different type of toxicity

		ASV (in Vials)	
		Mean	**SD**
Type of Toxicity	Hemotoxic	18.6	6.7
	Neurotoxic	14.2	5.0
	Local	10.0	0.0
P value		<0.001*	

Mean ASV given in hemotoxic snake bites was 18.6 ± 6.7 units, in neurotoxic snake bites was 14.2 ± 5 units and in locally toxic snake bites 10 units were used. This difference in mean ASV requirements significantly high among hemotoxic group.

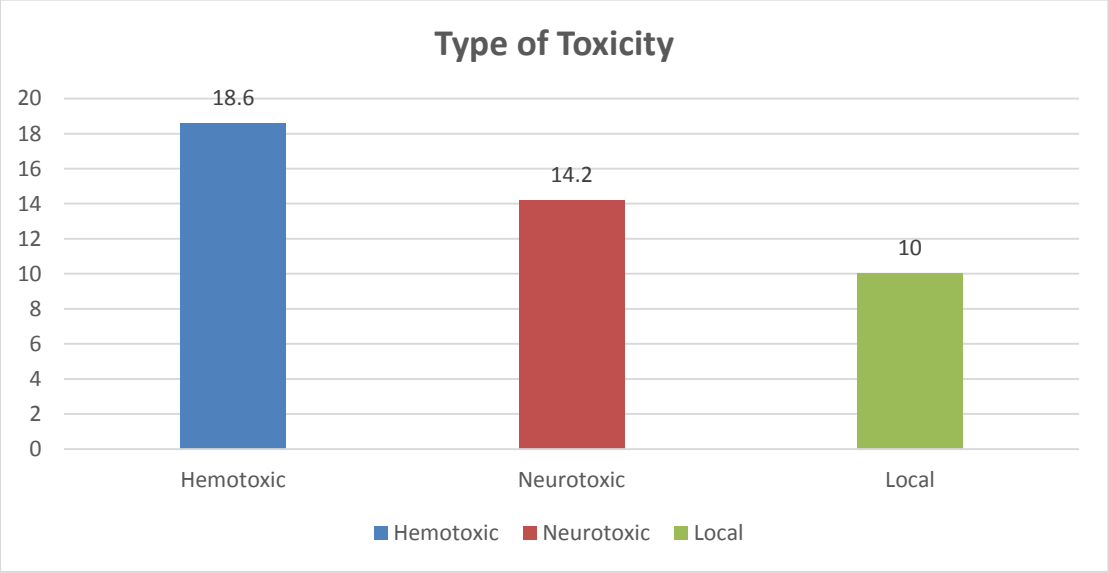

Chart 19: Bar diagram showing Mean ASV used in different type of toxicity

REACTION TO ASV

Table 21: Reaction to ASV

		Count	%
Reaction To ASV	Present	33	32.0%
	Absent	70	68.0%
	Total	103	100.0%

In this study 32% subjects had reaction to ASV.

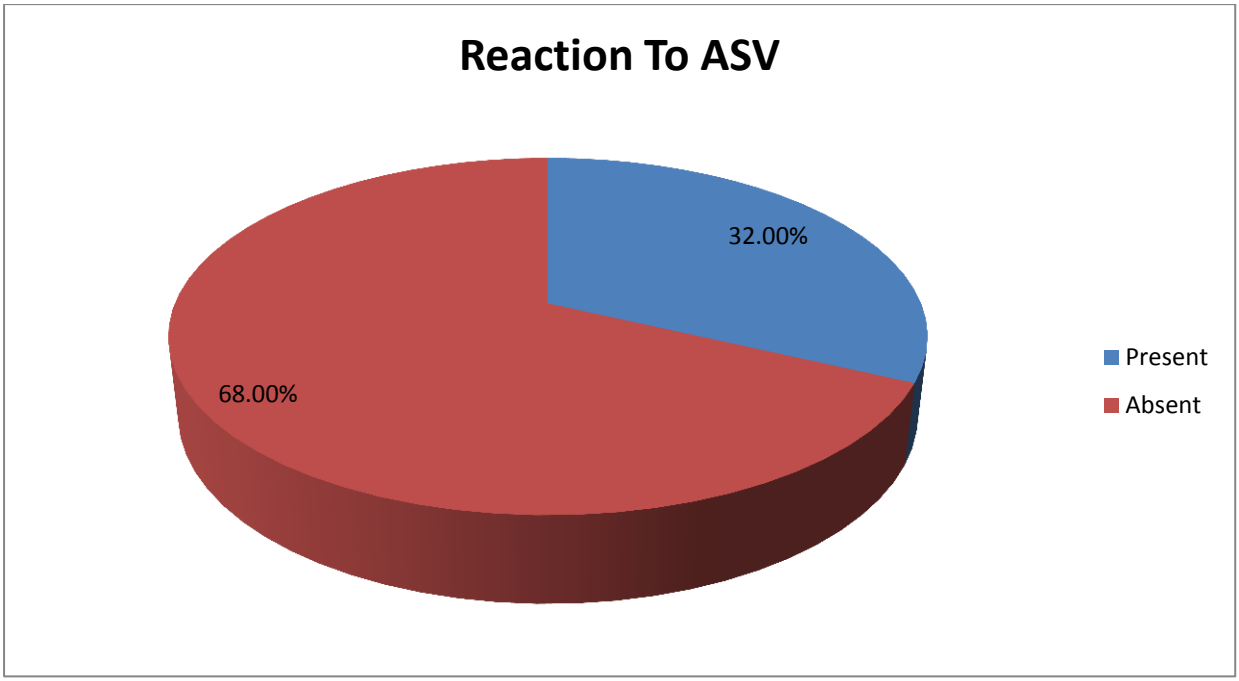

Chart 20: Pie diagram showing Reaction to ASV

LIFE THREATENING COMPLICATIONS

Table 22: Life Threatening Complications among subjects

		Count	%
Life Threatening Complications	ABSENT	80	77.7%
	ARF	11	10.7%
	CELLULITIS	9	8.7%
	MODS	2	1.9%
	DIC	1	1.0%
	Total	103	100.0%

22.3 % of subjects had life threatening complications. Most common life threatening complication observed was ARF (10.7%), followed by Cellulitis in 8.7%, MODS in 1.9% and DIC in 1% of subjects.

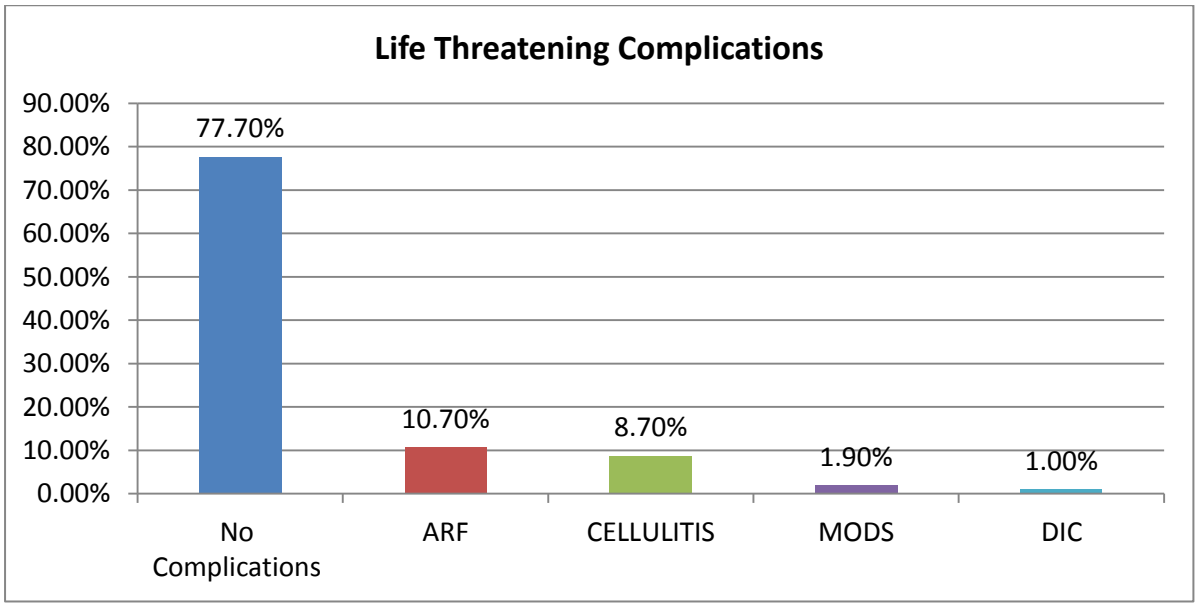

Chart 21: Bar diagram showing Life Threatening Complications among subjects

Table 23: Association between Time of presentation and Life Threatening Complications

Time of Presentation	Life Threatening Complications									
	ARF		CELLULITIS		DIC		MODS		Nil	
	Count	%	Count	%	Count	%	Count	%	Count	%
<6 hrs	3	27.3%	5	55.6%	0	0.0%	0	0.0%	69	86.2%
6 to 24 hrs	6	54.5%	4	44.4%	0	0.0%	1	50.0%	11	13.8%
>24 hrs	2	18.2%	0	0.0%	1	100.0%	1	50.0%	0	0.0%
Total	11	100.0%	9	100.0%	1	100.0%	2	100.0%	80	100.0%

$\chi 2 = 62.47$, df = 8, $p<0.001$*

Significant association was observed between Complications and time of presentation. 100% of DIC, 50% of MODS, 18.2% of ARF were seen among subject who presented after 24 hrs.

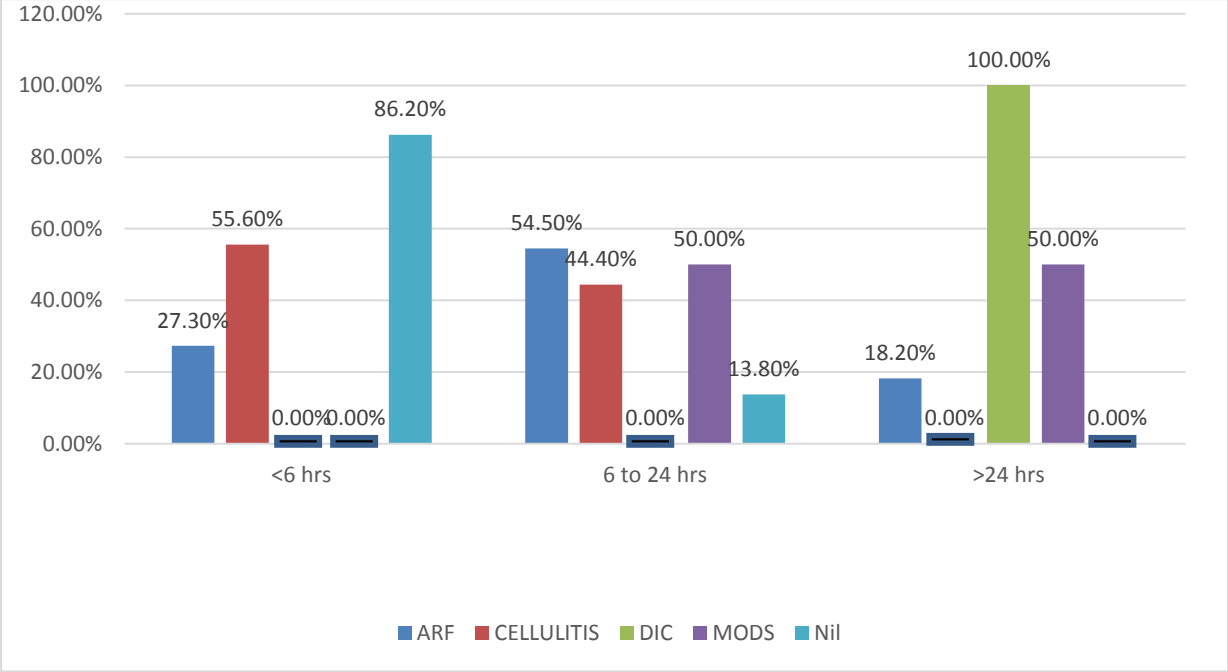

Chart 22: Bar diagram showing Association between Time of presentation and life threatening complications

Table 24: Association between life threatening complications and tourniquet usage in subjects

		Tourniquet			
		Tourniquet not used		Tourniquet Used	
		Count	%	Count	%
Life Threatening Complications	Present	6	26.1%	17	73.9%
	Absent	4	5.0%	76	95.0%

χ 2 = 9.061, df = 1, p= 0.003*

Significant association was observed between complications and tourniquet usage. i.e., among subjects with complications, 73.9% subject's tourniquet was used.

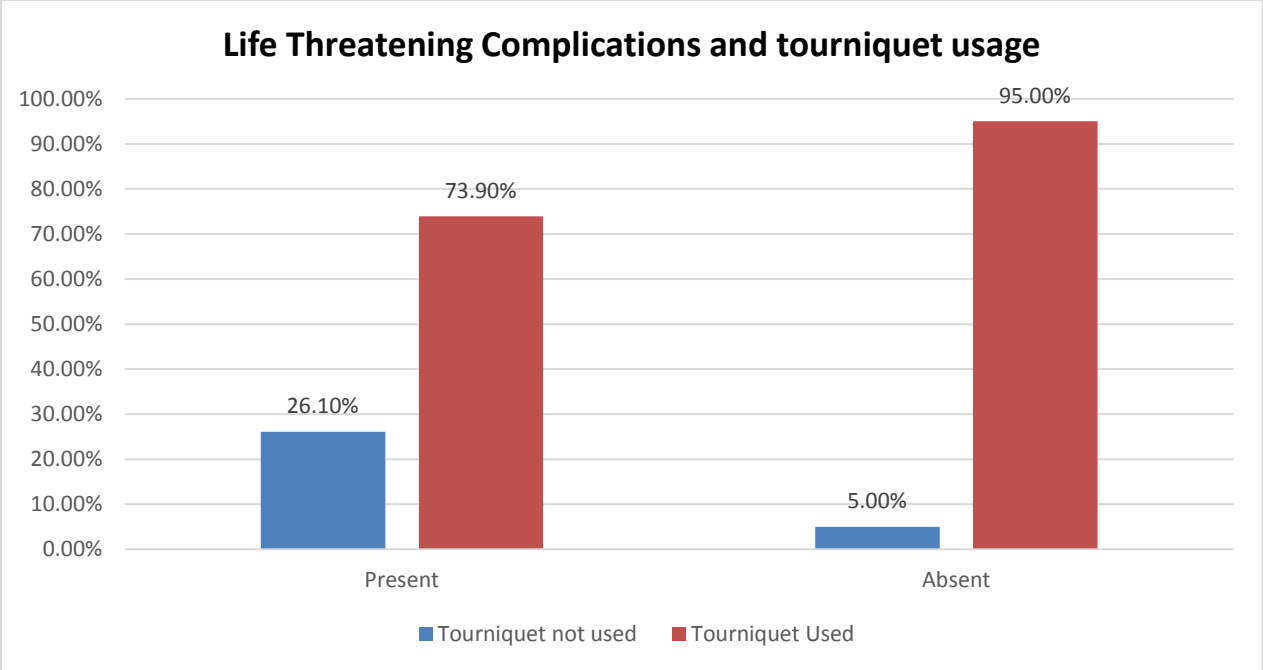

Chart 23: Bar diagram showing Association between life threatening complications and tourniquet usage in subjects

Table 25: Association between Type of Toxicity and Life Threatening Complications among subjects

		Type of Toxicity					
		Hemotoxic		Neurotoxic		Local	
		Count	%	Count	%	Count	%
Life Threatening Complications	ARF	9	16.1%	1	4.2%	1	4.3%
	Cellulitis	2	3.6%	2	8.3%	5	21.7%
	DIC	1	1.8%	0	0.0%	0	0.0%
	MODS	2	3.6%	0	0.0%	0	0.0%
	Nil	42	75.0%	21	87.5%	17	73.9%

χ 2 = 12.41, df = 8, p= 0.134

In Hemotoxic group, 16.1% developed ARF, 3.6% developed Cellulitis, 1.8% DIC, MODS in 3.6%. In Neurotoxic group, 4.2% had ARF and 8.3% had Cellulitis. In subjects having local toxicity 4.3% had ARF and 21.7% had Cellulitis. There was no significant difference in complication between two groups.

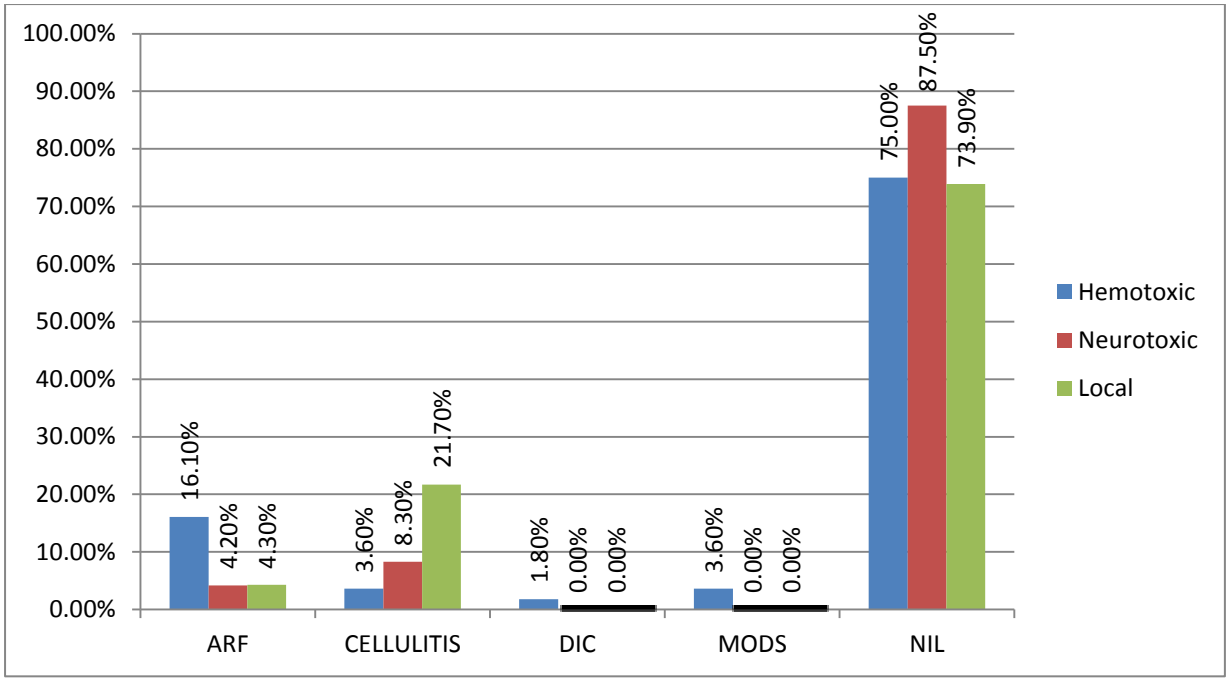

Chart 24: Bar diagram showing Association between Type of Toxicity and Life Threatening Complications among subjects

VENTILATOR SUPPORT

Table 26: Ventilator Support among subjects

		Count	%
Ventilator Support	No	85	82.5%
	Yes	18	17.5%
	Total	103	100.0%

In this study, 17.5% of subjects required ventilator support.

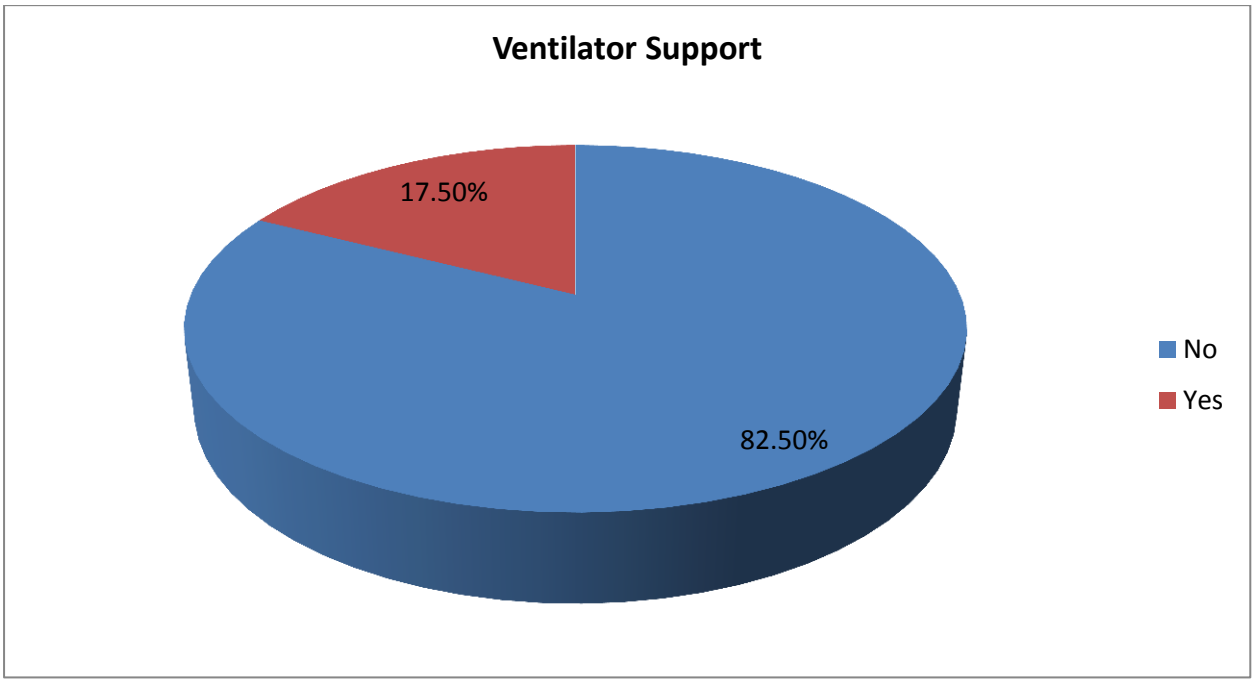

Chart 25: Pie diagram showing Ventilator Support among subjects

Table 27: Association between Type of Toxicity and Ventilator Support among subjects

		Type of Toxicity					
		Hemotoxic		Neurotoxic		Local	
		Count	%	Count	%	Count	%
Ventilator Support	No	46	82.1%	16	66.7%	23	100.0%
	Yes	10	17.9%	8	33.3%	0	0.0%

χ 2 = 9.061, df = 2, p= 0.011*

17.9% of subjects in hemotoxic group and 33.3% of subjects in neurotoxic group required ventilator support. None in local toxicity group required ventilator support.

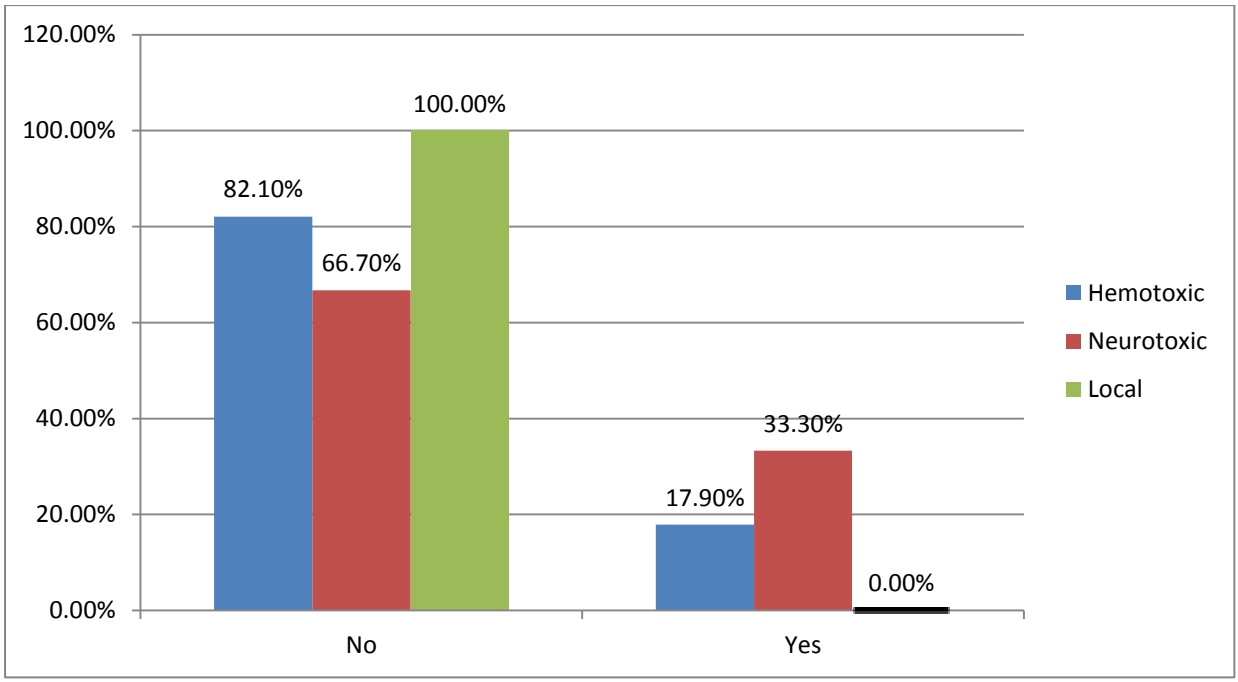

Chart 26: Bar diagram showing Association between Type of Toxicity and Ventilator Support among subjects

OUTCOME

Table 28: Outcome among subjects

		Count	%
Outcome	Complete Recovery	85	82.5%
	Debridement	10	9.7%
	Mortality	4	3.9%
	Hemodialysis	4	3.9%
	Total	103	100.0%

In this study 82.5% of subjects had complete recovery, 9.7% underwent debridement, 3.9% underwent hemodialysis and 3.9% died during the course of treatment.

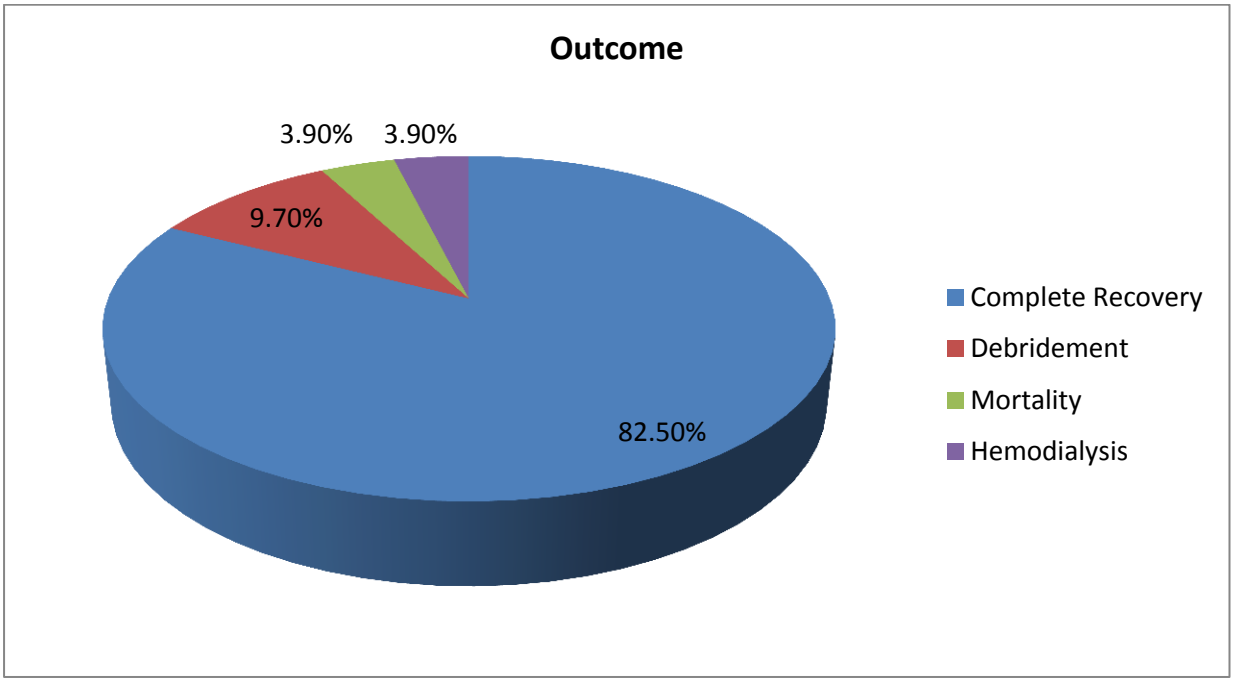

Chart 27: Pie diagram showing Outcome among subjects

Table 29: Association between Type of Toxicity and Outcome

		Type of Toxicity					
		Hemotoxic		Neurotoxic		Local	
		Count	%	Count	%	Count	%
Outcome	Complete Recovery	46	82.1%	21	87.5%	18	78.3%
	Mortality	4	7.1%	0	0.0%	0	0.0%
	Debridement	3	5.4%	2	8.3%	5	21.7%
	Hemodialysis	3	5.4%	1	4.2%	0	0.0%

$\chi 2 = 9.26$, df = 6, p= 0.159

In hemotoxic group, 7.1% died, 5.4% underwent debridement and 5.4% underwent hemodialysis. In Neurotoxic group 8.3% underwent debridement and 4.2% underwent hemodialysis. In local toxicity group 21.7% underwent debridement. There was no significant association between outcome and type of toxicity.

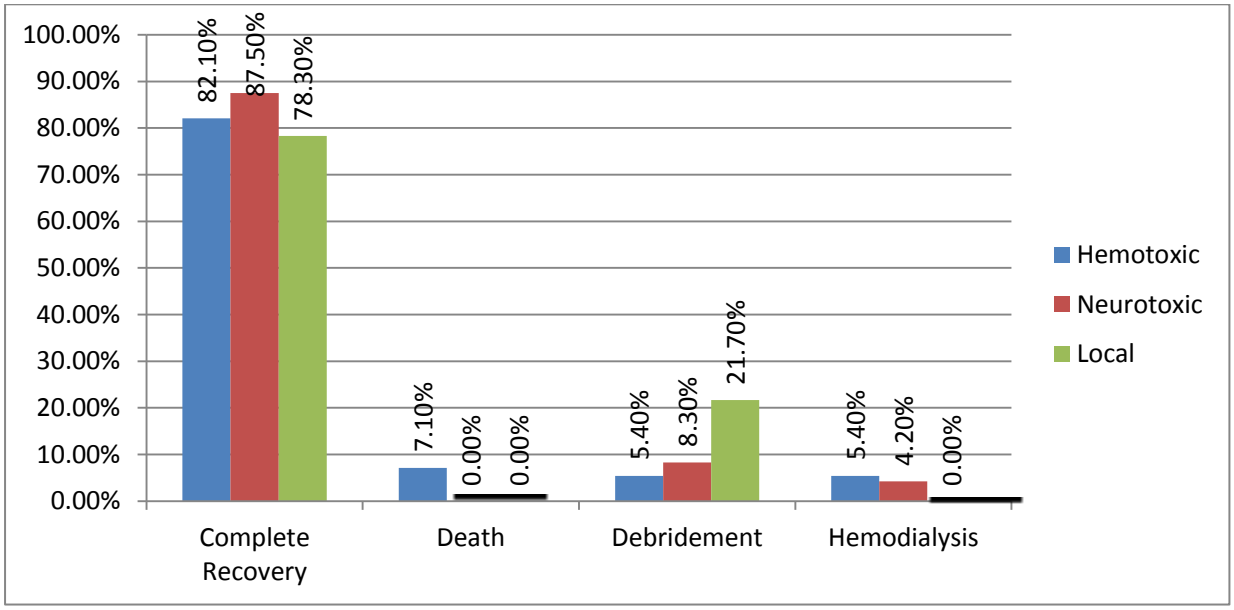

Chart 28: Bar diagram showing Association between Type of Toxicity and Outcome among subjects

DISCUSSION

DISCUSSION

Snakebite poisoning is one of the commonest public health problem in the tropics. It is an occupational hazard of agricultural workers and hunters in many tropical countries. Mortality in India from snakebite is about 15,000 per annum, whereas it is estimated to be 30,40,000 per annum worldwide. But unlike mortality from snakebite poisoning and the incidence of snakebite cannot ascertained as large number of cases go unnoticed, which may be attributed to treatment by local quacks or witch doctors or may be bites by non-poisonous snakes requiring no treatment.

AGE

Majority of subjects in this study were in 2nd and 3rd decade, i.e., among middle aged individuals with mean age of 37.83 ± 13.58 years. A similar study conducted by Sanket et al[65] and Gourav et al[66] also showed majority of bites among middle aged individuals i.e., among 2nd and 3rd decade as this is the most productive age group and were at risk for exposure while working in the field.

GENDER

In this study male to female ratio is 2:1. Similar higher male preponderance were reported in studies by Virendra et al[67] (3:1) and Gaurav et al[66] (4:1). This might be because of their involvement in farm/agriculture related activities and easy accessibility to the health care services as compared to females.

OCCUPATION

Majority of the cases of snake bites tend to occur among people with agriculture or farming as their chief occupation, in our study we observed similar results with 67% of our study population being farmers which was also seen in results of studies done by Sharma SK et al[68] (44%), Behcet AL et al[69] (87%), Sanket et al[65] (81%). The characteristics of snakebite have been attributed to the risk of exposure of these people to the snakes during their agricultural activities. This also shows that the high-risk group is in the low socioeconomic section of the population.

SEASON OF BITE

Incidence of snake bite was highest during the Monsoon (43.7%) and winter (41.7%) season. This is due to the fact that in monsoon and rainy season snakes venture out of their water-filled pits and also there is increased human activity in fields during this period as it is the sowing season. A similar trend was observed by Viramani SK et al[70] whereas a study by Gaurav et al[66] reported highest incidence of 51 % during summer.

SITE OF BITE

Lower extremities were the most observed bitten part of body in the present study(64.1%) and the common site was the feet followed by upper limb (35.9%). These findings are similar to the findings that of Virmani SK et al[70], Bhat RN[71], Virendra et al[67] and Gaurav et al[66]. Accidental and unintentional bites are more likely to occur in the lower limb as the person might unintentionally startle the snake with lower limbs being easily amenable for the bite,

especially when they are bare footed, while in the upper limb it may be seen with bites that occur during sleep.

TIME OF BITE

In the present study, the maximum incidence of snakebite occurred in morning (35.9%) followed by evening (30.1%) , afternoon (19.4) and night (14.6%) which was similar to studies reported by Chattopadhyay S et al[72] (61%) and Harbi NA[73] (53%). The reason for this may be due to involvement in agricultural activities more in the morning and evening as compared to the rest of the day. A higher incidence of bites at night was reported by Sanket et al[65] (72.66%) and Gaurav et al[66] (72.66%)

TIME OF PRESENTATION

Majority of subjects in the study presented with in 6 hrs (74.8%). 21.4% presented with in 6 to 24 hrs and 3.9% presented after 24 hrs. This helps in assessment of severity of envenomation, and administration of ASV in appropriate doses as the signs and symptoms develop in this vulnerable period. This observation was also made by Tarianj DD[74], Hati AK et al[3].

TOURNIQUET USE

In this study 90.3% patients presented to hospital with tourniquet tied proximal to bite site. Similar results were reported by Sharma SK et al[22] and Michael GL et al where 88% and 74% had used tourniquet respectively. This might be because of the apprehension and anxiety following the bites and also due to lack of awareness of first aid measures following snakebite.

TYPE OF SNAKE

In majority of the bites type of snake were not known (68.9%), 11.7% were cobra bites, 12.6% had viper bites and 6.8% had krait bites. Sanket et al[65] also showed that majority of the snakes were not identified (95%). This may be because of lack of knowledge about the types of snakes and due to anxiety and fear following snakebite.

LOCAL ENVENOMATION SYMPTOMS

Most common local envenomation symptoms in this study is swelling (47.6%), followed by it was pain in 43.7%, local bleeding 16.5% and gangrene in 9.7%. Swelling may be due to tourniquet applied proximal to the bite site which leads to obstruction of lymphatics and venous blood flow. Gaurav et al[66] also showed pain, local bleed, cellulitis and Gangrene in 35%, 32%, 34% and 6% respectively.

HEMOTOXIC ENVENOMATION

Most common hematological manifestation in this study is hematuria (23.3%) followed by local bleed in 18.4%, epistaxis in 15.5%, gum bleeding in 11.7%, hematemesis in 5.8%, hemoptysis in 2.9%.

Virendra et al[67] reported Gum bleeding in 7.95%, Hematuria in 10.22% and Hematemesis in 5.68%.

Sanket et al[65] reported gum bleed in 83.33%, Local Bleed in 7.14%, Haemoptysis in 4.76%, Epistaxis in 2.3%, Haematemesis in 4.76%, Malaena in 4.76%, Haematuria in 42.85%, Oliguria in 47.61%, Ecchymosis in 4.76%, Intracerebral bleed in 2.3%, Subconjunctival haemorrhage in 4.76%.

Gaurav et al[66] reported Local bleed in 83.33%, Gum bleed in 7.14%, Hemoptysis in 4.76%, Epistaxis in 2.3%, Hematemesis in 4.76%, Malena in 4.76%, Hematuria in 42.85%,

Oliguria in 47.61%, Ecchymosis 4.76%, Intracerebral hemorrhage in 2.3%, Subconjunctival hemorrhage 4.76%.

NEUROTOXIC ENVENOMATION

Most common neurological manifestation in this study is Ptosis (34%) i.e., all patients with neurotoxic envenomation had ptosis. This is because ptosis develops even with the small doses of neurotoxic venom in the body & is the first sign to manifest in cases of neurotoxic envenomation. This is followed by Blurring of vision (15.5%), Respiratory paralysis (14.6%), Ophthalmoplegia (8.7%), Unconsciousness (7.8%) and flaccid limb paralysis (1.9%).

Virendra et al[67] reported altered sensorium in 1.13%, Breathlessness in 18.44%, Ptosis in 86.66%, Head lag in 88.66% and Diplopia in 46.66%.

Sanket et al[65] reported Ptosis in 100%, Dysphagia in 42.85%, Ophthalmoplegia in 85.71%, Unconsciousness in 28.57%, Flaccid limb paralysis in 28.67% and Respiratory paralysis in 90.47%.

Gaurav et al[66] reported Ptosis in 100%, Dysphagia in 42.85%, Ophthalmoplegia in 85.71%, Unconsciousness in 28.57%, Flaccid limb paralysis in 28.67%, Respiratory paralysis in 90.47%.

20 MIN WHOLE BLOOD CLOTTING TIME

In 54.4% of subjects 20 WBCT showed no clotting and in 45.6% showed clotting. All the 54.4 % (56) where blood was not clotted belonged to Hemotoxic envenomation and 45.6 % where blood had clotted belonged to either to Neurotoxic or Local envenomation category. Out of 56 hemotoxic snakebites, only 24 patients had one or the other hemotoxic symptoms. Rest 32 patients had no signs or symptoms. But 20 WBCT was positive in all the 56

hemotoxic envenomation patients suggesting that venom has caused its effects on the body. This shows that 20 WBCT is a very good indicator of Hemotoxic envenomation.

TYPE OF ENVENOMATION

In the study 24.3% had hemotoxic envenomation, 22.3% had only local features, 17.5% had neurotoxic envenomation. Other subjects had combination of toxicity like 19.4% (Hematotoxic +Local), 9.7% (Hematotoxic +Neurotoxic), 1% (Hematotoxic +Neurotoxic + Local) and 5.8% (Neurotoxic +Local). This shows that even though the type of snake was not identified in majority of cases, Snakes causing predominantly hemotoxicity i.e., Viper could be most common snakes in this locality followed by neurotoxic snakes like Cobra and Krait.

Gaurav et al[66] showed hemotoxic snake bites (55.26%) were more common than neuroparalytic bites (27.63%). Similarly Sanket et al[65] showed Vasculotoxic snake bites (55.26%) were more common than neuroparalytic bites (27.63%). Nigam et al[43] and Sarangi et al[76] also reported high incidence of Hemotoxic envenomation followed by Neurotoxic envenomation.

ASV USAGE

Mean ASV given in hemotoxic snake bites was 186 ml, in neurotoxic snake bites was 142 ml and in locally toxic snake bites 100ml were used. The Maximum dosage as per protocol for Hemotoxicity is 300 ml, for neurotoxicity is 200 ml and for local envenomation is 100 ml. In this study 32% subjects had reaction to ASV. By following the protocol we could reduce the financial burden on the patients by reducing the number of ASV used majorly in Hemotoxic and Neurotoxic bites and also the risk of developing ASV reactions.

LIFE THREATENING COMPLICATIONS

In this study 77.7% had no other life threatening complications. Most common life threatening complication observed in the study subjects was ARF in 10.7%, cellulitis in 8.7%, MODS in 1.9% and DIC in 1% of subjects. Most of the complication occurred in patients who presented late to hospital i.e., after 6 hours of bite. While ARF was more common among Hemotoxic bites.

Out of 11 patients who presented with ARF, 3 patients had presented within 6 hours, 6 patients between 6 and 24 hours, 2 patients after 24 hours of bite. On initiation of ASV treatment, all the patients with ARF presenting within 6 hours and 2 patients presenting between 6 and 24 hours had complete recovery without requiring haemodialysis. 4 patients required haemodialysis but both the patients presenting to hospital after 24 hours of bite with ARF died in the course of the hospital stay. This shows that early presentation and initiation of treatment with ASV in patients with ARF has better outcome.

Cellulitis was more common in local toxicity patients who had come with tourniquet tied to the limb. This may be due to stasis of blood in periphery along with superadded infection during the bite. The obstruction to venous blood flow leads to increased concentration of venom in the local area & delay in activation of inflammatory mediators leading to muscle necrosis and increases the incidence of Cellulitis.

Tourniquet also causes obstruction to arterial blood flow resulting in gangrene. The most dreaded complications like MODS and DIC was also found in Hemotoxic envenomation suggesting that a careful monitoring and aggressive treatment must be given in cases of hemotoxic bites.

Virendra et al[67] reported cellulitis in 39.77%, Hypotension in 21.59%, acute renal failure in 13.63%, DIC in 19.31%, Cortical venous sinus thrombosis (CVT) in 1.13%, Delayed peripheral neuropathy 6.66% patients. Gaurav et al[66] reported ARF among 26%, cellulitis in 44.7% and DIC in 31.5%. In both of these studies the ASV was used without following any protocol. The incidence of complications was less in our study which suggests that proper usage of ASV as per protocol and early initiation of treatment helps in reducing the complications.

VENTILATOR SUPPORT

In this study 17.5% of subjects required ventilator support in total. 17.9% of subjects in hemotoxic group and 33.3% of subjects in neurotoxic group required ventilator support. So incidence of need for ventilator support is more in patients with neurotoxic bites. This may be because of neurotoxic envenomation leading to respiratory muscle paralysis.

OUTCOME

In the study 82.5% of subjects had complete recovery, 9.7% underwent debridement, 3.9% underwent hemodialysis and 3.9% died during the course of treatment. Mortality was seen in patients who presented late to hospital i.e., after 24 hours of bite and also with complications ARF, DIC and MODS.

Sanket et al[65] reported complete recovery in 72%, 10.5% underwent surgical debridement, 9.2 % required hemodialysis and mortality was seen in 7.9%. Gaurav et al[66] reported complete recovery in 43%, 31% had DIC, 10.5% underwent surgical debridement, 9.2% required hemodialysis and mortality was seen in 5.2%. In both these studies ASV was

used without following any particular protocol and the morbidity and mortality was much higher than our study.

In a study by Srimannarayana J et al[77], used three different regimens of treatment reported high mortality of 38.89%, 25%, and 26.67% respectively. Another study by Paul et al[78], which compared the outcome among low dose versus high dose ASV regimens showed mortality rate of 10% and 14% respectively. The mortality rate in these studies using different regimens was much higher than our study.

CONCLUSION

CONCLUSION

- Snakebites are common in 2nd and 3rd decade, i.e., among middle aged individuals with mean age of 37.83 ± 13.58 years as they are among the most productive age group and involved more in outdoor activities.

- Males are more affected than females with male to female ratio of 2:1 as they are more involved in outdoor activity and agriculture in this locality.

- Farmers are at higher risk of snakebites as compared with other occupation.

- Snakebites are more common in winter and Monsoon season as farmers are more active in agricultural work in this period.

- Snakebites are more common in lower limbs as compared to upper limbs as they are easily accessible during working in fields.

- Snakebites are more common in morning and evening as the farmers are actively involved in agricultural work in this time.

- Majority of the patients presented to hospital within 6 hours which is mainly due to anxiety and fear of death following snakebite and also due to easy availability of health care services to the people in this locality.

- Majority of snakebite patients come with tourniquet tied to their limbs which shows the lack of knowledge about the first aid measures to be taken following snakebite.

- Majority of snakes were not identified. Viper bites may be more common in view of more subjects having hematotoxicity followed by Cobra and Krait bites.

- Hemotoxic envenomation was more common followed by only local envenomation, Neurotoxic envenomation and then the combination of envenomation.

- Most common local envenomation symptoms includes swelling, followed by it was pain, local bleeding and gangrene

- Most common hematological manifestation includes hematuria followed by local bleed, epistaxis, gum bleeding, hematemesis, hemoptysis.

- Most common neurological manifestation includes Ptosis followed by Blurring of vision, Respiratory paralysis, Ophthalmoplegia, Unconsciousness and Flaccid limb paralysis.

- 20 WBCT is positive in all hemotoxic bites even if the patient doesn't presents with any symptoms of hemotoxicity which makes it a very good indicator of Hemotoxic envenomation.

- Mean ASV given in hemotoxic snake bites was 186 ml, in neurotoxic snake bites was 142 ml and in locally toxic snake bites is 100ml thus reducing the financial burden on

the patients by reducing the number of ASV used majorly in Hemotoxic and Neurotoxic bites and also the risk of developing ASV reactions. Reaction to ASV is very common, hence it should not be used without an indication.

- Most common life threatening complication observed in the study subjects was ARF, cellulitis, MODS and DIC. Most of the complication occurred in patients who presented late to hospital i.e., after 6 hours of bite. So early initiation of treatment with ASV reduces the risk of developing life threatening complications.

- Local complications like cellulitis were more common in patients who had come with tourniquet tied to the limb. By educating the people about the first aid measures we can reduce these complications. The most dreaded complications like MODS and DIC was found in Hemotoxic envenomation suggesting that a careful monitoring and aggressive treatment must be given in cases of hemotoxic bites.

- Ventilator support was required in 17.5% of patients. Neurotoxic patients required more ventilator support than hemotoxic patients due to respiratory paralysis.

- As a outcome, when treated the patients of snakebite with Indian standard protocol, 82.5% of subjects had complete recovery, 9.7% underwent debridement, 3.9% underwent haemodialysis and mortality was seen in 3.9% during the course of treatment. The outcome when compared to other studies where ASV was used without following any protocol, the morbidity and mortality was very high. This shows that by using the Indian Guidelines and protocol, we can reduce the financial burden on patients by reducing the ASV usage and also have a good clinical outcome.

- Mortality was seen in patients who presented late to hospital i.e., after 24 hours of bite and also with complications ARF, DIC and MODS. This shows that early presentation to hospital and early initiation of treatment with ASV reduces the mortality.

SUMMARY

SUMMARY

Snakebite poisoning is one of the commonest public health problems in the tropics. It is an occupational hazard of agricultural workers and hunters in many tropical countries like India and is one of the leading causes of morbidity and mortality among middle aged population. ASV, which is the only drug available in India to counteract the effects of poisonous venom, is being used injudiciously without following a particular protocol.

This was a prospective observational study done at a tertiary medical college hospital. 103 patients with snakebite fulfilling the inclusion criteria were included in the study. They were treated with ASV as per Indian guidelines and protocol given by Association of Physicians of India (API) in 2013.

- Majority of patients were in 2nd and 3rd decade, i.e., among middle aged individuals. Males were affected more as compared to females.

- Most common bites were in farmers and were highest during the Monsoon and winter season.

- Lower extremities were the most observed bitten part followed by upper limb and the maximum incidence of snakebite occurred in morning and evening.

- Majority of subjects presented within 6 hrs and complications were more in patients presenting late to hospital.

- Majority of patients presented to hospital with tourniquet tied proximal to bite site and cellulitis was more among the patients with tourniquet.

- Though type of snake was not known in most of the cases, viper and cobra bites were common among identified.

- Most common local envenomation symptoms are swelling and pain. Most common hematological manifestation in this study was hematuria, local bleed, epistaxis and gum bleeding. Most common neurological manifestation is Ptosis, Blurring of vision and Respiratory paralysis.

- 20 WBCT showed no clotting in Hemotoxic envenomation and clotted in Neurotoxic or Local envenomation.

- 24.3% had hemotoxic envenomation, 22.3% had only local features, 17.5% had neurotoxic envenomation. Other subjects had combination of toxicity. Mean ASV given in hemotoxic snake bites was 186 ml, in neurotoxic snake bites was 142 ml and in locally toxic snake bites 100ml were used.

- Most common life threatening complication observed were ARF, cellulitis, MODS and DIC. 17.5% of subjects required ventilator support in total.

- 82.5% of subjects had complete recovery, 9.7% underwent debridement, 3.9% underwent haemodialysis and mortality was seen in 3.9% during the course of

treatment. Mortality was seen in patients who presented late to hospital i.e., after 24 hours of bite and also with complications like ARF, DIC and MODS.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Warrell D. Researching nature's venoms and poisons. Trans R Soc Trop Med Hyg. 2009; 103(9):860-866.
2. Sam K, Khan M, Peeraly S, Kumar PG, Rao PG. Snake-bite Envenomation: A Comprehensive Evaluation of Severity, Treatment and Outcome in a tertiary Care South Indian Hospital. The Internet Journal of Emergency Medicine. 2009; 5(1).
3. Hati AK, Mandal M, De MK, Mukherjee H, Hati RN. Epidemiology of snakebite in the district of Burdwan, West Bengal. J Indian Med Assoc. 1992 Jun; 90(6):145-7.
4. Pillay VV. Modern medical toxicology. 2nd ed. New Delhi: Jaypee Brothers; 2001. p. 95-103.
5. Hayat AS, Khan AH, Shaikh TZ, Ghouri RA, Shaikh N. Study of snakebite cases at Liaquat university hospital Hyderabad/Jamshoro. J Ayub Med Coll Abbottabad. 2008; 20(3):125-7.
6. Bawaskar HS, Bawaskar PH. Profile of snakebite envenoming in western Maharashtra, India. Trans R Soc Trop Med Hyg. 2002; 96:79-84.
7. Viccellio P, editor. Emergency toxicology. 2nd ed. Philadelphia: Lippincott Raven publishers; 1998. p-1035.
8. Williams D, Gutierrez JM, Harrison R, Warrell DA, White J, Winkel KD et al. The Global Snake Bite Initiative: an antidote for snake bite. Lancet. 2010; 375:89-91.
9. Pe T, Mya S, Myint AA, Aung NN, Kuy KA, 0o T. Field trial of efficacy of local compression immobilization first-aid technique in Russell's viper (Daboia russelii siamensis) bite patients. Southeast Asian J Trop Med Public Health. 2000 Jun; 31(2):346-8.

10. Chauhan S, Faruqi S, Bhalla A, Sharma N, Varma S, Bali J. Pre-hospital treatment of snake envenomation in patients presented at a tertiary care hospital in North Western India. J venom Anim Toxins Incl Trop Dis [online]. 2005 [cited 2009 Nov. 3]; 11(3): 275-82. Available from : URL : http://www.scielo.br/scielo.php? Script = SCT_ abstract & PTd = S167891992005000 300006 & lng = en & nrm = TSO & tlng=en .
11. Kularatne SAM, Budagoda BDSS, Gawarammana IB, Kularatne WKS. Epidemiology, clinical profile and management issues of cobra (Naja naja) bites in Sri Lanka: first authenticated case series. Trans R Soc Trop Med Hyg. 2009; 103:924-30.
12. Bawaskar HS. Snake Venoms and Antivenoms: Critical Supply Issues. J Assoc Phys India. 2004; 52:11-13.
13. Master FJ. Snakes to Simillimum: Demystifying venoms. Belgium: B. Jain Archibel s.p.r.l.; 2008. p. 1-74.
14. Warrell DA. Snake bite. Lancet. 2010; 375:77-88.
15. Warell DA. Animal poisons. In: Manson-Bahr PEC, Bell DR, editors. Manson's tropical diseases. 19th ed. London: Bailliere Tindall; 1987. p. 855-74.
16. Warrell DA. Guidelines on Management of Snake-bites. New Delhi: WHO Regional office for South-East Asia; 2010. Available from: URL: http://www.searo.who.int/LinkFiles/BCT_snake_bite_guidelines.pdf.
17. Tilak R. Snakes. In : Bhalwar R, Gupta RK, Kunte R, Tilak R, Vaidya R, editors. Textbook of Public health and Community Medicine. 1st ed. Pune: Department of Community Medicine, Armed Forces Medical College in collaboration with WHO, India office, New Delhi. 2009. p. 966-8.
18. White J. Overview of venomous snakes of the world. In : Dart RC, editor. Medical toxicology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins;2004. p. 1543-56.

19. Menon JC, Joseph JK, Jose MP, Dhananjaya BL. Clinical Profile and Laboratory Parameters in 1051 Victims of Snakebite from a Single Centre in Kerala, South India. J Assoc Physicians India. 2016; 64:22-29.
20. The global burden of snakebite: a literature analysis and modeling based on regional estimates of envenoming and deaths. Geneva: WHO. 2008 Nov. Available from : URL: http://www.who.int/neglecteddiseases/integrated_mediasnakebite/en/index.html.
21. Calvete JJ, Cid P, Sanz L, Segura A, Villata M, Herrera M et al. Antivenomic assessment of the immunological reactivity of Echi Tab-Plus-ICP, an antivenom for the treatment of snakebite envenoming in sub-Saharan Africa. Am J Trop Med Hyg. 2010; 82(6):1194-201.
22. Sharma SK, Chappuis F, Jha N, Bovier PA, Loutan L, Koirala S. Impact of snakebites and determinants of fatal outcomes in Southeastern Nepal. Am J Trop Med Hyg. 2004; 71(2):234-8.
23. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM et al. Snakebite mortality in India: A nationally representative mortality survey. PLoS Negl Trop Dis 2011; 5(4): e1018. Available from : URL: http://www.plosntds.org/article/info:doi/10.1371/journal.pntd.0001018.
24. Simpson ID, Norris RL. Snakes of medical importance in India: Is the concept of "Big 4" still relevant and useful? Wilderness Environ Med. 2007; 18(1):2-9.
25. Kalantri S, Singh A, Joshi R, Malamba S, Ho C, Ezoua J et al. Clinical predictors of in-hospital mortality in patients with snakebite: a retrospective study from a rural hospital in central India. Trop Med Int Health. 2006 Jan; 11(1):22-30.
26. Harrison RA, Hargreaves A, Wagstaff SC, Faragher B, Lalloo DG. Snake envenoming: a disease of poverty. PLoS Negl Trop Dis 2009; 3(12): e569. Available

from: URL: http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0000569.

27. Reddy KSN. The essentials of Forensic medicine and toxicology. 29th ed. Hyderabad: Suguna Devi; 2010.500-2.
28. Smith MA. The fauna of British India, Ceylon: Reptilla andAmphibia, Vol III Serpents, Taylor and Francis, London 1943.
29. Kumar S, Usgaonkar RS. Myasthenia Gravis like picture resulting from snake bite. J Indian Med Assoc. 1968 May 1; 50(9):428-9.
30. Vad NE Morphology of Snakes. Thesis for M.Sc. Degree in Zoology in Haffkine Institute, Bombay, 1959
31. Pillary VV. Handbook of Forensic Medicine and Toxicology. 12th Edition, 2001: 345-351.
32. Indramani Jena and Sarangi. Snakes of Medical Importance and snake bite treatment, 1993.
33. Findlay Russell. Terrestrial and marine venomous snakes in Forensic Medicine a study in trauma and environmental hazards. London W.B. Saunders company. 1971; 3: 1437-45.
34. Reid HA, Thean PC, Martin WJ. Specific antivenene and prednisone in viper-bite poisoning: Controlled trial. Br Med J. 1963 Nov; 2:1378–1380.
35. Warell DA: Animal Toxins-Venomous bite and stings in Manson's Tropical Disease 20th, W.B. Saunders: 20 Ed. P. 68-95.
36. Mehtha PJ, Sainani GS. Bleeding following snake bite. J Assoc Physicians India.1984; 32 (5):389.

37. Kornalik F and Blomback B. Prothrombin activation induced by ecarin-a prothrombin converting enzyme from Echis carinatus vemon. Thromb Res. 1975 Jan; 6(1):57-63.
38. Saini RK, Arya RK, Singh S, Sharma S, Gupta VK, Pathania NS. Coagulation defects in snake bite poisoning. J Assoc Physicians India.. 1985; 33(2):148-151.
39. Reid HA., Theakston RDG. The management of snake bite. Bull World Health Organ. 1983; 61(6):885–895
40. Lallo DG, Trevett AJ, Saweri A, Naraqi S, Thekaston RD, Warrell DA. Snake bites by the Papuan taipan (Oxyuranus scutellatus canni): paralysis, hemostatic and electrocardiographic abnormalities, and effects of antivenom. Am J Trop Med Hyg. 1995 Jun; 52(6):525-31.
41. Dash SC, Ghosh SK, Mathew DC, Jha GN, Prasad W, Gewal KS. Neurotoxic snake bite. Dramatic Recovery following neostigmise therapy. 1976 Aug; 24(8):535-7.
42. Thomas L, Tyburn B, Katterlee J, Biao T, Mehadaovi H, Moravie V. Prognostic significance of clinical grading of patients envenomed by Bothrops lanceolatus in Martinique. Trans R Soc Trop Med Hyg. 1998 Sep-Oct; 92(5):542-5.
43. Nigam P, Tandon VK, Rajendra Kumar, Thacore VR, Lal Narrottam. Snake bite. A clinical study Indian J Med Sci. 1973 Sep; 27(9):697-704.
44. Ashish Gunwant Rao Wankhade. An unusual Russell's Viper Bite mark. Med Sci Law. 2004; 44:87-89.
45. Gold BS, Robert A. Venomous Snakebites Current Concepts in Diagnosis, Treatment and Management. Emerg Med Clin North Am. 1992 May; 10(2):249-67.
46. Gupta A, Rao PV. Aucte renal failure following snake bite. J Assoc Physicians India. 1988 Aug; 36(8):501-3.

47. Chugh KS. Snake bite induced acute renal failure in India. Kidney Int. 1989 Mar; 35(3):891-907.
48. Shastry JCM, Date A, Carman RH, Johny KV. Renal failure following snake bite. A clinicopathological study of nineteen cases. Am J Trop Med Hyg. 1977 Sep; 26:1032-8.
49. Lallo DG. The epidemiology of snake bite in central province and National Capital district, Papua New Guinea. Trans R Soc Trop Med Hyg. 1995 Mar-Apr; 89(2):178-82.
50. Watt G. Positive response to edrophonium in patients with neurotoxic envenoming by cobras. A placebo-controlled study. N Engl J Med. 1986 Dec; 315(23):1444-8.
51. Singh S, Dass A, Jain S, Varma S, Banerjee AK, Sharma BK. Fatal nonbacterial thrombotic endocarditis following viperine bite. Intern Med. 1998 Mar; 37(3):342-4.
52. Chuang TY, Lin SW, Chan RC. Guillain Barre Syndrome – An unusual complication after snakebite. Arch Phys Med Rehabil. 1996 Jul; 77(7):729-31.
53. Sean Patrick Nordt, Richard F Clark. Rattlesnakes and other cortalids. Clinical Toxicology Ford Delaney Ling Erickson Saunders. 2001; 109:863-877.
54. Mathew JL, Gera T. Ophitoxoxemia. Intern Med. 2000 June; 39(4):472-482.
55. Warrell DA. Disseminated intravascular coagulation caused by the carpet viper. Trial of heparin. Br J Haematol. 1976 Jul; 33(3):335-42.
56. Toby L. Envenomation coagulopathy in wounds from pit vipers. N Engl J Med 1981; 305:443-447.
57. Theakston RDG, Jonas MJJ, Reid HA. Micro-ELISA for detecting and assaying snake venom and venom antibody. Lancet. 1977 September; 24:639-641.
58. Viravan C et al. ELISA confirmation of acute and past envenoming by the Monocellate thai cobra. Am J Trop Med Hyg. 1986 Jan; 35(1):173-81.

59. Sarangi A, Jenal L, Sahoo H. A profile of snake bite poisoning with special reference to hematological, renal, nernological and electrocardiographic abnormalities. J Assoc Physicians India. 2016. 1977 August; 25:555-560.
60. Simpson ID. Management of Snakebite. The National, API WB branch. Update in Medicine. 2006;88-93.
61. Shibendu G, Prabuddha M, Tanmoy C. Management of Snake Bite in India. J Assoc Physicians India. 2016; 64:11-14.
62. National Snakebite Management Protocol. Directorate General of Health Services; 2009. Available from: URL: http://164.100.130.11:8091/nationalsnakebitemanagementprotocol.pdf.
63. Gosavi PA, Jaju JB, Pawar GR, Dharmadhikari SC. A study on the clinico-epidemiological profile and the outcome of snake bite cases in the tertiary care hospital. Int J Basic Clin Pharmacol. 2014; 3:298-302.
64. Singh S, Singh G. Snake Bite: Indian Guidelines and Protocol [Internet]. India: Association of Physicians of India; 2013 [cited 2013]. Available from http://www.apiindia.org/
65. Sanket M, Dhanesh M. A study of clinical profile of snake bite at a tertiary care centre. Int J Recent Sci Res. 2015; 6:6065-68.
66. Gaurav B, Mhaskar D, Anubhav A. A Study of Clinical Profile of Snake Bite at a Tertiary Care Centre. Toxicol Int. 2014; 21(2):203–208.
67. Virendra CP, Harsha VP, Avinash P, Vaibhav A. Clinical Profi le and outcome of envenomous snake-bite at tertiary care centre in western Maharashtra. Int j med public health. 2011; 1:28-38.

68. Sharma SK, Chappuis F, Jha N, Bovier PA, Loutan L, Koirala S. Impact of snakebites and determinants of fatal outcomes in Southeastern Nepal. Am J Trop Med Hyg 2004; 71(2):234-8.
69. Behcet AL, Orak M, Aldemir M, Guloglu C. Snakebites in adults from the Diyarbakır region in southeast Turkey. Turkish Ulus Travma Acil Cerrahi Derg. 2010; 16 (3):210-4.
70. Viramani SK, Dutt OP. A profile of snakebite poisoning in Jammu Region. J Indian Med Assoc. 1987; 185:132-134.
71. Bhat RN. Viperine snakebite poisoning in Jammu. J Indian Med Assoc. 1974; 63: 383-392.
72. Chattopadhyay S, Sukul B. A profile of fatal snake bite cases in the Bankura district of West Bengal. Trans R Soc Trop Med Hyg 2011; 18:18-20.
73. Harbi NA. Epidemiological and clinical differences of snake bites among children and adults in south western Saudi Arabia. J Accid Emerg Med 1999; 16:428-30.
74. Tarianga DD, Philip PJ, Alexander G, Maladens, Jeyaseelan L, Peter JV. Randomized controlled trial on the effective doses of anti-snake venom in cases of snakebite with systemic envenomation. J Assoc Physicians India. 1999 April; 147:369-371.
75. Michael GC, Thacher TD, Shehu IL. The effect of pre-hospital care for venomous snake bite on outcome in Nigeria. Trans R Soc Trop Med Hyg. 2011; 105:95-101.
76. Sarangi A, Jenal L, Sahoo H. A profile of snake bite poisoning with special reference to hematological, renal, rernological and electrocardiographic abnormalities. J Assoc Physicians India. 1977; 25:555-560.

77. Srimannarayana J, Dutta TK, Sahai A, Badrinath S. Rational use of anti-snake venom (ASV): Trial of various regimens in hemotoxic snake envenomation. J Assoc Physicians India. 2004; 52:788-93.
78. Paul V, Pratibha S, Prahlad KA, Earali J, Francis S, Lewis F. High-dose anti-snake venom versus low-dose anti-snake venom in the treatment of poisonous snake bites - A critical study. J Assoc Physicians India. 2004; 52:14-7.

ANNEXURES

INFORMED CONSENT FORM

STUDY TITLE: A CLINICAL STUDY OF TREATMENT OUTCOME IN COMPLICATED SNAKEBITES RECEIVING ASV AS PER INDIAN GUIDELINES AND PROTOCOL.

STUDY NUMBER:

SUBJECT'S NAME: **HOSPITAL NUMBER:**

AGE:

It is hoped that the knowledge of relevant prognostic factors might be useful for early identification of patients at high risk requiring intensive care treatment. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. We will collect the treatment and relevant details from your hospital record. This information collected will be used for only dissertation and publication. The institutional ethical committee has reviewed this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

I understand that I remain free to withdraw from the study at any time and this will not change my future care. I have read or have been read to me and understood the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of information that will be collected and disclosed during the study. I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction. I, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information for dissertation and publication only.

Signature or thumb impression of the subject: Date:

Name and signature of the witness: Date:

Name and signature of person obtaining consent Date:

PROFORMA FOR DATA COLLECTION

NAME: **IP/OP NO:**

AGE: **DOA:**

GENDER: **OCCUPATION:**

ADDRESS:

DETAILS OF SNAKEBITE

SITE OF BITE:

PRESENCE OF FANG MARKS: SINGLE/ DOUBLE

TIME OF BITE:

TIME OF HOSPITAL ADMISSION:

INTERVAL BETWEEN BITE AND ADMISSION:

OCCUPATIONAL/ NON OCCUPATIONAL:

DETAILS OF SNAKE

SNAKE: IDENTIFIED/ NOT IDENTIFIED

GENERAL PHYSICAL EXAMINATION:

PULSE: PALLOR:

BLOOD PRESSURE: ICTERUS:

RESPIRATORY RATE: CYANOSIS:

TEMPERATURE: CLUBBING:

SPO2: LYMPHADENOPATHY:

OEDEMA:

SIGNS OF ENVENOMATION

LOCAL ENVENOMATION	P/A	HEMOTOXIC FEATURES	P/A
PAIN:		BLEEDING FROM BITE SITE:	
SWELLING:		BLEEDING FROM GUMS/ GINGIVA:	
CELLULITIS:		EPISTAXIS:	
BLEEDING:		ECCHYMOSIS/ PURPURA/ PETECHIAE:	
		HEMATURIA:	
		HEMETEMESIS:	
		HEMOPTYSIS	

NEUROTOXIC FEATURES	P/A	CARDIOTOXIC FEATURES	P/A
PTOSIS:		HYPOTENSION:	
OPHTHALMOPLEGIA:		CARDIAC ARRYTHMIAS:	
UNCONSCIOUSNESS:		ECG CHANGES:	
RESPIRATORY PARALYSIS:			
FLACCID LIMB PARALYSIS:			

P- PRESENT; A- ABSENT

CENTRAL NERVOUS SYSTEM:

RESPIRATORY SYSTEM:

PER ABDOMEN:

CARDIOVASCULAR SYSTEM:

INVESTIGATIONS

1. 20 WBCT
2. CBC- HEMOGLOBIN:
   TOTAL COUNT:
   PLATELET COUNT:
3. URINE ROUTINE AND MICROSCOPY
4. RENAL FUNCTION TESTS
   B.UREA:
   S.CREATININE:
5. BLEEDING TIME:
   CLOTTING TIME:
6. ECG
7. CHEST X RAY
8. OTHER INVESTIGATIONS

IMPRESSION

VENOMOUS/ NON VENOMOUS:
LOCAL ENVENOMATION:
HEMOTOXIC/ NEUROTOXIC:

TREATMENT

ASV

TOTAL DOSE:

ANY ADVERSE REACTIONS:

NATURE OF ADVERSE REACTION:

OTHER DRUGS:

OTHER COMPLICATIONS:

RENAL INVOLEMENT:

RESPIRATORY PARALYSIS:

SHOCK:

GANGRENE/ CELLULITIS:

SURGICAL INTERVENTION:

VENTILATOR SUPPORT

YES/NO:

NO OF DAYS:

DIALYSIS:

OUTCOME

COMPLETE RECOVERY/ DISABILITY (MORBITY)/ DEATH (MORTALITY)

KEY TO MASTER CHART

GENDER: M- MALE, F- FEMALE

SEASON:

M- MONSOON (JUNE-SEP)

W- WINTER (OCT-FEB)

S- SUMMER (MAR-MAY)

SITE OF BITE:

UL- UPPER LIMB,

LL- LOWER LIMB

TIME OF BITE:

M- MORNING

A- AFTERNOON

E- EVENING

N- NIGHT

TIME OF PRESENTATION:

A- <6HRS, B- 6-24HRS, C- >24 HRS

TYPE OF TOXICITY:

H- HEMOTOXIC ENVENOMATION

N- NEUROTOXIC ENVENOMATION

L- LOCAL ENVENOMATION

VARIABLES:

Y – PRESENCE OF THE VARIABLE

N – ABSENCE OF THE VARIABLE

SL NO	HOSP NO	AGE	GENDER	MONTH	SEASON	SITE OF BITE	TIME OF BITE	TIME OF PRESENTATION	OCCUPATION	TYPE OF SNAKE	LOCAL ENVENOMATION				HEMOTOXIC ENVENOMATION							NEUROTOXIC ENVENOMATION						TYPE OF TOXICITY	ASV	COMPLICATIONS	VENTILLATOR SUPPORT	OUTCOME
											PAIN	LOCAL BLEED	SWELLING	GANGRENE	Local bleed	Gum bleed	Hemoptysis	Epistaxis	Hematemesis	Hematuria	20 WBCT	Ptosis	Blurred vision	Ophthalmoplegia	Flaccid limb paralysis	Unconsciousness	Respiratory paralysis					
1	80784	50	F	NOV	W	LL	M	B	AGRICULTURE	VIPER	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	Y	N	N	N	N	10	ARF	N	HEMODIALYSIS
2	83262	45	M	DEC	W	UL	M	C	AGRICULTURE	VIPER	N	N	N	N	N	N	N	Y	N	Y	NOT CLOTTED	Y	Y	Y	N	N	Y	H+N	20	ARF	Y	HEMODIALYSIS
3	99464	35	F	JAN	W	UL	M	A	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	Y	N	N	Y	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
4	98850	35	F	JAN	W	LL	E	B	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	Y	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
5	92700	54	F	JAN	W	LL	M	B	AGRICULTURE	NOT KNOWN	Y	Y	Y	Y	Y	N	N	Y	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	CELLULITIS	N	DEBRIDEMENT
6	116913	40	F	FEB	W	UL	A	A	HOUSE WIFE	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
7	108948	50	M	FEB	W	LL	E	A	AGRICULTURE	NOT KNOWN	Y	Y	N	N	Y	Y	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
8	109909	65	M	FEB	W	LL	E	A	AGRICULTURE	KRAIT	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	Y	Y	Y	N	N	N	N+L	10	N	N	COMPLETE RECOVERY
9	76946	35	M	NOV	W	LL	E	A	BUSINESS	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	Y	N	N	N	N	10	N	N	COMPLETE RECOVERY
10	73577	45	M	NOV	W	LL	E	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
11	68890	45	F	OCT	W	LL	M	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
12	68522	26	M	OCT	W	LL	A	B	BUSINESS	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
13	64834	70	M	OCT	W	UL	E	A	AGRICULTURE	NOT KNOWN	N	N	Y	N	N	N	N	N	N	NN	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
14	61433	35	M	OCT	W	LL	M	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
15	61426	29	M	OCT	W	LL	E	B	BUSINESS	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	Y	N	N	N	N	10	N	N	COMPLETE RECOVERY
16	60075	40	F	OCT	W	LL	M	A	HOUSE WIFE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
17	133031	20	M	APRIL	S	LL	E	A	STUDENT	VIPER	N	N	Y	N	N	Y	N	Y	Y	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	ARF	N	COMPLETE RECOVERY
18	128521	18	M	MAR	S	LL	E	A	STUDENT	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
19	128068	26	F	MAR	S	LL	N	B	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	Y	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
20	146265	42	M	MAY	S	LL	M	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	Y	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
21	143386	30	F	NOV	W	UL	M	B	HOUSE WIFE	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	Y	N	Y	Y	N	20	N	Y	COMPLETE RECOVERY
22	152056	29	M	NOV	W	UL	E	A	BUSINESS	COBRA	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N+L	10	N	N	COMPLETE RECOVERY
23	149515	40	M	NOV	W	LL	M	A	AGRICULTURE	VIPER	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
24	164856	45	M	JULY	M	UL	M	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
25	158021	28	F	JUNE	M	UL	E	A	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
26	162399	21	M	JUNE	M	UL	E	B	AGRICULTURE	NOT KNOWN	Y	Y	Y	Y	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	CELLULITIS	N	DEBRIDEMENT
27	158494	19	M	JUNE	M	UL	E	A	STUDENT	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
28	157388	35	M	JUNE	M	LL	A	B	AGRICULTURE	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
29	153299	30	F	JUNE	M	UL	E	A	HOUSE WIFE	COBRA	Y	N	Y	Y	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	N	N	N+L	20	CELLULITIS	N	DEBRIDEMENT
30	269971	40	M	FEB	W	LL	A	A	AGRICULTURE	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
31	275423	32	F	APRIL	S	LL	N	B	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
32	272024	35	M	MAR	S	LL	N	B	AGRICULTURE	NOT KNOWN	Y	N	Y	Y	N	N	N	Y	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	ARF	N	DEBRIDEMENT
33	277810	45	F	DEC	W	LL	M	B	AGRICULTURE	NOT KNOWN	Y	N	Y	Y	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	CELLULITIS	N	DEBRIDEMENT
34	277434	25	F	DEC	W	LL	N	A	BUSINESS	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
35	277072	24	M	DEC	W	UL	M	B	BUSINESS	NOT KNOWN	N	N	N	N	N	Y	N	N	N	Y	NOT CLOTTED	Y	N	N	N	N	N	H+N	20	N	N	COMPLETE RECOVERY
36	281472	45	M	APRIL	S	LL	N	A	AGRICULTURE	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	20	N	N	COMPLETE RECOVERY
37	279204	20	M	APRIL	S	LL	M	A	BUSINESS	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
38	278016	48	F	DEC	W	UL	M	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
39	283251	20	M	DEC	W	LL	E	A	BUSINESS	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
40	287004	33	M	MAY	S	UL	E	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
41	283670	20	M	APRIL	S	UL	N	A	AGRICULTURE	NOT KNOWN	N	N	N	N	Y	N	N	Y	Y	Y	NOT CLOTTED	N	N	N	N	N	N	H	30	N	Y	COMPLETE RECOVERY
42	288269	42	M	MAY	S	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
43	293786	19	M	MAY	S	UL	E	A	STUDENT	NOT KNOWN	N	N	N	N	N	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
44	301913	45	M	JUNE	M	LL	N	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	Y	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
45	301771	62	M	JUNE	M	UL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
46	301469	36	M	JUNE	M	UL	A	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	Y	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
47	301051	30	M	JUNE	M	LL	N	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
48	301002	18	M	JUNE	M	LL	M	A	STUDENT	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
49	297414	28	M	JUNE	M	LL	M	B	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	Y	N	Y	N	NOT CLOTTED	Y	Y	Y	N	Y	Y	H+N+L	30	ARF	Y	COMPLETE RECOVERY
50	291910	35	M	MAY	S	LL	N	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
51	197122	45	F	SEP	M	LL	E	A	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
52	194821	25	F	SEP	M	LL	A	A	HOUSE WIFE	VIPER	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
53	192890	32	M	SEP	M	LL	A	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
54	192809	40	M	SEP	M	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
55	190485	35	M	SEP	M	LL	A	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
56	185745	50	F	AUG	M	LL	A	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	Y	N	N	NOT CLOTTED	Y	N	N	N	N	Y	H+N	30	N	Y	COMPLETE RECOVERY
57	187507	22	M	AUG	M	LL	A	A	BUSINESS	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	N	Y	N+L	20	N	Y	COMPLETE RECOVERY
58	186168	30	M	AUG	M	UL	A	A	AGRICULTURE	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	Y	Y	N	20	N	Y	COMPLETE RECOVERY
59	175182	25	F	JULY	M	LL	E	B	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	Y	N	N	N	Y	Y	H+N	30	N	Y	COMPLETE RECOVERY
60	174111	21	M	JULY	M	LL	E	A	AGRICULTURE	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	Y	N	20	N	Y	COMPLETE RECOVERY
61	172292	28	M	JULY	M	LL	M	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
62	170027	45	F	JULY	M	UL	E	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	Y	N	Y	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
63	170467	30	M	JULY	M	LL	N	A	AGRICULTURE	COBRA	Y	N	Y	Y	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	Y	N+L	20	CELLULITIS	Y	DEBRIDEMENT
64	168005	20	M	JULY	M	LL	M	A	STUDENT	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
65	166136	60	F	JULY	M	UL	E	A	AGRICULTURE	NOT KNOWN	N	N	Y	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	Y	N+L	20	N	Y	COMPLETE RECOVERY
66	309713	28	M	JULY	M	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
67	308293	38	F	JULY	M	UL	N	C	HOUSE WIFE	VIPER	N	Y	Y	N	Y	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	ARF	N	HEMODIALYSIS
68	303243	28	M	JUNE	M	UL	N	B	AGRICULTURE	VIPER	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
69	302704	55	M	JUNE	M	UL	E	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
70	304619	45	F	JUNE	M	UL	M	B	AGRICULTURE	NOT KNOWN	Y	N	Y	Y	N	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	CELLULITIS	N	DEBRIDEMENT
71	318187	75	F	AUG	M	LL	E	A	AGRICULTURE	VIPER	Y	N	Y	N	N	N	Y	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
72	312147	28	F	JULY	M	UL	E	A	HOUSE WIFE	NOT KNOWN	N	N	N	N	N	N	N	Y	N	Y	NOT CLOTTED	Y	Y	Y	N	N	Y	H+N	30	N	Y	COMPLETE RECOVERY
73	210728	60	M	OCT	W	LL	M	A	AGRICULTURE	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	Y	Y	N	20	N	Y	COMPLETE RECOVERY
74	208143	24	M	OCT	W	UL	N	A	STUDENT	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
75	207154	35	M	OCT	W	LL	E	A	AGRICULTURE	NOT KNOWN	Y	N	Y	Y	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	10	CELLULITIS	N	DEBRIDEMENT
76	205240	22	M	OCT	W	UL	N	A	STUDENT	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	Y	N	N	N	Y	N	20	N	Y	COMPLETE RECOVERY
77	203640	35	M	OCT	W	LL	E	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
78	203477	40	F	OCT	W	UL	A	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	Y	N	Y	N	NOT CLOTTED	N	N	N	N	N	N	H+L	10	ARF	N	COMPLETE RECOVERY
79	201005	22	M	SEP	M	LL	A	A	STUDENT	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
80	321523	38	M	AUG	M	LL	A	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	Y	N	N	N	N	N	H+N	20	N	N	COMPLETE RECOVERY
81	224047	80	M	SEP	W	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	Y	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
82	334920	35	F	SEP	W	UL	A	A	HOUSE WIFE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
83	332034	48	M	AUG	M	UL	E	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
84	331433	40	F	AUG	M	UL	M	B	AGRICULTURE	VIPER	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	ARF	N	HEMODIALYSIS
85	265615	28	M	MAR	S	LL	M	A	BUSINESS	NOT KNOWN	Y	N	Y	N	N	N	N	Y	N	Y	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
86	265546	52	M	MAR	S	UL	A	A	AGRICULTURE	VIPER	Y	Y	Y	Y	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	CELLULITIS	N	DEBRIDEMENT
87	260647	48	F	FEB	W	LL	M	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	10	N	N	COMPLETE RECOVERY
88	258657	40	F	FEB	W	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	Y	N	N	N	Y	N	H+N	20	N	N	COMPLETE RECOVERY
89	251832	68	M	FEB	W	LL	E	A	AGRICULTURE	COBRA	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
90	250399	65	M	JAN	W	UL	A	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	N	N	COMPLETE RECOVERY
91	242663	40	M	JAN	W	UL	A	A	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	10	N	N	COMPLETE RECOVERY
92	329925	45	F	AUG	M	LL	M	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	N	Y	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H+L	20	N	N	COMPLETE RECOVERY
93	226411	59	F	NOV	W	LL	A	C	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	Y	N	Y	N	Y	NOT CLOTTED	N	N	N	N	N	N	H	30	MODS	Y	DEATH
94	307815	58	M	JULY	M	LL	M	C	AGRICULTURE	VIPER	N	N	N	N	N	N	N	Y	N	Y	NOT CLOTTED	Y	Y	N	Y	Y	Y	H+N	30	DIC	Y	DEATH
95	214276	25	M	OCT	W	LL	M	B	BUSINESS	NOT KNOWN	N	N	N	N	N	N	Y	N	Y	Y	Y	NOT CLOTTED	N	N	N	N	N	N	H	30	ARF	Y	DEATH
96	173362	26	M	JULY	M	UL	N	B	STUDENT	NOT KNOWN	N	N	N	N	N	N	Y	N	Y	Y	Y	NOT CLOTTED	Y	Y	Y	Y	Y	Y	H+N	30	MODS	Y	DEATH
97	178901	35	M	AUG	M	LL	E	B	AGRICULTURE	KRAIT	N	N	N	N	N	N	N	N	N	N	CLOTTED	Y	N	N	N	N	N	N	N	10	N	N	COMPLETE RECOVERY
98	200446	40	M	SEP	M	UL	A	A	AGRICULTURE	NOT KNOWN	Y	Y	Y	Y	Y	N	N	N	N	N	CLOTTED	N	N	N	N	N	N	L	10	CELLULITIS	N	DEBRIDEMENT
99	202540	35	M	OCT	W	LL	E	A	AGRICULTURE	VIPER	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	Y	N	N	N	N	N	H+N	20	ARF	N	COMPLETE RECOVERY
100	306585	50	M	JUNE	M	LL	M	B	AGRICULTURE	NOT KNOWN	Y	N	Y	N	N	N	N	N	N	Y	CLOTTED	N	N	N	N	N	N	L	10	ARF	N	COMPLETE RECOVERY
101	312133	25	M	JULY	M	LL	M	A	AGRICULTURE	VIPER	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY
102	194971	40	F	DEC	W	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	Y	Y	N	N	NOT CLOTTED	N	N	N	N	N	N	H	10	N	N	COMPLETE RECOVERY
103	133399	50	M	DEC	W	LL	M	A	AGRICULTURE	NOT KNOWN	N	N	N	N	N	N	N	N	N	N	NOT CLOTTED	N	N	N	N	N	N	H	20	N	N	COMPLETE RECOVERY