HAEMATOLOGICAL AND COAGULATION PROFILE IN SNAKE ENVENOMATION

By

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Dissertation submitted to the

Sri Devaraj Urs Academy of Higher Education and Research,

Tamaka, Kolar, Karnataka

DOCTOR OF MEDICINE

IN

PATHOLOGY

Under the guidance of

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April 2015

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This is to certify that, the ethics committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved the dissertation work of **Dr. SHUBHAM AGARWAL**, a postgraduate student in the Department of Pathology of Sri Devaraj Urs Medical College entitled "**HAEMATOLOGICAL AND COAGULATION PROFILE IN SNAKE ENVENOMATION "** to be submitted to the Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar.

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ACKNOWLEDGEMENT

It is most appropriate that I begin by expressing my immense gratitude to the Almighty lord for his blessings.

My continued reverence and acknowledgement to my beloved teacher and guide Dr CSBR Prasad, professor, department of pathology who graced my study officially and at the same time informally by his constant support and expert advice.

I express my deep sense of gratitude and humble thanks to Dr Harendra Kumar M.L.professor and hod, for his support, advice constant encouragement in preparing the dissertation.

I would like to thank Dr. Uday Kumar who hand picked this topic for me , graced my study officially and his constant support and expert advice. his encouragement , wise constructive judgement the painstaking effort to weed out errors and his affection during course of study leaves me permanently indebted to him. I dedicate the good part of the work to him.

I convey my deepest regards and earnest gratitude to my co- guide and professor Dr A Raveesha, for his support, advice and constant encouragement in preparing this dissertation.

I express my deep and immense gratitude and humble thanks to Dr Sharita MN for her advice, unconditional help and encouragement throughout the study.

I thank Dr Suresh TN, Dr S Das, professors, and Dr Vidyavathi K, Dr Hemalatha A, Dr Manjula, associate professors for their constant guidance and encouragement in preparing this dissertation.

I wish to express my sense of gratitude to all the assistant professors, Dr Swaroop, Dr Shilpa, Dr Sushma for their kind help in preparing this dissertation.

I express my sincere thanks to my friends and colleagues Dr Priya T Rajan, Dr haithra.

I thank my junior colleagues Dr Rakshith, Dr veena, Dr Yashaswini, Dr Geetanjali,Dr Nishit, Dr karthik, Dr Shubhra, Dr Ankita for helping me in completing this vast work.

I am infinitely obliged to my father Dr Dinesh kumar Agarwal and my mother Mrs. Sunita Agarwal who supported my decision to be a pathologist, helped me realise my dreams and also my sister Dr Shruti Agarwal for being pillars of strength.

My special thanks to all my unnamed close friends and relatives for their consent encouragement and inspiration throughout my study.

I am thankful to Dr Rahul ASGR for his guidance in statistics.

Lastly I am thankful to technical staffs Mr.Gowri Shankar,Mr Veerendra,Mr Syed Nazeemuddin, Mr Prashanth B.N, Mr Bhaskar, Mr Rehman and Mrs Surekha and all non teaching staff for their invaluable help without whom this study would not have been possible

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LIST OF ABBREVIATIONS

Sl No	Abbreviation	Expansion
1	ALP-	Alkaline Phosphatase.
2	APTT-	Activated Partial Thromboplastin Time.
3	ASV-	Anti snake venom.
4	AV-	Atrio Ventricular.
5	CK-	Creatine Kinase.
6	CPK-	CreatinePhospho Kinase.
7	DIC-	Disseminated Intra Vascular Coagulation.
8	ECM-	Extra Cellular Matrix.
9	HCT-	Heamatocrit.
10	HMWK-	High Molecular Weight Kininogen.
11	INR-	International Normalized Ratio.
12	MCH-	Mean corpuscular hemoglobin.
13	MCHC-	Mean corpuscular hemoglobin concentration.
14	MCV-	Mean corpuscular volume.
15	MPV-	Mean platelet volume.
16	PBI-	Pressure Bandage and Immobilization.
17	PCT-	Plateletcrit.
18	PDW-	Platelet distribution width.
19	PL-	Phospholipid.
20	PT-	Prothrombin time.
21	RBC-	Red Blood Cells.
22	SP-	Specific Poisoning.

23 TFPI- Tissue Factor Pathway Inhibitor.

24 TT- Thrombin Time.

25 vWF- von Willebrand Factor.

26 WBC- White Blood Cells.

ABSTRACT

Background :

Snake bite is a major health problem in India occurring most frequently in summer and rainy season. In India it is estimated that about 20,00,00 snake bites ocuur per year, of which 20,000 die of snake envenomation. There are mainly 4 species of snakes in India which are common in rural areas- Indian cobra, Krait, Russel's viper, and Saw scaled viper. Saw scaled viper accounts for 80 % of snake bites. Almost all snake bites occur in rural areas (97%). Out of which (59%) are men and (41%) are women.

Bleeding and coagulation abnormalities are a common complication of snake bite, but there is paucity of scientific information about clinical importance of blood indices and abnormalities in coagulation parameters. This study is undertaken to analyze the characteristics of blood indices and coagulation parameters at different intervals after envenomation and to define a safe observation period after suspected snake bite.

Objectives

1. To determine various changes in coagulation parameters after snake envenomation.

2. To determine the first abnormal test result associated with severe envenomation.

3. To demonstrate variation in RBC indices (MCV, MCH, MCHC) and platelet indices (Platelet count, MPV, PCT, PDW) at admission and after 12 hours of admission.

Materials and methods

- Detailed history, physical examination of patients was done.
- Examination of various signs for bleeding abnormality.
- Oral consent was taken from the patient. In case the patient is minor, consent was taken from guardians.
- Blood was drawn by a 23 guage needle with syringe into K3EDTA and 3.2% sodium citrate vacutainers. The plasma was then aliquoted in ependoff tubes.
- The sample was analysed for complete blood counts and coagulation studies "PT, aPTT, TT and Fibrinogen" on admission and after 12 hours of admission to the hospital.

Results

Total number of snake bite cases admitted in casualty was 146. Out of these 146 cases, only 53 cases had signs of envenomation which was included in our study. 33 (62.2%) out of 53 cases showed mild envenomation and 20(37.7%) cases had severe envenomation. Age of the patients ranged from 17-85 yrs. Most of them were males with male to female ratio of 1.7:1. 49.1% of the patients were admitted during rainy season between May and august. 69.9% of cases were bitten in the night . The most common site was lower extremities. Platelet count was decreased in 4(7.5%) cases and all these cases remained prolonged 12hrs after admission. The common complications seen in these cases were bleeding (18.8%), neurotoxicity manifesting as giddiness and unconsciousness (15%), cellulitis (3.6%) and local tissue reaction (62.2%). PT and APTT were prolonged in 14(26.4%) cases. Out of these 14 cases, 2

cases were prolonged even after 12 hrs of admission. Thrombin time was prolonged in 17 cases (32%). Out of these, 3 cases were prolonged even after 12 hrs of admission. Fibrinogen concentration was decreased in 6(11.3%) cases. 3 cases were prolonged even after 12 hrs of admission.

Conclusion

First line of coagulation markers (PT, APTT, fibrinogen and thrombin time) should be considered as first line of investigations for any suspected coagulation abnormality in snake bite patients.

If there is any abnormality in the first line parameters, then second line of specific markers can be entertained if required, to pinpoint the level of defect.

PT and APTT was the first abnormal test result which we found in our study after snake envenomation and concluded that 12 hrs was the safe period to rule out any complications following envenomation.

There was no significant changes in the RBC indices (MCV, MCH, and MCHC) and platelet indices (MPV, PCT, PDW) after snake envenomation except platelet count which was low in 4 out of 53 cases which may be due to toxic effects of venom on platelets.

Key words: Envenomation, PT, APTT, TT, Fibrinogen, haematotoxicity.

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INTRODUCTION

India is inhabited by more than 60 species of venomous snakes. Some of the most common species found in India are spectacled cobra (Naja naja), Common krait (Bungarus caeruleus), Saw scaled viper (Echis carinatus) and Russell's viper (Daboia russelii)[1].

After being bitten by a poisonous snake, individuals may develop local pain, edema, systemic complications, acute renal failure, neurologic abnormalities, hemorrhage, infarctions and ultimately resulting in death [2]. Coagulopathy is a common manifestation in some of these cases and its abnormality can be detected by blood coagulation tests.

There are very few references in the literature related to coagulation parameter abnormalities after snake bite, evaluation of their seriousness and the length of the follow up period. Therefore we have undertaken this study to throw some light on the need of various coagulation tests and the duration of safe observation period after a suspected snake bite.

Envenomation is defined as occurrence of snakebite with the evidence of tissue damage, resulting in the spectrum of clinical symptoms and laboratory abnormalities from milder, localized injury of the tissue, to systemic illness including hypotension, neuromuscular dysfunction and coagulopathy[3].

Snake venom contains various types of enzymatic and non enzymatic toxins. Few toxins damage blood vessels and cause bleeding while others cause activation of coagulation factors and results in coagulation. Yet another type of venom causes sedation and neurotoxicity. Few types of snake venoms are cardiotoxic.

OBJECTIVES

1. To determine various changes in coagulation parameters after snake envenomation.
2. To determine the first abnormal test result associated with severe envenomation.
3. To demonstrate variation in RBC indices (MCV, MCH, MCHC) and platelet indices (Platelet count, MPV, PCT, PDW) at admission and after 12 hours of admission.

REVIEW OF LITERATURE

Majority of the patients with suspected snake bite do not develop envenomation. The accepted policy is to observe the patients and to have serial blood samples tested for upto 24 hrs after a bite, and also after removal of any first aid such as pressure bandages with immobilization[4]. This practice is not totally fool proof as delayed envenomation can occur in some cases.

According to one study from South Queensland, some hospitals discharge patients without symptoms and normal blood test results 4 to 6 hrs after the bite. But there is dearth of literature in other geographical regions like India[4].

One study suggests that the combination of tests for Prothrombin time - International Normalised Ratio (PT-INR), Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), and Creatine Kinase (CK) level combined with serial neurological examinations is able to reliably detect envenomated patients within 12 hrs[4] . No single test is sufficient to exclude severe envenomation within 12 hrs, so combination of tests is more appropriate. The study supports an observation period of 12 hrs for suspected snakebite, with repeat laboratory testing and neurological assessments performed on admission and at 6hrs and 12 hrs after the bite. Although pressure bandage and immobilization (PBI) were used for most patients and may have delayed the onset of envenomation in some, the majority had evidence of envenomation on admission despite the use of pressure bandage and immobilization. Current recommendations are that the repeat blood tests should be performed 1 hr after removal of effective PBI[4].

Most literature suggests that only 5% to 10% of snakebite patients develop severe envenomation. Coagulation studies are the most useful early laboratory parameters to detect or assess the status of envenomation[4].

Coagulopathy caused by poisonous snake bite is a clinically significant complication leading to hemorrhage, infarction and some case fatalaties[2].

According to Retzios et al [(5)], snake venom forms fibrin by working like thrombin on fibrinogen molecules. During normal stable fibrin formation, there is removal of both fibrinopeptide A and B. During fibrin polymer formation by snake bite there is removal of only fibrinopeptide A, so the resulting polymer formed is unstable and vulnerable to fibrinolysis and phagocytosis by

reticuloendothelial cells[2] resulting in various coagulation abnormalities like defibrination, isolated thrombocytopenia or Disseminated Intravascular Coagulation (DIC).

Various other studies have shown that the prevalence of coagulopathy and DIC was different according to the type of venom, location and time length of the bite as it affected the absorption of venom into the blood[5].

According to a study done by Winker et al, decrease in Hct (hematocrit), Protein level in blood, ALP(alkaline phosphatase) and Cholesterol levels after snake bite was seen. The decrease in Hct was thought to be caused by toxicity of snake venom on blood and lower levels of proteins, albumin and cholesterol were thought to be due to the leakage and their loss outside the blood locally or systematically because of the injured vessel wall and the increased permeability of the blood vessels due to venom cytotoxicity[6].

Winker et al[6] reported that the more serious a snakebite is, the lower is the cholesterol level and albumin level. In this study, when coagulopathy and various clinical symptoms of snake bite were related and analysed statistically, leukocytosis and rhabdomyolysis were associated with coagulopathy group and hemolysis and rhabdomyolysis associated with DIC group[6].

When rhabdomyolysis was observed after snake bite envenomation, coagulopathy was seen to be occurring five times more often in the patients with rhabdomyolysis than without rhabdomyolysis. Rhabdomyolysis releases many tissue factors from the damaged tissues into the blood and the factors released activate the extrinsic pathway of coagulation pathway and leads to consumption coagulopathy[2].

The complications in snake bite cases are mainly due to hemorrhage and in rare cases infarction. Most of the cases with coagulopathy following snakebite improves spontaneously without any untoward complication. The period of morbidity was seen to be 6-7 days based on PT abnormally and thrombocytopenia[2].

A few snakebite cases by poisonous snakes are termed dry when little or no venom is injected into the person or there are no symptoms of snakebite.

Envenomation is defined as occurrence of snakebite with the evidence of tissue damage, resulting in the spectrum of clinical symptoms and laboratory abnormalities from milder,

localized injury of the tissue, to systemic illness including hypotension, neuromuscular dysfunction and coagulopathy[3]. Various treatment modalities exist for suspected envenomation like advanced life support, immobilization of affected limb, local wound debridement, tetanus immunization and analgesics.

Types of signs and symptoms	Severity of envenomation		
	Minimal	**Moderate**	**Severe**
LOCAL	Swelling, erythema, or ecchymosis confined to the site of the bite.	Progression of swelling, erythema, or ecchymosis beyond the sight of the bite.	Rapid swelling, erythema or ecchymosis involving the entire body part.
SYSTEMIC	No systemic signs or symptoms	Non-life threatening signs and symptoms (nausea, vomiting, perioral paresthesias, and mild hypotension.	Markedly severe signs and symptoms (hypotension, altered sensorium, tachycardia, tachypnea and respiratory distress)
Coagulation	No coagulation abnormalities or other important laboratory abnormalities.	Mildly abnormal coagulation profile without clinically significant bleeding; mild abnormalities on other laboratory tests.	Markedly abnormal coagulation profile with evidence of bleeding or threat of spontaneous hemorrhage; results of other laboratory tests may be severely abnormal.

Table 1: Guidelines for assessing the severity of Pit viper envenomations[7].

Patients are usually observed for a period of 6-8 hours[5]. Antivenom is usually given if the patient shows signs of progressive injury, with worsening of the localized injury of the tissue, systemic manifestation or coagulation abnormality proved by laboratory testing.

As of now, there are no clear guidelines for ordering coagulation markers in patients with minimal or moderate envenomation, nor in those who do not receive anti venom.

Most of the physicians order routine coagulation markers on patients with snakebites, irrespective of the type of snake or severity of envenomation. The cost of platelet counts, Prothrombin time, APTT, and fibrinogen concentrations are significant and contribute to the expense of the management of these patients. Patients may also have to bear the extra cost due to unnecessary longer stay in the hospital or emergency department.

HEMOSTASIS & SNAKE VENOM:

Hemostasis is a tightly regulated process which maintains blood flow through the vasculature and leads to thrombosis if there is any tissue injury[8]. Hemostasis is the resultant of combined function of coagulation factors, extracellular matrix, platelets, vascular endothelium and fibrinolytic system[9].

In response to vascular injury and exposure to ECM proteins, collagen and vWF, circulating platelets adhere to vascular endothelium, followed by activation and later aggregation of platelets to form platelet plug[10].

Coagulation factors are activated through Intrinsic and Extrinsic pathways resulting in the formation of stable fibrin meshwork, which makes the platelet plug more stable and provides strength to it.[9].

After entry into the patient, toxins target hematologic system by interfering with coagulation factors resulting in clotting abnormalities and hemorrhage resulting in severe blood loss. Snake venom toxin interfere with intrinsic or extrinsic or common pathways of blood coagulation resulting in anticoagulant effect[11, 12]. Specific or particular venom affects a specific coagulation factor. These specific actions of venoms include effect on factors V, VII, X, Prothrombin, thrombin like activity or depletion of specific coagulation factors like fibrinogen[6].

The four most common venomous snakes of Indian subcontinent are Naja naja, D.russelii (Russell viper), Echiscarinatus (Saw scaled viper) and Bungarus caeruleus (Krait) [11].

N.naja and B.caeruleus belongs to elapidae while D.russelii and E.carinatus belongs to viperidae family. Viperid venoms are pro coagulant in nature while elapid venoms are anticoagulant[13].

Both, D.russelii and E.carinatus venoms show pro coagulant effect, while venom of E.carinatusis is more potent in its action.

The mechanism of pro coagulant effect in both the cases is due to activation of factors V, X (D.russelii) and Prothrombin (E.carinatus) [14].

Among elapid venoms, N.naja have strong anticoagulant property due to fibrinolytic, platelet inhibiting activity and factor VIII hydrolyzing activity[9, 15].

In addition, N kaothia venom from north eastern region of India also shows vWF hydrolyzing activity. Envenomation by common krait (B.ceruleus) is mildly anti coagulant. However its action on coagulation cascade is not prominent enough to be detected[16].So, krait bite can be confused with a dry bite.

Envenomation by D.russelii and E.carinatus is characterized by consumption coagulopathy, following activation of factors X,V (D.russelii) and Prothrombin (E.carinatus) resulting in depletion of plasma fibrinogen eventually leaving the blood incoagulable[17].

Further hematological alterations common in victims envenomated by viperidae snakes include prolonged bleeding time, prolonged clotting time, anemia, systemic bleeding and hemorrhage. In addition, hemostatic alterations specific for D.russelii envenomation include rapid intravascular coagulation, venous thrombosis, and hypofibrinogenemia[17]. In case of N.naja envenomated victims, no prominent hemostatic alterations are observed with only less than 3% of victims showing prolonged Prothrombin time[16].

Analysis of sequence similarity and homogeneity of snake venom toxins can give additional information into the differential and common actions of venom toxins on coagulation factors[9].

"Dry bite" should not be mistaken for krait bites where the coagulation alterations are negligible.

Whenever possible ,exact identification of snake , based on specific coagulation alteration must be assessed[9].

The effect of venom components on blood coagulation depends on the amount of venom injected and sometimes low doses of venom will not show any alteration even if the venom is relatively more toxic.

Sometimes, the changes or defects in haemostasis may be only trivial and error in identifying the snake species by the physician can aggravate the problem.

Therefore, a thorough and deep knowledge of limitations and appropriate measures to overcome them will be useful.

In a study done by Hayat et al in the university of Hyderabad, they observed 60 snakebite cases involving both genders with an age ranging from 8 to 55 yrs. In their study they observed that 57 (95%) cases were of viper bites and had hemostatic abnormalities and 3(5%) were of Elapid bites which were neurotoxic and had neuroparalytic symptoms[18].

Graham et al, tried to find out that which laboratory parameters turned abnormal after severe envenomation and how long the test parameter took to become abnormal after suspected snakebite. So, through these, they tried to determine and assess the safe observation period for a patient after a suspected snake bite[3].

Their study included 478 patients from a period of 2002 to 2009, out of which 75 cases were of minor envenomation, 163 were non envenomated and 240 patients had severe envenomation. They subjected all the patients to atleast 3 sets of parameters comprising of (PT-INR, aPTT, CK) for a minimum of 12 hrs observation period. They concluded that these laboratory parameters including the neurological assessments were able to identify nearly all severe envenoming cases within 12hrs of the bite[19].

Soogarum et al in their study conducted in Thailand on green pit viper, found the effect of venom on hematologic parameter. The venom is seem to have a thrombin like effect in vitro while defibrinating effect in vivo. They found out that there was a significant decrease in the total platelet count and also mean platelet volume in severely envenomated cases. These changes were thought to be due to the effect of green pit viper toxin on platelet morphology[20].

SNAKES

There are three families of venomous snakes in South-Eastern Asia: Elapidae, Viperidae andColubridae.

Elapidae: have relatively short fixed front (proteroglyph) fangs.

This family includes cobra, king cobra, krait, coral snake, Australian snake and sea snake (found all over the world except Europe).

Elapidae are comparatively longer, thinner, uniform-coloured snakes with large smooth symmetrical scales (plates) on the top (dorsum) of the head.

Cobra usually raises the front part of the body off the ground and spread and flattens the neck to form a hood.

Several species of cobras are capable of spitting their venom for over one metre or more towards the eyes of enemies.

Venomous sea snakes have flat tails and less ventral scales.

Viperidae usually have long fangs which are folded flat against the upperjaw but, when the snakes strike, they are usually erected.

There are two subfamilies, typical vipers (Viperinae) and pit vipers (Crotalinae).

The Crotalinae have special sense organs, to detect their warm-blood victim. Its situated between the nose and eye.

Viperidae are short, thick-body snakes with many small rough scales on the top of the head and characteristic patterns of coloured markings on the dorsal surface of the body.

Viperidae inhabiting in India:

Typical vipers (sub-family Viperinae):

1. Western Russell's viper (Daboiarusselii)
2. Saw-scaled or carpet vipers Echiscarinatus

Colubridae

Two species which are important in south east asia. Red necked keel back Rhabdophissubminiatus and Yamakagashi R tigrinus.

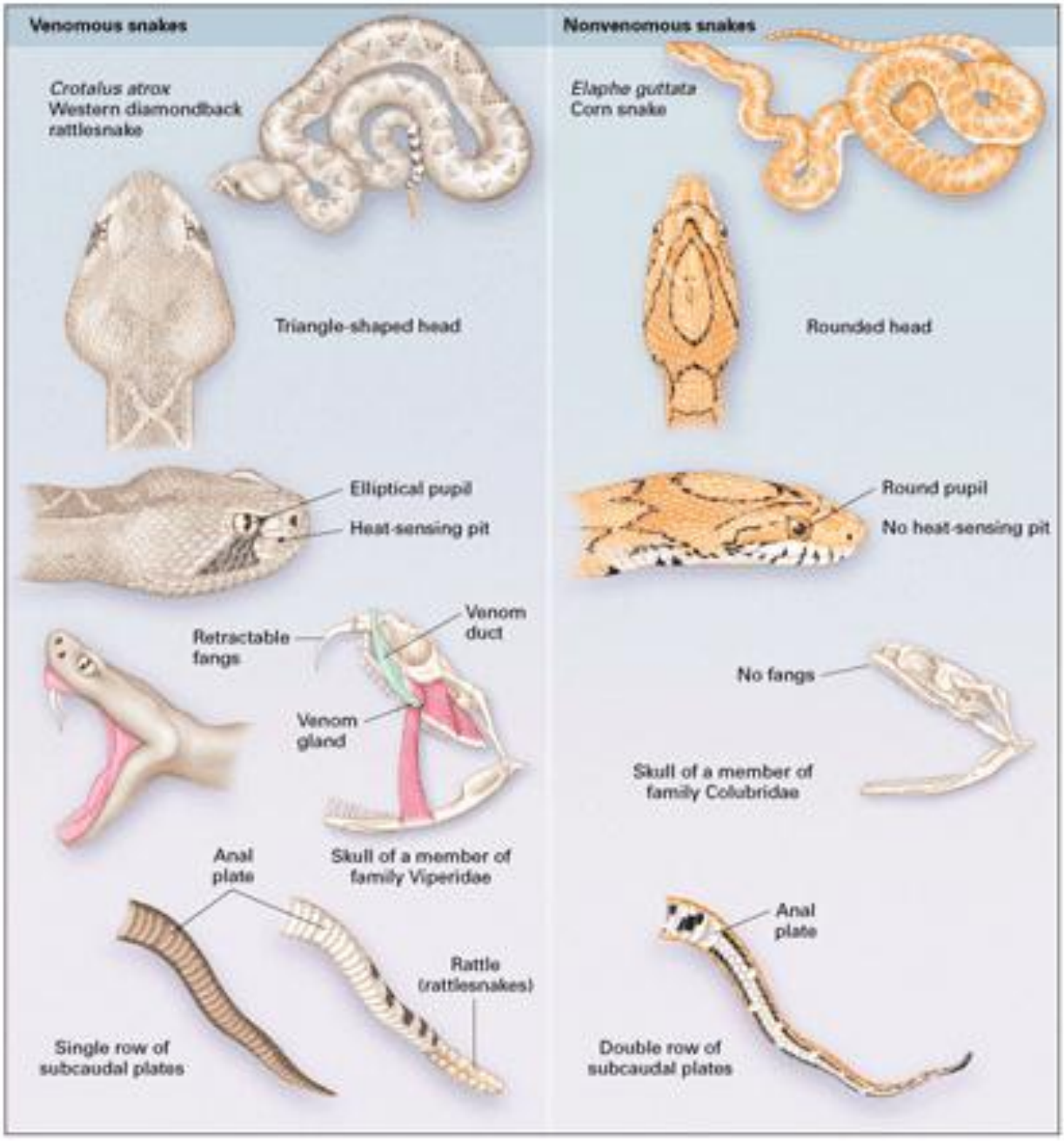


Fig 1: **DIFFERNCE BETWEEN VENOMOUS AND NON-VENOMOUS SNAKES**

1	Belly scales seen by turning the snake with belly upwards	Large and cover entire width of the belly.	Small like those on the back or moderately large but they do not cover the entire breadth.
2	Head scales	Small (viper) or may be large and with a) Conspecious pit between the eye and nostril (pit viper) b) Third latial touches the eye and nasal sheilds. (Cobra, king cobra and coral) c) Central row of scales on back enlarged and under surface of the mouth with only four infralatials , the fourth being longest (Krait)	Large with exception for pit viper, cobra and Krait.
3	Fangs	Two long grooved or canalized fangs like hypodermic needles.	Multiple, shoot and solid teeth.
4	Tail	Compressed	No much compressed
5	Habits	Usually noctural	Not so
6	Bite mark	Two fang mark with or without small mark of other teeth.	A number of small teeth marks in a row.

Table 2: HOW TO DIFFERENTIATE BETWEEN POISONOUS & NON POISONOUS SNAKES[21]

Fig 2: Russell's Viper (Daboiarusselii**)**

The Russell's Viper is a stout bodied snake.

Like all the vipers it is a nocturnal snake.

It is therefore frequently encountered by rural workers, as they are carrying out general agricultural activities.

There are two key identification features, the first is a series of chain-like or black edged almond shaped marks along the snakes back and flanks.

The second distinguishing mark is a white triangular mark on the head with the apex of the triangle pointing towards the nostrils.

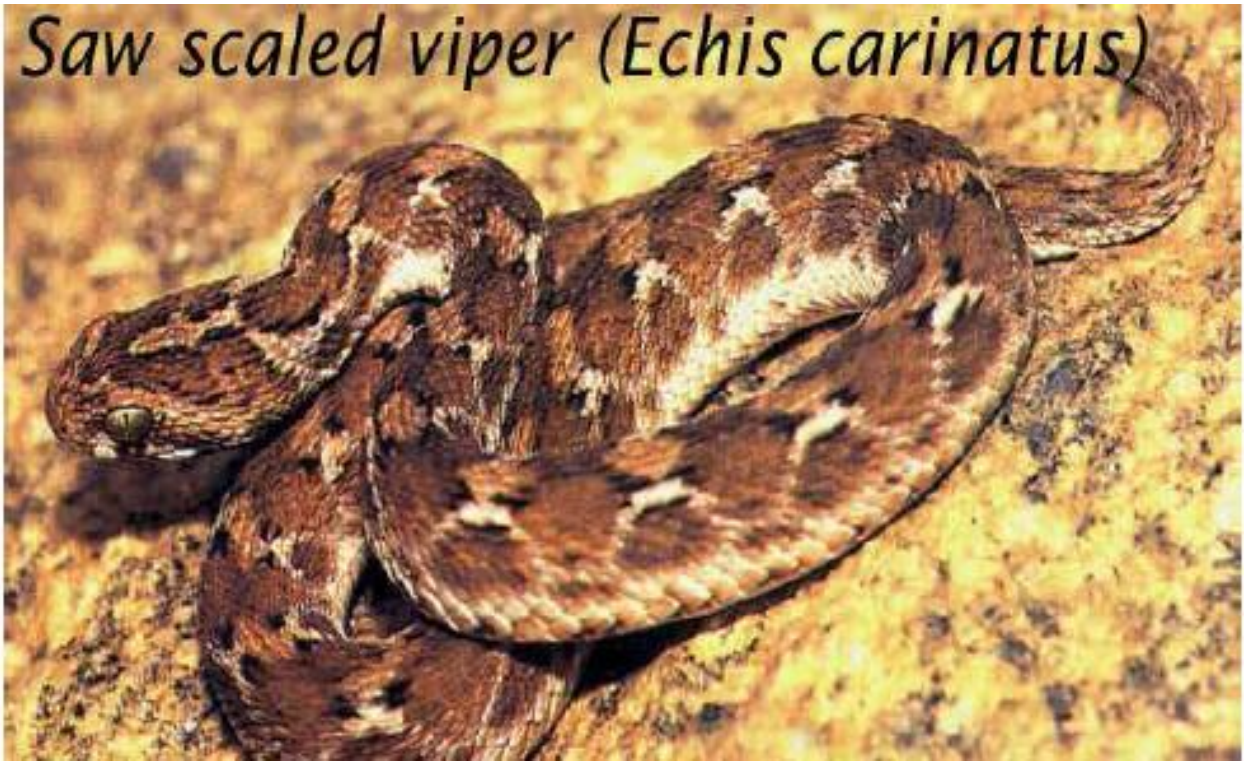


Fig 3: Saw scaled Viper (Echiscarinatus**)**

The southern Indian Saw Scaled Viper is a small snake, usually between 30 and 40 centimeters long.

The northern Indian species (*Echissochureki*) is much larger.

It inhabits mainly dry arid climates.

One of the key identification features of this species is the posture it adopts when it is agitated.

In addition, there are often wavy hoop like markings down both sides of the Saw Scales body. On the head, there is usually a white or cream arrow shaped mark, pointing towards the front of the head, often compared to the shape of a bird's foot.

Fig 4: INDIAN COBRA (Naja naja) WITH HOOD AND SHAPE OF HEAD

The Spectacled Cobra[1], is probably India's most well recognized snake.

The hood markings of the spectacle like mark, distinguishes this snake from other species, and its habit of rearing up when alarmed makes it distinctive but not definitive as other species do this.

Fig 5: Common Krait (Bungarus caeruleus)

The Common Krait is a nocturnal snake.

Its primary diet is other snakes.

It can be found all over Peninsular India and often seeks habitation near human dwellings.

The Common Kraits the most poisonous snake in India and its venom is neurotoxic in nature.

The Krait is black with a white belly.

The most important snake species from a medical point of view are given below, according to the following definitions (WHO, 2010)[22]:

CATEGORY 1: Highest medical importance**:** Highly venomous snakes which are common or widespread and cause numerous snake-bites, resulting in high levels of morbidity, disability or mortality.

CATEGORY 2: Secondary medical importance**:** Highly venomous snakes capable of causing morbidity, disability or death, but (a) for which exact epidemiological or clinical data are lacking or (b) are less frequently implicated because of their behavior, habitat preferences or occurrence in areas remote to large human populations.

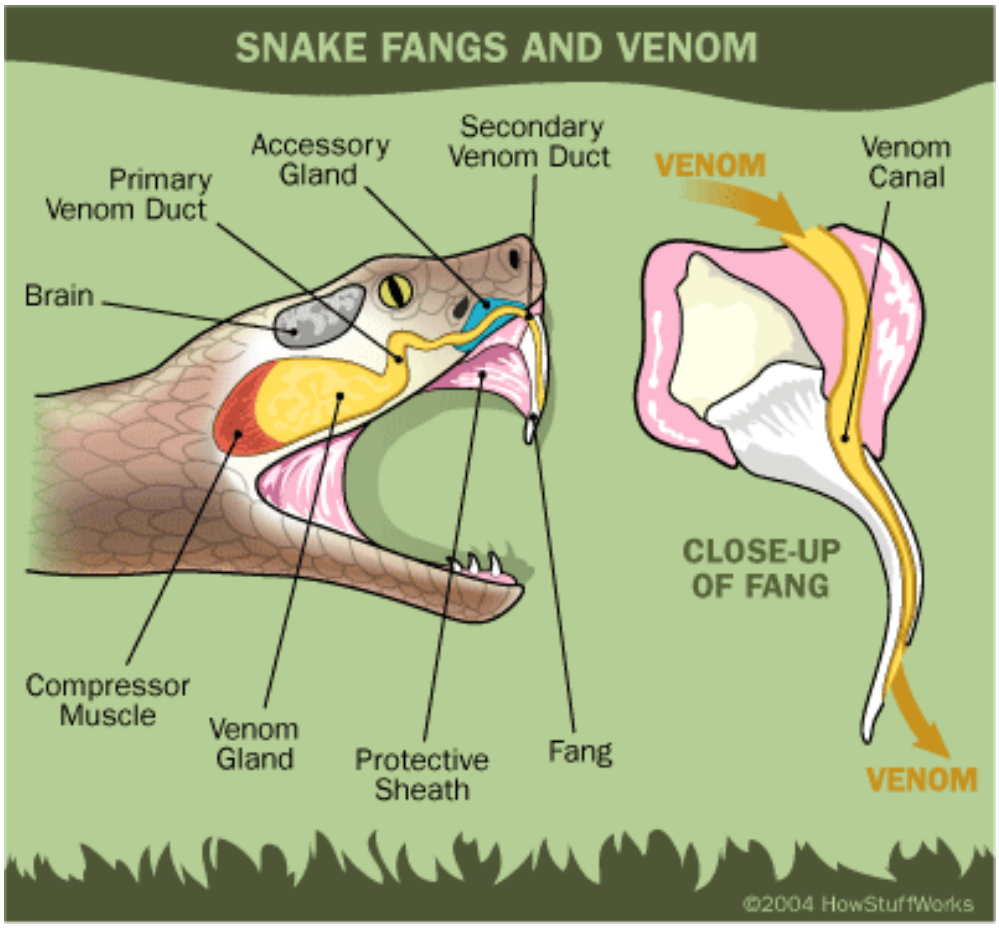


Fig 6: VENOM APPARATUS

If a human is bitten, venom is usually injected subcutaneously or intramuscularly.

The average dry weight of venom injected at a strike is approx 60 mg in Naja naja, 13mg in E carinatus and 63 mg in D russelii.

Venom composition

More than 90% of snake venom (dry weight) is protein.

Each of the venoms contains over a 100 proteins namely: enzymes (constituting 80-90% of viperid and 25-70% of elapid venoms), non-enzymatic polypeptide toxins, and non-toxic proteins such as nerve growth factor.

Venom enzymes

These include digestive hydrolases, hyaluronidase, and activators/inactivators of physiological processes.

Most venoms contain lamino acid oxidase, phosphomono- and diesterases, 5'nucleotidase, DNAase, NAD nucleosidase, phospholipase A2 and peptidases.

Zinc metalloproteinase haemorrhagins:

Damage vessels, causing bleeding.

Procoagulant enzymes

Venoms of Viperidae and some Elapidae and Colubridae contain serine proteases and other procoagulant enzymes that are thrombin-like/activates factor X, prothrombin and other clotting factors.

These enzymes stimulate blood clotting with formation of fibrin in the blood. Ironically, this process results in incoagulable blood because most of the fibrin clot is broken down immediately by the body's own plasmin fibrin breaking down system ;and sometimes below 30 minutes of the bite, the levels of clotting factors becomes so less that the blood doesnt clots.

Some venoms contain multiple antihaemostatic factors.

For example, Russell's viper's venom contains toxin, that activates factors V, X, IX and XIII, fibrinolysis, protein C, platelet aggregation, anticoagulation and hemorrhage.

Phospholipase A2 (lecithinase)

The most widespread and extensively studied of all venom enzymes.

It damages mitochondria, RBCs, WBCs, platelets, peripheral nerve endings, skeletal muscle, vascular endothelium, and other membranes.

Causes neurotoxicity, sedation, leads to the auto pharmacological release of histamine and anti-coagulation.

Acetylcholinesterase:

Although usually found in venom of elapids, it doesn't contribute to their neurotoxicity.

Hyaluronidase:

Promotes spread of venom via tissues.

Proteolytic enzymes (metalloproteinases; endopeptidases/hydrolases) and polypetidecytotoxins (cardiotoxins):

Oedema, caused by increased vascular permeability blistering, bruise and necrosis at the site of the bite.

Venom polypeptide toxins ("neurotoxins"):

Postsynaptic (α) neurotoxins.

They bind to acetylcholine receptors at the motor end plate.

Presynaptic (β) neurotoxins.

These release Ach at the nerve endings at neuromuscular junctions, and then damages the endings, which prevents further release of transmitters.

Quantity of venom injected , (dry bites)

It depends on the species and size of snake, the efficiency of the bite, whether one/two fangs penetrated the skin and whether the strikes were in repetition. Because of inefficiency of the snake to inject venom or the loss of snake's control of venom discharge, a small number of bites by venomous snakes does not result in the injection of sufficient venom to cause clinical symptoms.

Snakes do not finish their store of total venom, even after repeated strikes, and they are no less venomous after eating their prey .

Although larger snakes usually inject more venom than smaller snakes of

the same species, the venom of small, young vipers may be rich in some

dangerous components of venoms, such as those which disturb haemostasis.

GRADES OF SYSTEMIC POISONING (SP)[23]

SP0- Nil No systemic poisoning

SP1- Mild blood clotting of poor quality, No symptoms of poisoning.

SP2- Moderate Nonclotting blood, positive tourniquet test, tachycardia, transient hypotension, vomiting, pain in abdomen, headache.

SP3- Severe bleeding, neutrophilia, persisting hypotension, diarrhoea, renal failure, cardiotoxicity evident by ST-T changes, raised CPK, bradycardia, first or second degree AV block, atrial tachyarrythmias, ventricular extrasystoles, drowsiness, Ptosis/glossopharyngeal palsy.

SP4- Dangerous rapidly developing neuroparalysis, perisistent shock, hyper kalemia, Ventricular tachycardia, complete heart block or cardiac arrest.

NEUROTOXIC GRADING OF COBRA AND KRAIT BITES[23]:

Grade Description Clinical features

I Mild ptosis

II Moderate Ptosis, glossopharyngeal palsy

III Severe Ptosis, glossopharyngeal palsy and palatal palsy Respiratory failure.

IV Very severe Clinical features of severe type may develop in quick succession within

2 or 3 hours.

Pathophysiology:

Snake venom is serous in nature and contains numerous enzymes, proteins, aminoacids, etc.

Some of the enzymes are proteases, collagenases, arginine ester hydrolases, hyaluronidasess, phospholipidases, metallo-proteinases, endogenases, autocoids, thrombogenic enzyme.

These enzymes also act like toxins on different types of tissues of the human body, grouped under neurotoxins, nephrotoxins, hemotoxins, cardiotoxins, cytotoxins, which can result in organ dysfunction or destruction of cells.

The amount of enzymes and quanlity of enzymes and other clinical constituents differ with different speciesand subspecies, and the response of the victims to these substances are also different,therefore resulting in different features in different individuals.

For example - hyaluronidase allows rapid spread of venom through subcutaneous tissues by disrupting mucopolysaccharides, and phospholipase A2 has esterolytic effect on the red blood cell membrane and causes hemolysis.

It also promotes muscle necrosis.

Thrombogenic enzymes helps in the formation of relatively weaker fibrin clot, which in turn activatesplasmin and finally resulting in hemorrhages.

Venom of some snakes causes neuromuscular blockade at pre or post synaptic level.

In addition to above it causes endothelial cell damage which results in increased vascular permeability. In short, snake venom acts on various systems / organs /tissues of the body.

PHYSIOLOGY OF COAGULATION

Normal hemostatic mechanism has 5 different components: Blood vessels, platelets, plasma coagulation factors and their inhibitors and fibrinolytic system. All these factors work together to maintain the blood in fluid state normally and causes coagulation when needed. So, deficiency or increase in any of the components may lead to thrombosis or hemorrhage. Snake venom toxins which cause bleeding and hemoorhage usually or most often cause defect in coagulation cascade. Coagulation cascade comprises of Extrinsic pathway, Intrinsic pathway and Common pathway.

There are two systems involved in coagulation[24].

Intrinsic

Extrinsic

Common pathway

Following are the coagulation factors

I FIBRINOGEN

II PROTHROMBIN

III THROMBOPLASTIN

IV CALCIUM

V PROACCELERIN, LABILE FACTOR

V I PROCONVERTIN

VIII ANTI HEMPPHILIC FACTOR A OR GLOBULIN

IX CHRISTMAS FACTOR, ANTI HEMOPHILIC FACTOR 8,

PLASMA THROMBHOPLASTIN COMPONENT

X STUART PROWER FACTOR

XI PLASMA THROMBOPLASTIN ANTECEDENT

XII HAGEMAN FACTOR

XIII FIBRIN STABILIZING FACTOR

HMWK FITZGERALD FACTOR

PRE-K PRE-KALLIKREIN

KA KALLIKREIN

PL PLATELET PHOSPHOLIPID

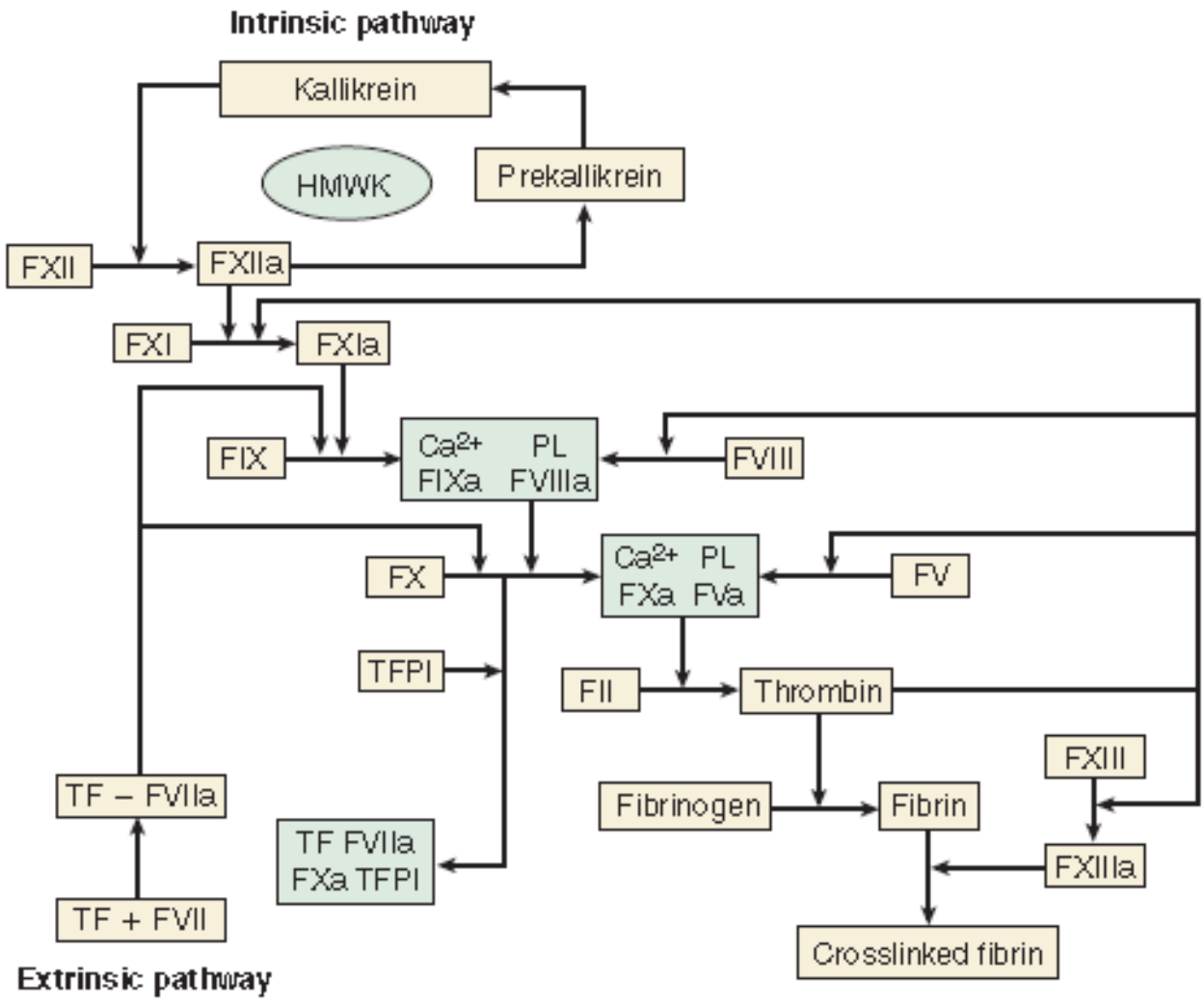


Fig 7: Coagulation cascade[25]

THE CLOTTING MECHANISM[24]

Whenever there is endothelial injury or injury to vessel wall there will be loose aggregation of platelets forming temporary hemostatic plug and later converted into the definitive clot by coagulation and fibrin mechanism.

Fibrin formation involves a cascade of enzymatic reactions and a series of clotting factors.

The fundamental reaction is conversion of the soluble plasma protein fibrinogen to insoluble fibrin.

First step in this direction is activation of factor X which is done either by Extrisic or Intrinsic pathway.

Activated factor X converts Prothrombin to thrombin which then catalyse the conversion of fibrinogen to fibrin.

The process of converting fibrinogen to fibrin usually involves the release of 2 pairs of polypeptides from each fibrinogen molecule. The remaining portion, fibrin monomer, then polymerizes with other monomer molecules to form fibrin.

The fibrin is initially a loose meshwork of interlacing strands of fibrin. Then it is converted by the formation of covalent cross-linkages to a dense, tight aggregate (stabilisation). This latter reaction is catalyzed by activated factor XIII and it requires calcium ions.

The investigations for clotting abnormalities are divided into First line and Second line investigations.

First line investigations gives a general idea in broader terms as to which area of the clotting mechanism is defective. It comprises of PT, APTT, TT, Fibrinogen concentration and platelet count.

Second line investigations comprises of investigations for specific factors or specific defects which could be pinpointed after first line investigations.

Therefore, first line investigations are recommended for the snakebite patients attending in the emergency department to save time and money[25].

D. russelii and E. carinatus – Defibrination.

N. naja – Factor VIII hydrolysis.

Knowledge of these specific effects of venom toxins on specific factors may give an idea of the snake species and thus can help the physician to administer specific monovalent anti snake venom rather than non specific polyvalent antivenom[26].

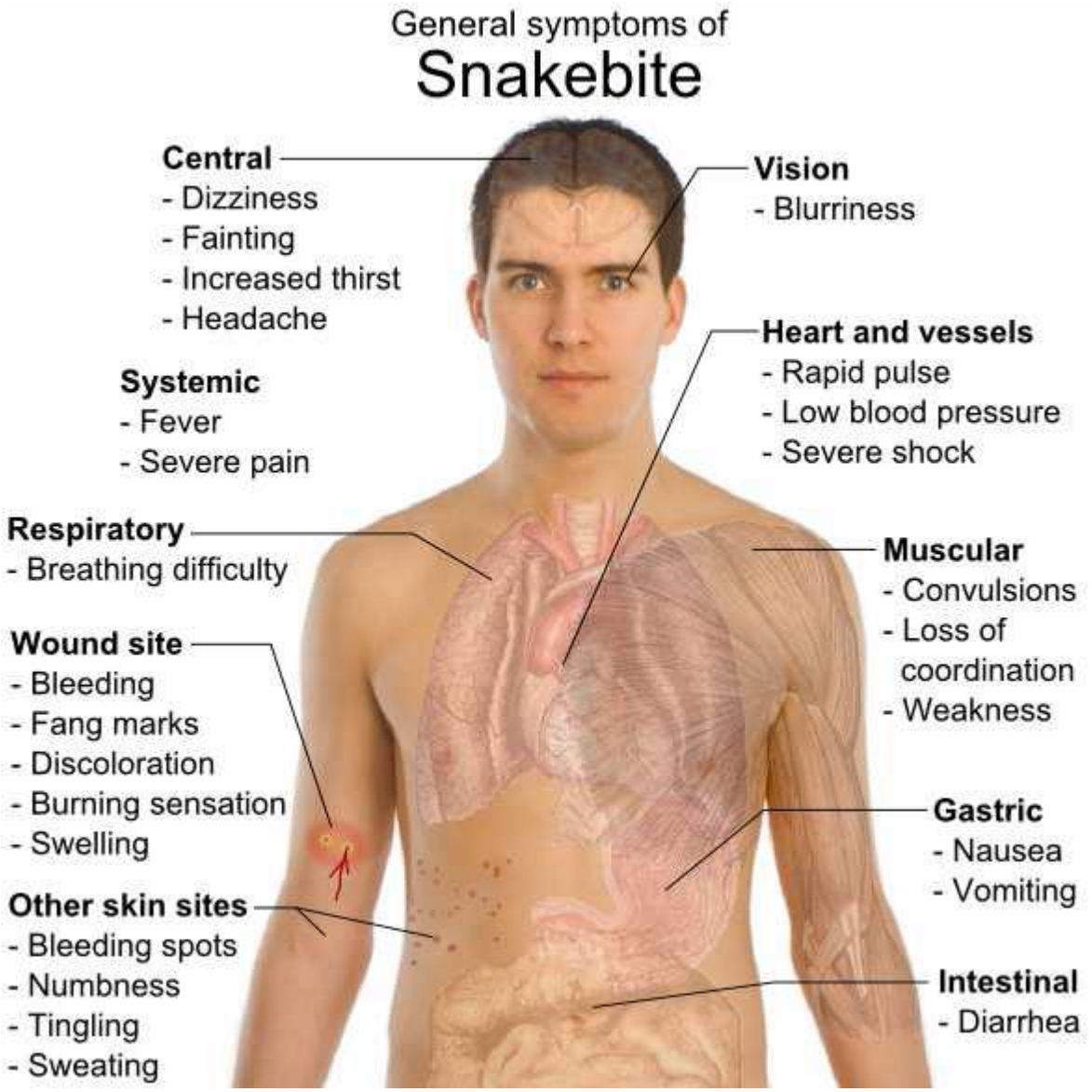


Fig 8: Signs and symptoms of snakebite.

Signs and Symptoms of Elapid envenoming:

General symptoms[22]:

Marks of fangs, localised pain, localised bleed, bruising, inflammation of lymphatics, enlargement of the lymph nodes, signs of inflammation like swelling, redness, and heat, blister formation, local infections, formation of abscess and presence of necrosis. Presence of nausea,vomiting, malaise, abdominal ache, weakness, drowsiness. Presence of swelling andlocalised pain with or without redness or discoloration at the bite site, and localnecrosis and/blisters/ bullae seen(Cobra).

Cardiovascular signs and symptoms(Viperidae)[22]

Visual disturbances, dizziness, shock, presence of hypotension, cardiac arrhythmias, pulmonary oedema, conjunctival oedema (chemosis).

Neurotoxic effects

symptoms of paralysis, like presence of ptosis with or without double vision, or ophthalmoplegia. The patient may complain of difficulty in focussing with both the eyes and heaviness in the eyelids. There may also be involvement of the sense organs like taste and smell sensations.

. Vision difficulty, breathing and speech problems.

. Paralysis of jaw/ tongue may also lead to upper airway obstruction and aspiration of secretions because of the inability of the patient to swallow.

. Presence of hypoxia due to insufficient ventilation may cause cyanosis, alteration of sensorium and also may lead to coma. This is sometimes a life threatening situation and should be dealt with urgent intervention.

. Paradoxical respiration, due to intercostal muscles paralysis may also be present.

Krait bites usually present symptoms in early mornings along with paralysis that can be mistakenfor a stroke. Stomach ache may suggest submucosalhaemorrhages inthe stomach.

Renal (Viperidae, sea snakes)[22]

Loin (lower back) pain, haematuria, haemoglobinuria,
myoglobinuria, oliguria/anuria, symptoms and signs of uraemia (acidotic breathing,hiccups, nausea, pleuritic chest pain etc).

Acute phase

Shock, hypoglycaemia.Hyponatraemia has been observed in victims of krait, due to natriuretic hormone like activity in the venom. Stomach pain may suggest submucosalhaemorrhages in the stomach (Krait).

Chronic phase(months to years after the bite)
Weakness, loss of hair, loss of libido, amenorrhoea, testicular atrophy, hypothyroidism.
Haemorrhagic infarction of the anterior pituitary resulting in Sheehan's-like syndrome (pan-hypopituitarism) after Russell's viper bite.

Bleeding and clotting disorders (Viperidae)
Traumatic bleeding from fang marks.
Spontaneous systemic bleeding - from gums , epistaxis, bleeding into the ears, intracranial haemorrhage, haemoptysis , haematemesis, rectal bleeding ormelaena, haematuria, vaginal bleeding, ante-partum haemorrhage in pregnantwomen, bleeding into the mucosae (e.g.

conjunctivae), skin (petechiae, purpura,Discoidhaemorrhages and ecchymoses) and retina.

Consequences of snake-bite[22]

Victims of snake-bite may suffer from any of the following:

1. Local envenoming limited to the part of the body that has been bitten. These effects may be debilitating, sometimes permanently.
2. Systemic envenoming involving organs and tissues away from the part of the body that has been bitten. These effects may be life threatening and debilitating.
3. Effects of anxiety due to the frightening experience of the bitten person.
4. Effects of first-aid and other pre-hospital treatments that may cause misleading clinical features.

Long-term complications (sequelae) of snake-bite[22]

At the site of the bite, loss of tissue may result in necrosis or amputation.

Chronic ulceration, infection, osteomyelitis, contractures, arthritis or arthrodesis may cause severe physical disability.

Malignant transformation may occur in skin ulcers after many years of snake bite.

Chronic kidney disease (renal failure) occurs after bilateral cortical necrosis (Russell's viper and hump-nosed pit viper bites) and chronic pan hypopituitarism or diabetes insipidus after Russell's viper bites in Myanmar and South India[16].

Chronic neurological deficit is seen in the few patients who survive intracranial haemorrhages and thromboses (Viperidae).

MATERIAL AND METHODS

Sample size calculation

$N=4PQ/d^2$

WHERE:

P= prevalance

Q= 100-P

d= allowable error (5%-20% of P)

In this study : P=70, d=13.

N=50.

Source of Data :

Blood samples from patients with history of snake bite are collected admitted in R.L.Jalappa Hospital and Research Center attached to Sri Devaraj Urs Medical College, Tamaka, Kolar beginning from Jan 2013 to June 2014.

Method of collection of data :

- Detailed history, physical examination of patients was done.
- Examination of various signs for bleeding from the site of bite, oral cavity, epistaxis and petechiae.

- Oral consent was taken from the patient. In case the patient is minor, consent was taken from guardians.
- Blood was drawn by a 23 guage needle with syringe into K3EDTA and 3.2% sodium citrate vacutainers. The plasma was then aliquoted in ependoff tubes.

The sample was analysed for complete blood counts and coagulation studies "PT, aPTT, TT and Fibrinogen" on admission and after 12 hours of admission and the patients were followed up till 24 hrs and only PT and APTT was performed on those patients into the hospital.

The tests were run by using Start analyser (STAGO) which is a four channel coagulation instrument to run in vitro tests which detect the clots based on electromagnetic sensors.

We preferred this instrument as it is more accurate and precise than the optical sensors.

INCLUSION CRITERIA:

All patients admitted to R L Jalappa Hospital with h/o snake bite with envenomation.

EXCLUSION CRITERIA:

Any other envenomation eg: Scorpion, Spider and non venomous snakes.

VARIOUS METHODS TO DETERMINE CLOTTING ASSAY

- Manual method
- Electromechanical method
    - -Impedance
    - -Steel ball
- Photo optical method
    - -Scattered light detection for clotting assay.
    - -Transmitted light detection for chromogenic assay.
    - -Transmitted light detection for immune assays.
    - -Nephelometry.
- Percentage detection method.
- Rate method.

PT:

- Blood is collected in a vacutainer with 3.2% sodium citrate as an anti-coagulant in the ratio of 1:9.
- The blood is centrifuged for 10 min at 2500g.
- The cuvette strips are placed in the incubation area for prewarming at 37 degree for 3 min.
- After incubation of the cuvette, 50 micro litre of plasma is dispensed into the cuvette and the timer is started for an incubation period of 60 sec.
- When the instrument starts to beep. The cuvettes are transferred to the test column area.
- 100 micro litrereagentprewarmed at 37 degree C is added pressing the pipette key.
- PT results are obtained and are expressed as seconds.

APTT:

Blood is collected in a vacutainer with 3.2% sodium citrate as an anti-coagulant in the ratio of 1:9.

The blood is centrifuged for 15 min at 2500g. Plasma is collected in plastic tubes.

The cuvette strips are placed in the incubation area for prewarming at 37 degree C for 3 min.

50 micro litre of plasma and reagent are dispensed into the cuvette and the timer is started for incubation of 180sec. When the instrument starts to beep the cuvettes are transferred to the test column area.

50 micro litre of 0.025 $CaCl_2$prewarmed at 37 degree C is dispensed after pressing the pipette key.

aPTT results are obtained from the machine and expressed as seconds.

Fibrinogen concentration:

Collect blood in a vacutainer with 3.2% sodium citrate as an anti-coagulant in the ratio of 1:9.

Centrifuge the blood for 10 min at 2500g to obtain the plasma.

Dilute the patients using Owren-Koller buffer solution to get 1:20 dilution. Cuvette strips are placed in the incubation area for pre warming at 37^0C for 3 min. Place a ball in each cuvette.

Start the timer for an incubation of 60 sec.

When the instrument beeps, transfer the cuvettes to the test column area. 50 microlitre of reagent pre warmed at 37^0C is dispensed after pressing the pipette key.

If the clotting time for 1:20 dilution of the plasma is being assayed as < 5 sec, the plasma is retested at 1:40 dilution and the result multiplied by 2.

If the result is being assayed as > 60 sec, the plasma is retested at 1:10 dilution and the result is divided by 2.

Fibrinogen level is expressed as g/l or mg/dl.

Thrombin time:

Collect blood in a vacutainer with 3.2% sodium citrate as an anti-coagulant in the ratio of 1:9.

Centrifuge the blood for 10 min at 2500g.

Collect the plasma in plastic tubes.

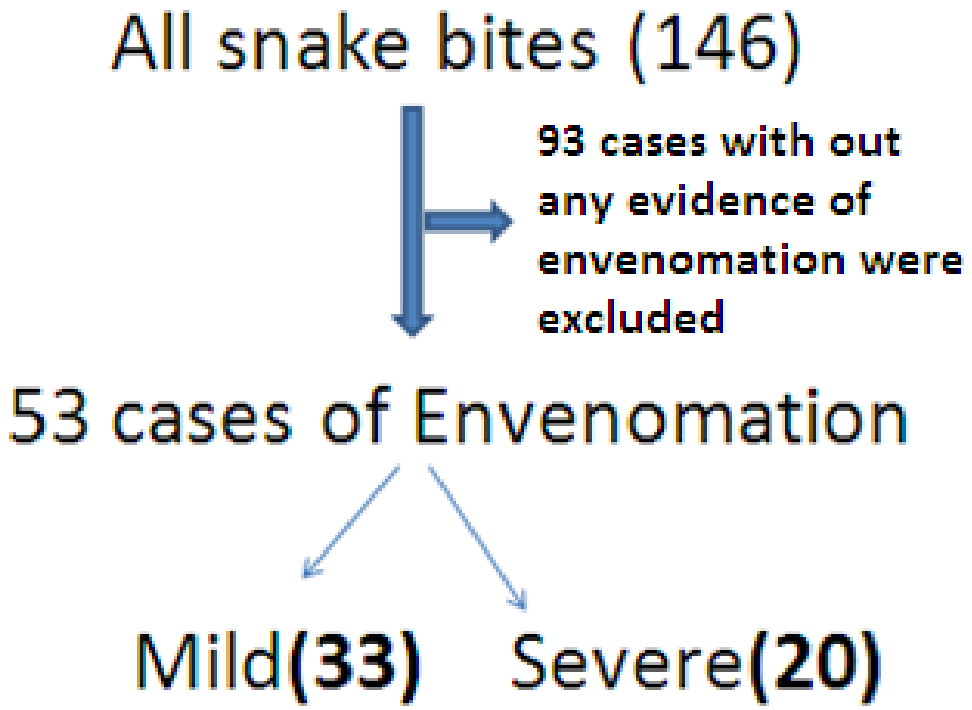
Place the cuvette strips in the incubation area for pre warming at37^0C for 3 min.

Dispense200microlitre of plasma into the cuvette with simultaneous start of the timer for an incubation of 120sec. When the instrument starts to beep, transfer the cuvettes to the test column area. 200 microlitre of thrombin reagent pre warmed at 37^0C is dispersed into the cuvette containing plasma after pressing the pipette key.

Thrombin time is expressed in seconds.

Results and analysis:

Total number of snake bite cases admitted in casualty was 146. Out of these 146 cases, only 53 cases had signs of envenomation which was included in our study.33 (62.2%) out of 53 cases showed mild envenomation and 20(37.7%) cases had severe envenomation. Age of the patients ranged from 17-85 yrs(Table 1). Most of them were males with male to female ratio of 1.7:1(Table 4). 49.1% of the patients were admitted during rainy season between May and august (Table 5). 69.9% of cases were bitten in the night (Table 6). The most common site was lower extremities (Table 7). Platelet count was decreased in 4(7.5%) cases and all these cases remained prolonged 12hrs after admission (Table8). The common complications seen in these cases were bleeding (18.8%), neurotoxicity manifesting as giddiness and unconsciousness (15%), cellulitis (3.6%) and local tissue reaction (62.2%) (Table 9). PT and APTT were prolonged in 14(26.4%) cases. Out of these 14 cases, 2 cases were prolonged even after 12 hrs of admission (Table 11 & 12). Thrombin time was prolonged in 17 cases (32%). Out of these, 3 cases were prolonged even after 12 hrs of admission (Table 13). Fibrinogen concentration was decreased in 6(11.3%) cases. 3 cases were prolonged even after 12 hrs of admission (Table 14).


All snake bites (146)
93 cases with out any evidence of envenomation were excluded
53 cases of Envenomation
Mild(33)
Severe(20)

Age	Frequency	Percent
10-25yrs	8	15.1
26-40yrs	14	26.5
41-55 yrs	19	35.8
56-70 yrs	6	11.3
71-85 yrs	6	11.3
Total	53	100

Table 3: Distribution of snake bite cases according to age.

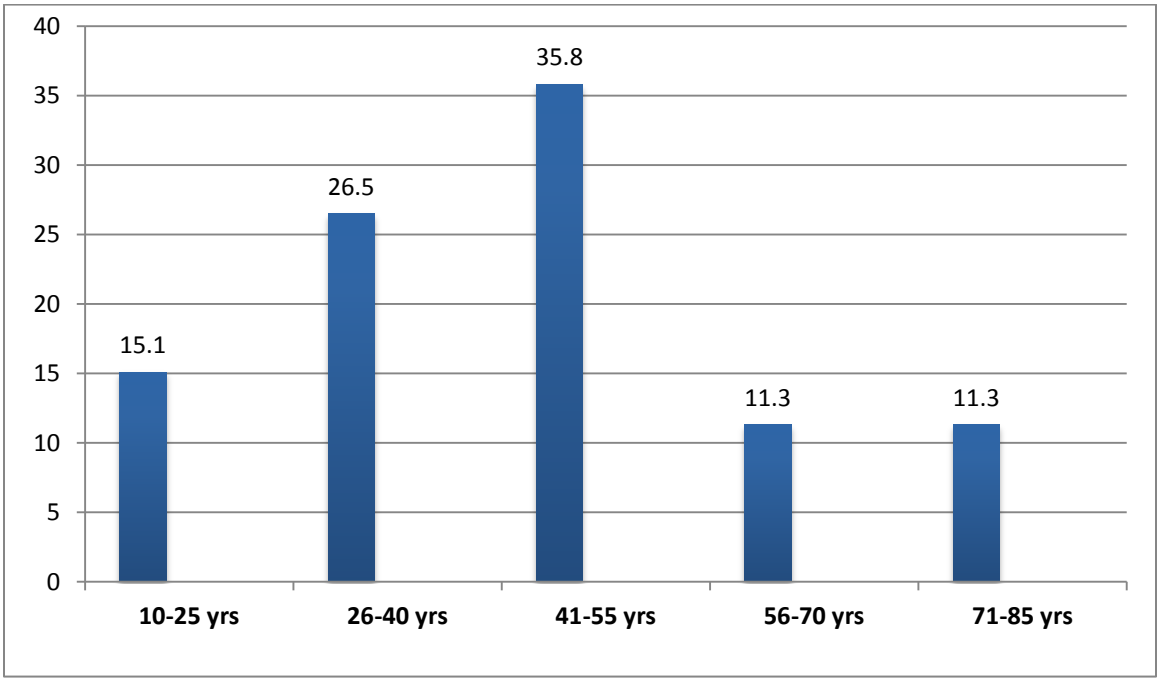


Fig 9: Age wise distribution of cases with snake envenomation cases

Sex wise distribution	Frequency	Percent
Male	34	64.1
Female	19	35.9
Total	53	100

Table 4: Distribution of snake bite cases according to gender.

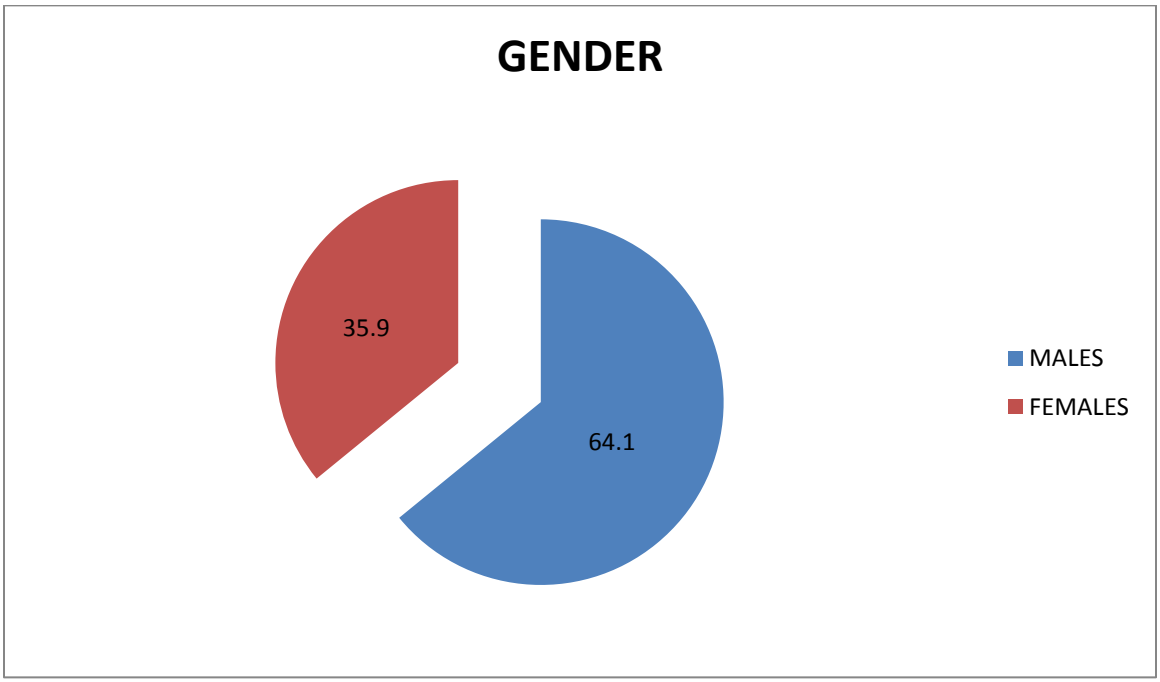


Fig 10: Comparison of gender distribution among snake envenomation cases.

Seasonal distribution	Frequency	Percent
Jan-April	13	24.5
May-Aug	26	49.1
Sep-Dec	14	26.4
Total	53	100

Table 5: Seasonal distribution of cases

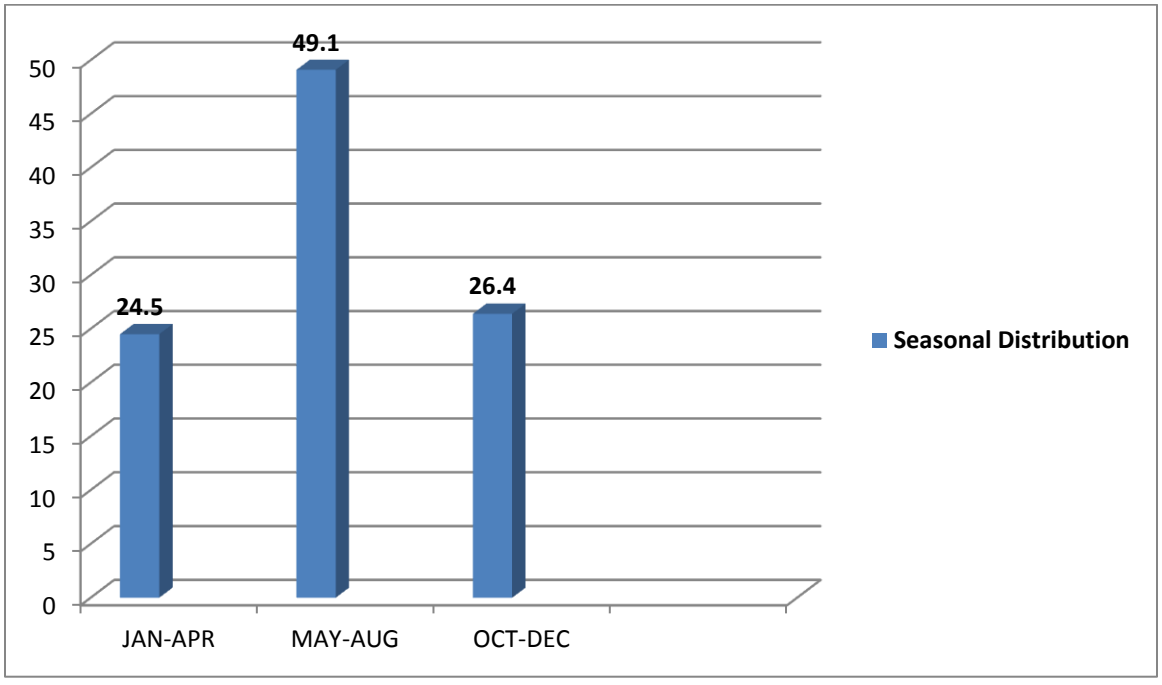


Fig 11: Season wise distribution of snake bite cases.

Time of bite	Frequency	Percent
Day	16	30.1
Night	37	69.9
Total	53	100

Table 6: Distribution of cases according to Time of bite.

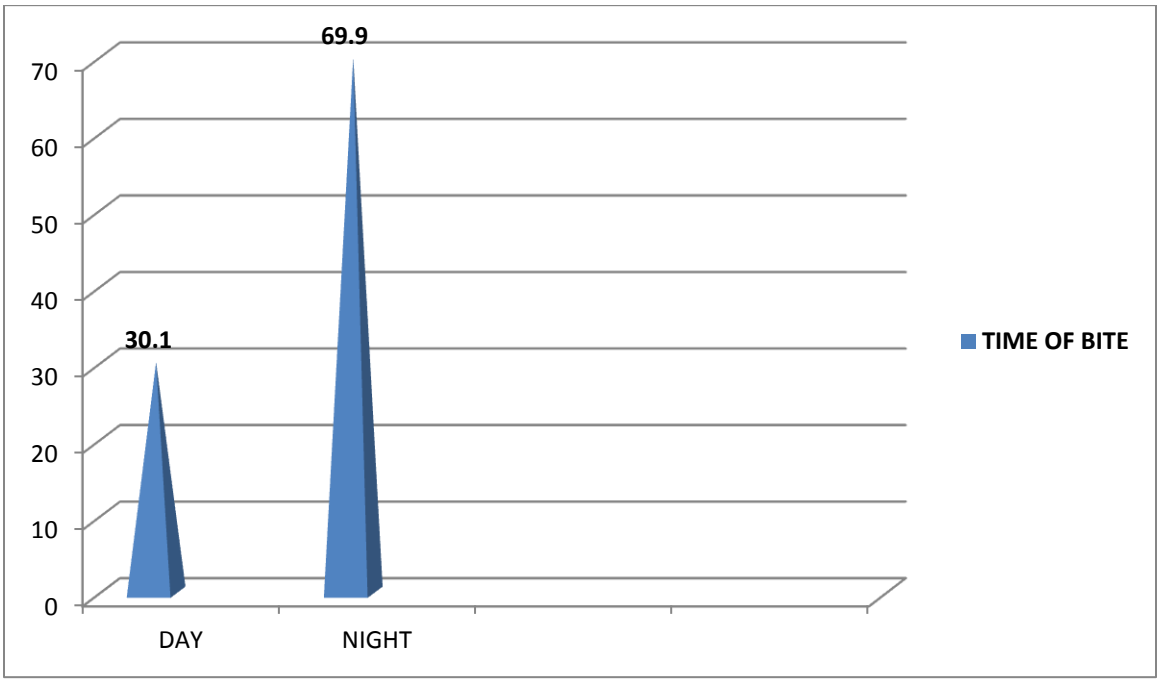


Fig 12: Distribution of snake bite cases according to time of bite.

Site of bite	Frequency	Percent
Toe, leg, foot	34	64.1
Finger, forearm, hand	13	24.5
Others	6	11.4
Total	53	100

Table 7: Distribution of snake bite cases according to Site of Bite.

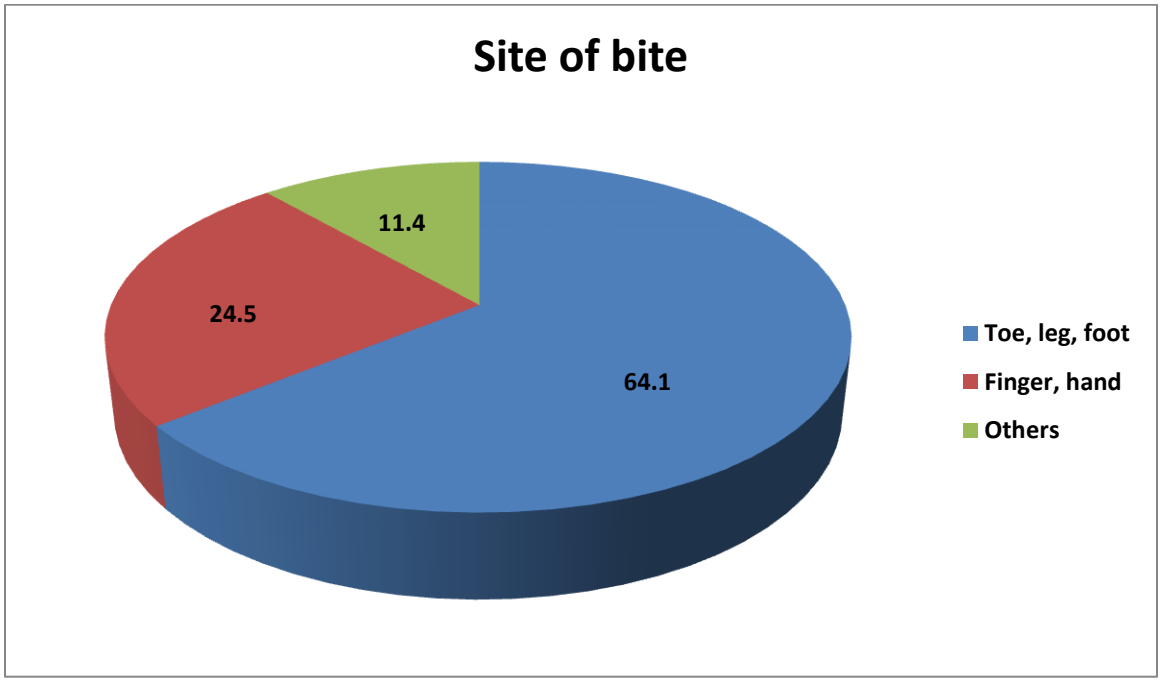


Fig 13: Distribution of snake bite cases according to site of bite.

Platelet count	At admission		After 12 hrs	
	Frequency	Percent	Frequency	Percent
<1 lack	4	7.5	4	7.5
>1 lack	49	92.5	49	92.5
Total	53	100	53	100

Table 8: Distribution of cases on the basis of platelet count.

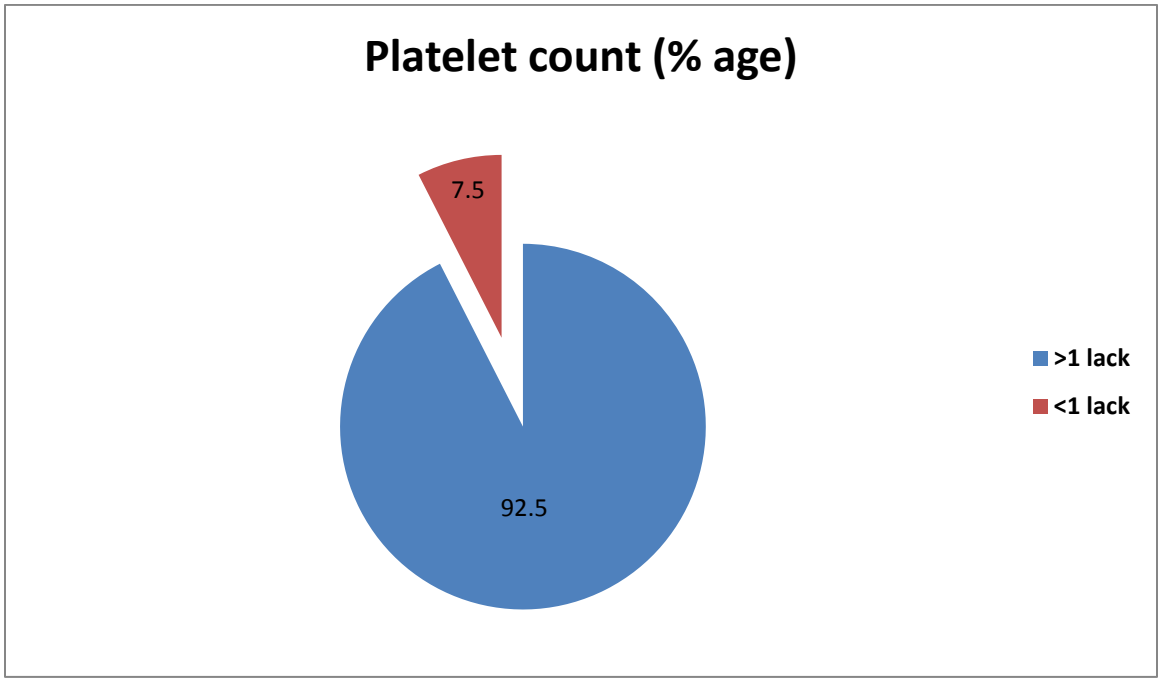


Fig 14: Distribution of thrombocytopenia cases in our study.

Complications	Frequency	Percent
Bleeding	10	18.8
Giddiness	4	7.5
Unconciousness	4	7.5
Cellulitis	2	3.6
Local tissue reaction	33	62.6
Total	53	100

Table 9: Distribution of cases on the basis of complications/prominent clinical manifestations.

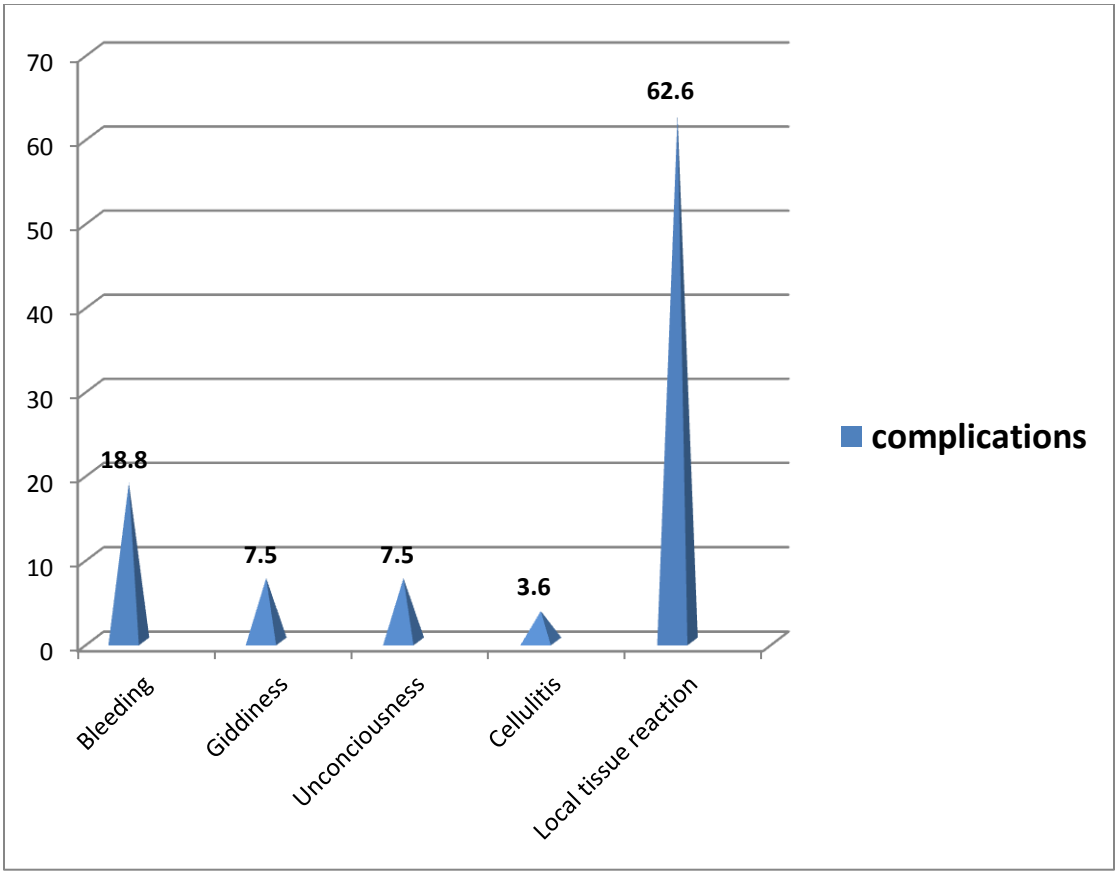


Fig 15: Distribution of cases according to complications.

Time of admission	Frequency	Percent
<6 hrs	35	66.2
6-24 hrs	16	30.1
>24 hrs	2	3.7
Total	53	100

Table 10: Distribution of cases according to time of admission.

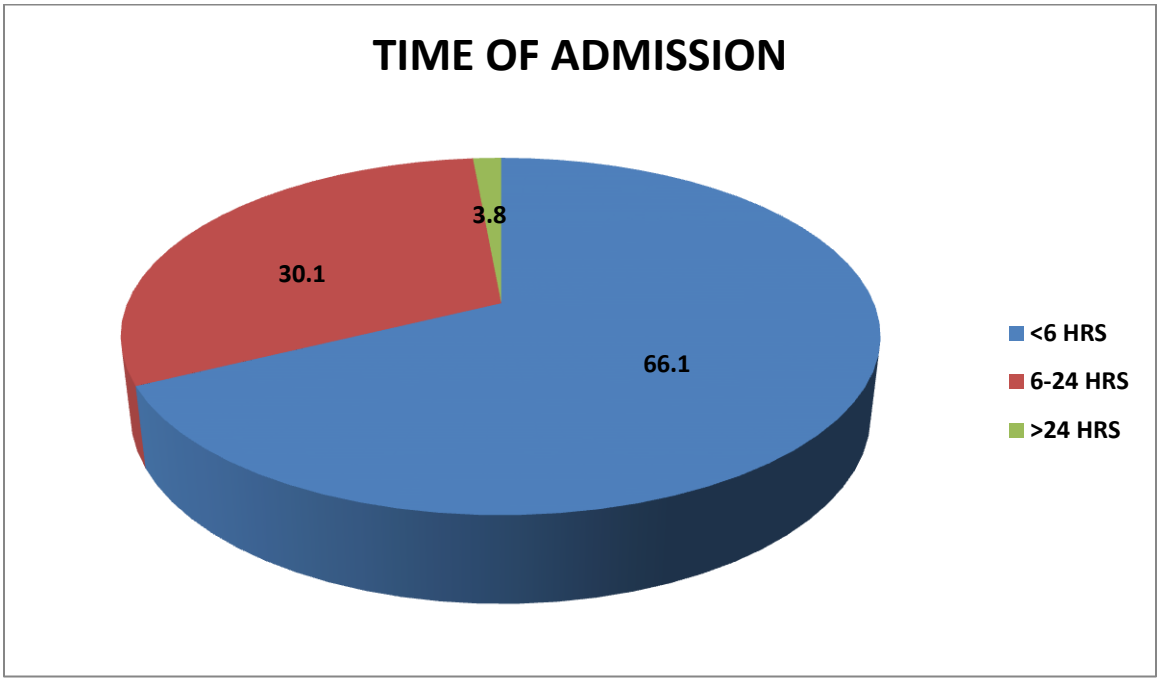


Fig 16: Distribution of cases according to time of admission.

Prothrombin time	At admission		After 12 hrs	
	Frequency	percent	Frequency	Percent
Prolonged	14	26.4	2	3.7
Normal	39	73.6	51	96.3
Total	53	100	53	100

Table 11: Comparison of Prothrombin time at the time of admission with 12 hrs after admission.

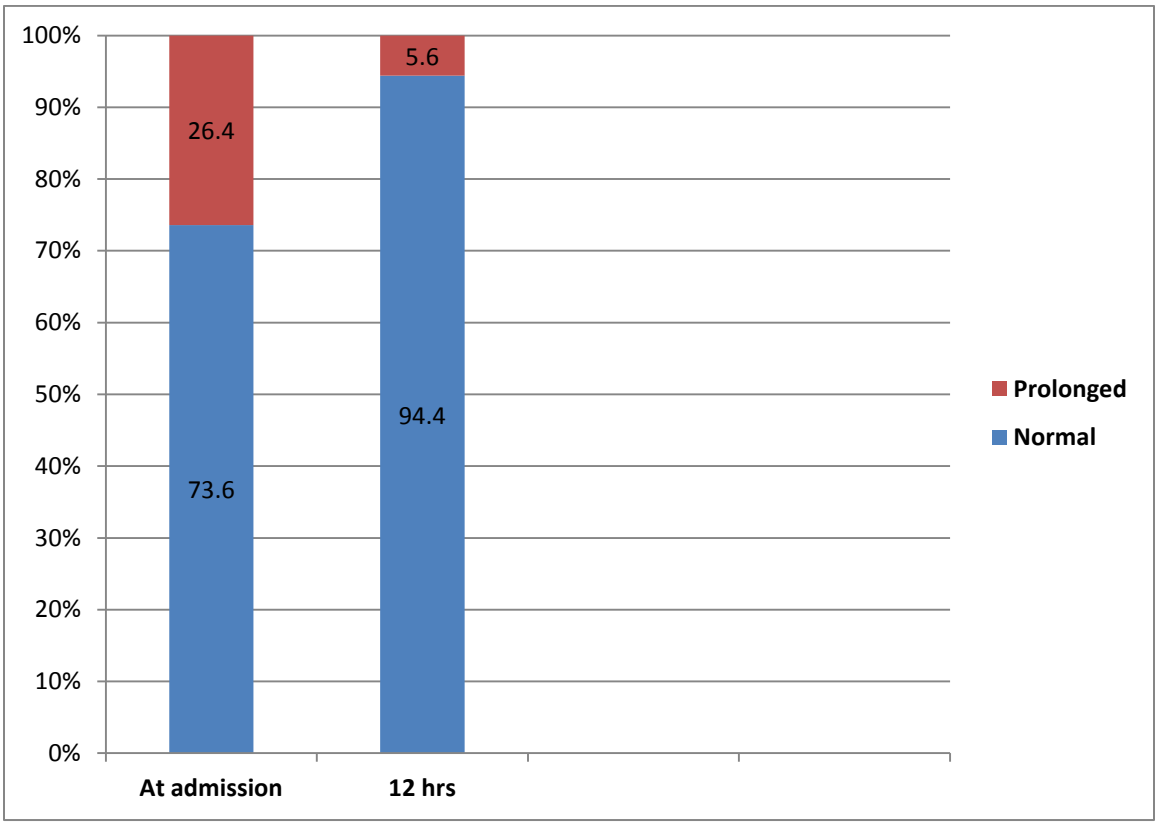


Figure 17: Comparison of PT at Admission and 12 hours following admission

APTT	At admission		After 12 hrs	
	Frequency	Percent	Frequency	Percent
Abnormal	14	26.4	2	3.7
Normal	39	73.6	51	96.3
Total	53	100	53	100

Table 12: Comparison of APTT at the time of admission with 12 hrs after admission.

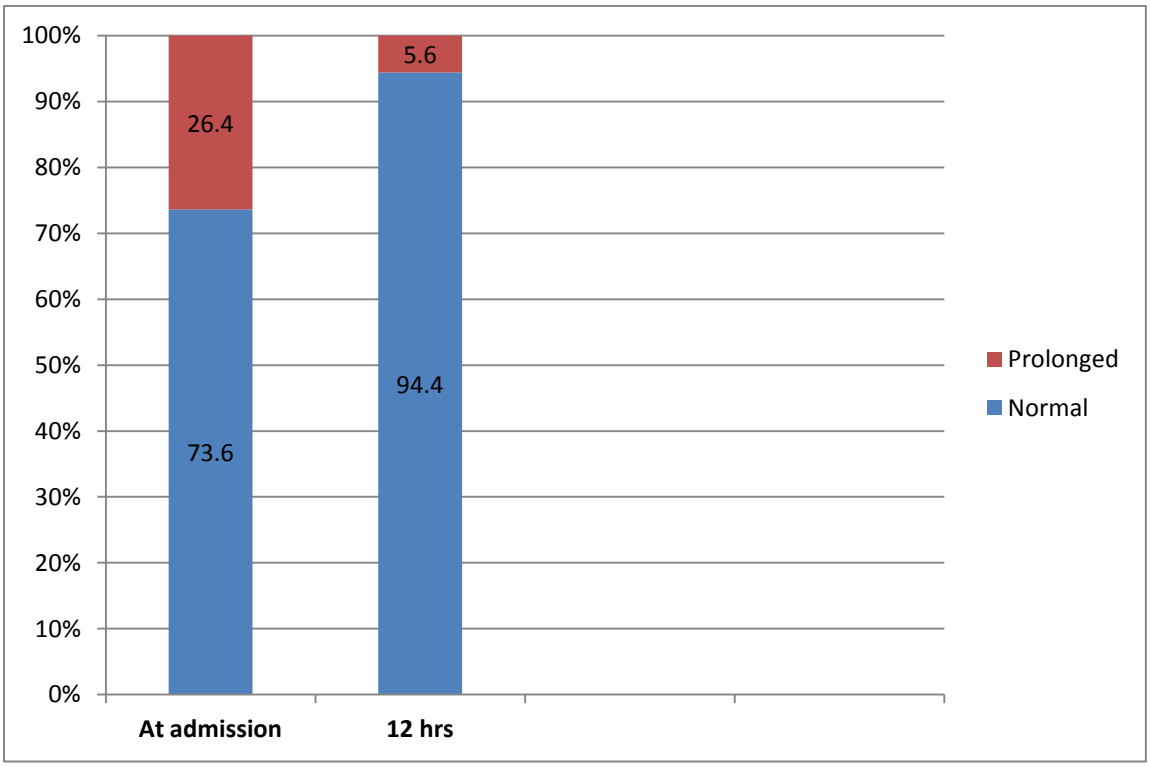


Fig 18: Distribution of normal and abnormal APTT at admission and after 12 hrs of admission.

Thrombin Time	At admission		After 12 hrs	
	Frequency	Percent	Frequency	Percent
Abnormal	17	32	3	5.6
Normal	36	68	50	94.4
Total	53	100	53	100

Table 13: Distribution of cases showing thrombin time abnormalities at admission and after 12 hrs of admission.

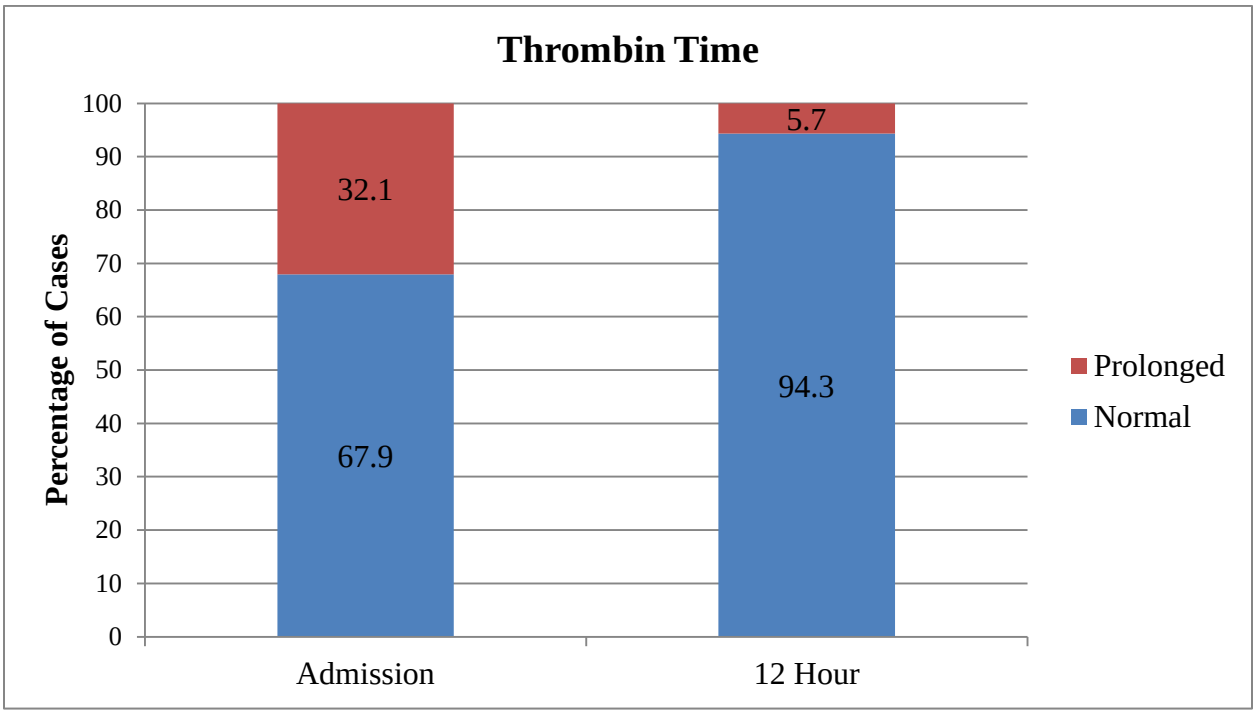


Fig 19: Comparison of Thrombin Time at the time of admission with 12 hrs after admission.

Fibrinogen	At admission		After 12 hrs	
	Frequency	Percent	Frequency	Percent
Decreased	06	11.3	3	5.6
Normal	47	88.7	50	94.4
Total	53	100	53	100

Table 14: Comparison of fibrinogen concentration between patients at the time of admission and after 12 hrs.

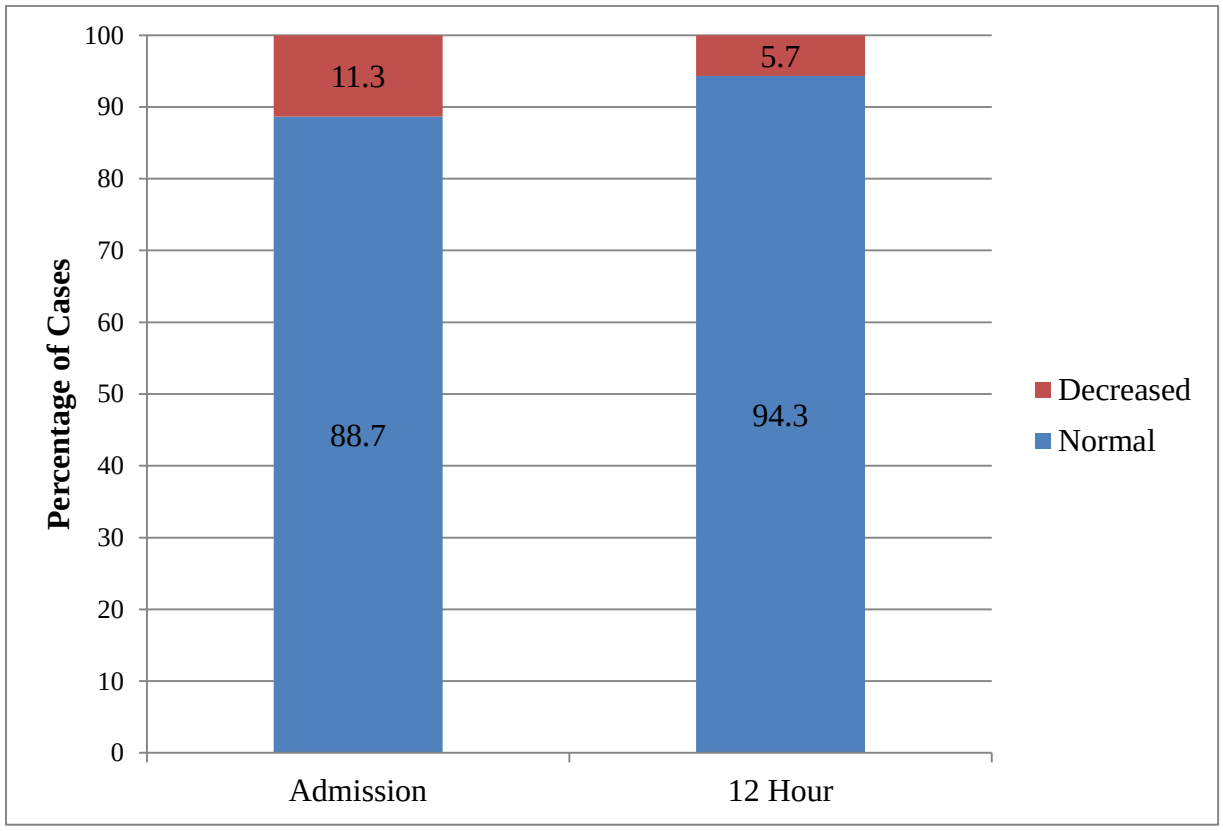


Fig 20: Distribution of cases according to Fibrinogen abnormaliries.

DISCUSSION

- This study showed 26.5% incidence of snake bite in age group of 26-40 yrs and 35.8% incidence in 41-55 yrs of age group. (table 3).

- Most of the farmers working in the fields (including females) belong to the age group of 26-55 years. The reason being, these age group persons are in their productive years and there is more chances for them to come in contact with the snakes while working in the fields and become victims to snake bites.

- Males showed a higher incidence (64%) as compared to females (36%) which may be because predominantly males were involved in farming (table 4).

- This is in accordance with another study done by Hayat AS[18] who also saw increased incidence of snake bite in male gender but the M:F ratio in his study was 4:1.

- Most of the patients were from the rural area. More vegetation in rural areas and which may be conducive ecology for the reptiles to inhabit.

- Most of our snakebite (49.1%) cases occurred during the period of May to August which is also the monsoon season and that might be the reason of increased activity of snakes and hence increased incidence of snakebite cases (table 5)

- Most of the cases (69.9%) occurred at night in our study, when the person is either sleeping or walking around in the dark to switch on the pump to fill water in the fields as electricity comes in night time in rural areas(table 6)and may accidently step on the snake. This finding was different from another study done by Hayat AS[18] who noted a 40% occurance of snake bite cases in night.

- In this study we found out that the most common site of snake bite was lower extremity (64.1%) (table 7) which was in accordance with the study done by Hayat AS[18] who found it to be 80%.

- In this study we found out that thrombocytopenia was present in 7.5% of the snake bite patients (table 8) which continued to be the same after 12 hrs while in another study done by Moriarity et al[7] showed that thrombocytopenia was present in 14.3% cases in his study.

- Out of 53 patients, 7 patients developed neurotoxicity.

- 3 patients developed both haematotoxicity and neurotoxicity. This may have happened as the venom may have contained both hematotoxic and neurotoxic components (table 9).

- Since most of our patients had haematotoxicity, and local reaction in the form of swelling and redness it can be concluded that viper bites are much more common than cobra bites in this region of Karnataka state.

LOCAL REACTION

- Most common local reaction we observed were swelling at the site of bite.
- Fang marks were identified in all the cases.
- The most common bleeding manifestation that we observed in our study was bleeding from the site of bite and petechiae.
- This was considered as an evidence of systemic envenomation.
- Bleeding was continuous in patients having severe envenomation and experienced considerable blood loss due to the coagulation disorder.
- 4 of such patients needed blood transfusion.
- In other patients bleeding was mild.
- Neurological symptoms were observed in 7 patients.
- Among these 3 patients had combined features of haematotoxicity and neurotoxicity. These patients had continuous bleeding from the site of bite with ptosis.
- 3 patients had only neurological symptoms with respiratory distress.

- Remaining one patient developed ptosis and difficulty in speaking and swallowing.
- 66% of the patients were admitted within first 6 hours of the bite , 30% in between 6 – 24 hours of the bite and 4% came after 24 hour with severe complication of bleeding manifestation.
- Most of our patients were admitted within 6 hours after the bite.
- It can be concluded that this may be due increased awareness of people regarding complication and availability of treatment for snakebite in hospital.

- According to our study, Values of Prothrombin time at the time of admission and after 12 hrs of admission are as follows (fig 11)

While the values of Prothrombin time according to a study done by Moriarity et al are as follows:

PT		
	Moriarity et al	Present study
Mild Envenomation	1/35 (2.9%)	0/33
Severe Envenomation	3/8 (37.5%)	14/20 (70%)

Table 15: Comparison of PT values between study done by moriarity et al and our study

APTT		
	Moriarity et al	Present study
Mild Envenomation	4/35 (11.4%)	0/33
Severe Envenomation	3/8 (37.5%)	14/20 (70%)

Table 16: Comparison of APTT values between study done by moriarity et al and our study.

Fibrinogen concentration		
	Moriarity et al	Present study
Mild Envenomation	0/6 (2.9%)	0/33
Severe Envenomation	2/6 (37.3%)	6/20 (30%)

Table 17: Comparison of Fibrinogen values between study done by moriarity et al and our study

Comparison of platelet count after envenomation between study done by moriarity et al and present study.

Platelet count		
	Moriarity et al	Present study
Mild Envenomation	2/36 (5.5%)	1/33 (3%)
Severe Envenomation	1/7 (14.3%)	3/20 (15%)

Table 18: Comparison of Fibrinogen values between study done by moriarity et al and our study

Comparison of platelet indices between study done by sooragum s et al and present study.

Sooragum S et al[20]	Present study
Study of effect of green pit viper on platelet indices showed that total platelet count and mean platelet volume (MPV) were significantly decreased.	In our study, there were 4 cases of decrease in platelet count out of 53 cases.

In a study done by Graham et al he concluded that combination of INR, APTT, CK level and serial neurological examination within 24 hrs is sufficient as safe observation period.

Whereas in present study, we found out that combination of PT, APTT, TT and fibrinogen levels for a period of 12 hrs can be considered as reliable indicators to exclude envenomation.

We also noticed a difference between time taken for coagulation parameters to become normal after administration of anti snake venom, in a study done by Dempfle et al and our present study

Dempfle et al[27]	Present study
He concluded that intra venous administration of anti snake venom resulted in normalized coagulation parameters within 48 hrs.	We found out that 51 out of 53 cases showed normalization of coagulation markers 12 hrs after administration of anti snake venom.

SUMMARY

Snake bite is a common cause of morbidity and mortality in rural India. The four most common venomous snakes in Indian sub continent are Naja naja(Indian Cobra), D russelii(Russell Viper), Echinus carinatus (Saw scaled viper) and Bungarus caeruleus(Krait).

Envenomation is defined as occurrence of snake bite with evidence of tissue damage resulting in clinical symptoms and laboratory abnormalities.

146 cases of snake bite were admitted in casualty department of R.L. Jalappa hospital, Kolar.

53 cases showed symptoms of envenomation.

33 cases had mild envenomation and 20 cases had severe envenomation. The common complications seen in these cases were bleeding, giddiness, unconsciousness, cellulitis and local tissue reaction. PT and APTT were prolonged in 26% of cases at the time of admission.

3% of cases showed prolonged PT and APTT even after 12 hrs of admission.

Thrombin time was prolonged in 32% of cases.5.6% of cases were prolonged even after 12 hrs of admission.

Fibrinogen concentration was decreased in 11.3% of cases. 5.6% of cases showed decreased fibrinogen even after 12hrs of admission.

First line of coagulation markers comprising of PT, APTT, TT, fibrinogen concentration and platelet count are pre requisites for early detection of coagulation abnormality following envenomation.

Our study showed that 12 hrs was sufficient to safely exclude envenomation.

If the patient had altered coagulation test which returned to normal after administration of ASV within 12 hrs, they can be safely discharged.

In the coagulation parameter were prolonged after 12 hrs after the administration of anti snake venom, prolonged observation is necessary to obviate the complication.

CONCLUSION

First line of coagulation markers (PT, APTT, fibrinogen and thrombin time) should be considered as first line of investigations for any suspected coagulation abnormality in snake bite patients.

If there is any abnormality in the first line parameters, then second line of specific markers can be entertained if required, to pinpoint the level of defect.

PT and APTT were the first abnormal test result after snake envenomation. 12 hrs observation was the safe period to rule out any complications following envenomation if the coagulation tests return to normal with Anti snake venom.

There was no significant changes in the RBC indices (MCV, MCH, and MCHC) and platelet indices (MPV, PCT, PDW) after snake envenomation except platelet count which was low in 4 out of 53 cases which may be due to toxic effects of venom on platelets.

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ANNEXURE-I

PROFORMA

- NAME
- AGE
- SEX
- TYPE OF SNAKE
- SITE OF BITE
- PHYSICAL EXAMINATION

1 hr of admission

Hematological parameters

- MCV -
- MCHC -
- PLATELET COUNT -
- PCT -
- MPV -
- PDW -

Coagulation profile

- PT -
- APTT -
- THROMBIN TIME -
- FIBRINOGEN TIME -

12 hr of admission

Hematological parameters

- MCV -
- MCHC -
- PLATELET COUNT -
- PCT -
- MPV -
- PDW -

Coagulation profile

- PT -
- APTT -
- THROMBIN TIME -
- FIBRINOGEN TIME -