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ACUTE RENAL FAILURE IN HAEMOTOXIC SNAKE ENVENOMATION

BRANCH – I

M.D. (GENERAL MEDICINE)

MARCH - 2008

DISSERTATION SUBMITTED FOR

M.D. DEGREE EXAMINATION

THE TAMILNADU

CERTIFICATE

This is to certify that the dissertation titled ACUTE RENAL FAILURE IN HAEMOTOXIC SNAKE ENVENOMATION submitted by Dr.M.Johnsi Rani to the faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.D., Degree (General Medicine) is a bonafide research work carried out by her under our direct supervison and guidance.

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I, Dr. M. JOHNSI RANI, solemnly declare that the dissertation titled ACUTE RENAL FAILURE IN HAEMOTOXIC SNAKE ENVENOMATION has been prepared by me.

This is submitted to the Tamilnadu Dr. M.G.R., Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D., Degree Branch I (General Medicine).

Place : Madurai **Dr. M. JOHNSI RANI**

Date :

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CONTENTS

ACUTE RENAL FAILURE IN HAEMOTOXIC SNAKE ENVENOMATION

INTRODUCTION:

Acute renal failure is characterized by a deterioration in the renal function over a period of hours to days, resulting in the failure of the kidney to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis.

In India about 60% cases of acute renal failure occurs in medical wards, 20% in the surgical side and remaining 20% in obstetrical conditions. In medical settings diarrhoeal disorders account for 15% of cases, snakebites for 10% of cases, another 5-10% with poisonings such as copper sulphate.

Snakebite envenomation is a frequently encountered problem in tropical countries like India, especially in the remote rural areas of south India. Most of the victims are middleaged farmers. The only specific treatment of a poisonous snakebite is antivenom. Serotherapy must be initiated as early as possible to save the life and to avert complications such as renal failure. The main object of this study is to highlight the evaluation of renal failure among the snake envenomation and the consequences their after.

AIM OF THE STUDY

- To find out the incidence and etiology of acute renal failure among the snake envenomation cases.
- To evaluate renal failure in cases of snake envenomation with relation to age, sex, tourniquet application, onset of treatment since the snakebite,and preexisting anaemia.
- To study the time of onset of renal failure since the snakebite and the role of supportive therapy and haemodialysis in the management of acute renal failure.
- To study the bleeding diathesis and any other complications and unsual presentations following the envenomation.
- To find out the incidence and probable cause of death among snake envenomation cases and the time of death after the snake bite.

REVIEW OF LITERATURE

SNAKES:

It belongs to phylum–chordate, class-ophidia reptilia, order-squamata, suborder-ophidia. OPHIDIA means SNAKES (or) SERPENTS.

Ophitoxaemia is the rather exotic term that characterizes the clinical spectrum of snakebite envenomation. Of the 2500-3000 species of snakes distributed world wide, about 500 are venomous. (13) Based on the morphological characteristics including arrangement of scales /dentition /osteology /myology /sensoryorgans etc., snakes are categorized into families. The families of venomous snakes are Atractaspididae, Elapidae, Hydrophidae and Viperidae.

The major families in the Indian subcontinent are **Elapidae**, which includes Common Cobra, King Cobra and Krait, **Viperidae**, which includes Russell's viper, Pit Viper and Saw Scaled Viper and **Hydrophidae**, which are the sea snakes. Of the 52 poisonous species identified in India, majority of bites and consequent mortality is attributable to only 5 species viz ophiophagus Hannah (King Cobra), NajaNaja (Common cobra) Daboia Russelli (Russell's viper), Bungarus caeruleus (krait) and Echis carinatus. (Saw-scaled viper)

The snakes whose bites are known to cause acute renal failure in India includes, Russell Viper, SawScaled Viper. Since, majority of snakes are non-venomous, it is important to know the anatomical differences between venomous and nonvenomous snakes. This will help to obviate needless administration of potentially harmful antivenom in every case of snakebite.

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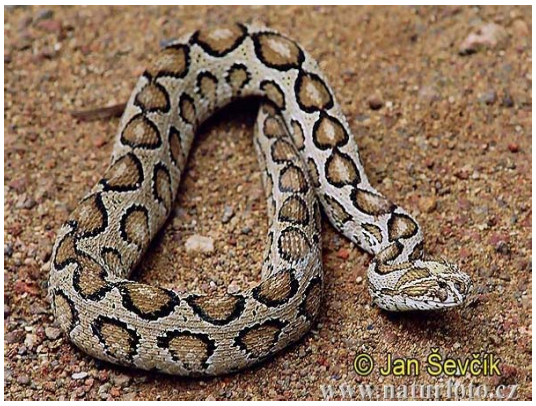
HAEMOTOXIC SNAKES



RUSSELL'S VIPER

SAW SCALED VIPER

PIT VIPER (MALAYAN)

IDENTIFICATION AND ANATOMY OF HAEMOTOXIC SNAKES

Saw-Scaled viper

Scientific Name : Echis carinatus.

Other common Names : Carper viper, "Phoorsa"

Geographical distribution : All over India (especially plains and deserts)

Physical characteristics: The Saw Scaled Viper is a small snake, about 1 ½ to 2 feet long, and is usually brown in colour. There is a wavy white line along the entire length of each flank, while diamond-shaped markings extend over the back, numbering usually 25 to 30. The head is triangular with small scales. A characteristic whitish, arrow shaped (or) Crow's Foot mark is often present on the head.

The Saw Scaled Viper is named as such because its scales are serrated. When agitated, it throws itself into a double coil (in the manner of a " Figure of eight") and rubs the coils together vigorously, producing a harsh, rasping sound, akin to the sound of a sandpaper being scraped over a rough surface. At the sametime, it also hisses loudly by exhaling forcefully through the nostrils. The Echis is an aggressive snake and may bite on the slightest provocation. The pupils are vertical and it is viviparous.

Habitat: These snake prefer desert regions, and is often found basking in the sun during the daytime, among rocks or in sandy soil. It may enter human habitation especially tents, in search of it`s prey.

Life span : 2 to 5 years or more.

Nature of venom : Vasculo and haemotoxic.

Russell`s Viper

Scientific name : Daboia russelli, Vipera russelli

Geographical distribution : All over India

Physical characteristics:

This is a brownish, stout snake, growing up to several feet in length. The head is triangular, with a 'V'shaped mark (apex pointing forward) and is covered with small scales. There are 3 rows of chained dark spots over the entire body. Pupils are vertical. Fangs are long, channelised, and hinged, being erected at the time of striking. The Russell's viper is known to hiss loudly when agitated and is viviparous.

Nature of venom : Vasculo and haemotoxic.

Pit viper

The head is covered with shields and a pit is present in between the eyes and the nostrils, which has a thermo receptor.

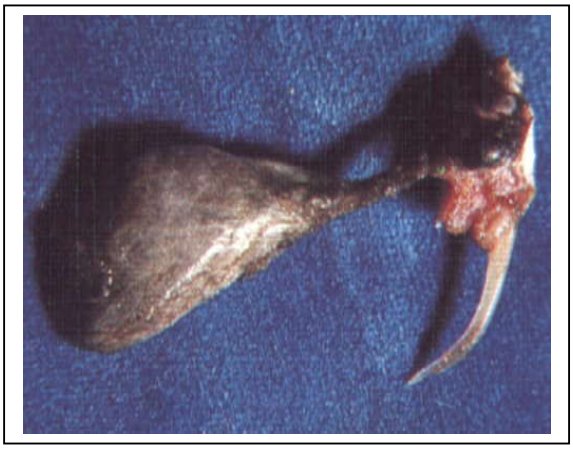
Snake Venom (21)

Source: It is the saliva secreted by the modified parotid glands of a venomous snake. Cobra venom is faint transparent yellow and is slightly viscous. Russell's viper venom is white or yellow. The concentration of venom shows diurnal and seasonal variation. Bites inflicted at nights and immediately after hibernation are the most severe. Venom travels in the body through lymphatics and superficial veins. (21).

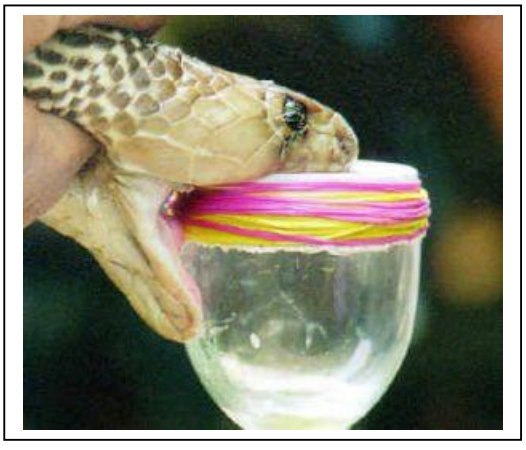
Snake venom, the most complex of all poisons is a mixture of enzymatic and nonenzymatic compounds, as well as other nontoxic proteins, carbohydrates and metals. There are over 20 different enzymes including phospholipases A2, B, C, D, hydrolases, phosphatases (acid as well as alkaline), proteases, esterases,

SNAKE VENUM

GREEN MAMBA WITH FRONT FANGS



VENOM GLAND AT FANG



VENOM EXTRACTION

acetylcholinesterase, transaminase, hyaluronidase, phosphodiaesterase, nucleotidase, ATPase and nucleosidases. (DNA &RNA). (1)

The nonenzymatic components are loosely categorized as neurotoxins and haemorrhagens (16). Different species have differing proportions of most if not all of the above mixtures. This is why poisonous species were formerly classified exclusively as neurotoxic, haemotoxic or myotoxic.

Pathophysiology of ophitoxaemia

The pathophysiologic basis for morbidity and mortality is the disruption of normal cellular functions by these enzymes and toxins. Some enzymes such as hyaluronidase disseminate venom by breaking down tissues barriers. (9).

The variation of venom composition from species to species explains the clinical diversity of ophitoxaemia. There is also considerable variation in the relative proportions of different venom constituents within a single species throughout its geographical distribution, at different seasons of the year and as a result of ageing.

Various venom constituents have different modes of action. Ophitoxaemia leads to increase in the capillary permeability which may cause loss of blood and plasma volume into the extravascular space.(13) This accumulation of fluid in the interstitial space is responsible for edema. The decrease in the intravascular volume may be severe enough to compromise circulation and lead on to shock. Snake venom also has direct cytolytic action causing local necrosis and secondary infection, a common cause of death in snakebite patients. The venom of Elapidae may also have direct neurotoxic action leading to paralysis of the muscles and respiratory failure, cardiotoxic effect causing cardiac arrest, myotoxic and nephrotoxic effects.

Ophitoxaemia also causes alteration in the coagulation activity leading to bleeding which may be severe enough to kill lthe victim. PhospholipaseA2 in Russell Viper Venom induce spheroechinocytosis which may produce hypoxic cell injury (Napathorn .S.) (66).

EPIDEMIOLOGY OF SNAKE BITE (13)

Snakebite remains a public health problem in many countries even though it is difficult to be precise about the actual number of cases. It is estimated that the true incidence of snake envenomation could exceed 5 million per year. About 1,00,000 of these develop severe sequelae. The global disparity in the epidemiological data reflects variations in health reporting accuracy as well as the diversity of economic and ecological conditions.

To complicate matters further, accurate records to determine the exact epidemiology or even mortality in snakebite cases are also generally unavailable (1). Hospital records fall far short of the actual number owing to dependence on traditional healers and practitioners of witchcraft etc. It has been reported that in most developing countries, upto 80% of individuals bitten by snakes first consult traditional practitioners before visiting a medical centre. Owing to the delay several victims die during transit to the hospital.

According to Reid, venomous snakes have two types of bites, the first type being a business bite inflicted when the snake is after a prey. In this case, a large amount of venom is injected and to victim dies rapidly. The second type of bite is as a matter of defence or warning and little or no venom is injected, the snake's object being to escape. When a venomous snake, bites human beings, it generally uses the

second type of bite. Therefore, over 50% of the victims have minimal or no poisoning and only 25% develop serious systemic symptoms.

While snakebite is observed in all age groups the large majority (90%) are in males aged 11-50 years. The predominance of male victims suggests a special risk of outdoor activity (14). The high incidence of snakebite between 04.00 hours to mid night corresponds well with the period of maximum outdoor activity observed in most studies. The incidence of snakebite shows a distinct seasonal pattern closely related to rainfall and temperature which compels the reptiles to come out of their shelter.(14)

A large number of bites occur in fields, most individuals are unable to spot the snake due to tall grass and crops. The observation that the most frequent site of bite is the lower extremity suggests that in most cases the snake is inadvertently trodden upon. Among host factors, people involved in occupations and lifestyles requiring movement in dense undergrowth or undeveloped land, are the worst affected. These include farmers, herders, and hunters and workers on development sites.

Morbidity and mortality resulting from snakebite envenomation also depends on the species of snake involved, since estimated " Fatal dose" of venom varies with species. In the Indian seething, almost 2/3 of bites are attributed to Saw Scaled Viper (as high as 95% in some areas like Jammu) (18), about ¼ to Russell's Viper and small proportions to Cobra & Kraits.Among the various species, the average yield per bite in terms of dry weight of lyophilized venom is 60 mg for Cobras, 63 mg for Russell's Viper, 20 mg for Krait and 13mg for Saw Scaled Viper.

The respective “Fatal doses” are much smaller viz 12mg for Cobra, 15mg for Russell’s Viper, 6 mg for Krait and 8 mg for Saw Scaled Viper.(21) However, clinical features and outcomes are not as simple to predict because every bite does not result in complete envenomation. (22). Epidemics of snakebite following floods owing to human and snake population getting concentrated together have been noted in Pakistan, India and Bangladesh.

How serious a problem is snakebite in INDIA?

Swaroop reported about 2,00,000 bites and 15,000 deaths in INDIA due to snakebite poisoning as far back as 1954 (6). Based on an epidemiological survey of 28 villages with a total population of nearly 19,000 individuals in Burdwan district of West Bengal state, Hati et al worked out an annual incidence of 0.16% and mortality rate of 0.016% per year.

Maharashtra, has the highest incidence, reporting 70 bites per 1,00,000 population and mortality of 2.4per 1,00,000 per year.(11) The other states with a large number of snake bites cases include West Bengal, Tamilnadu, Utter Pradesh and Kerala(1).

The Hindu – Magazine June 13 2004:

Actually we do not have upto date data, as the statistics are not very clear or simply absent. The latest survey was done in 1972 by Dr. Sawai and Dr.Homma of the JAPAN Snake Institute, the report concluded that about 10% of deaths are of the victims who come to the hospital and about 90% die outside, having gone for other remedies like manthra and magic. It is very different now after 30 yrs.

Based on the recent preliminary survey that Janaki and Romulus Whitaker did in Kerala, West Bengal and Rajesthan, they found the awareness about ASV is much higher now than it was 1972 and majority of snakebite victims now come to hospitals. Actual Incidence of snakebite is increasing, by destroying the forest and creating agricultural lands, we are increasing the prey base of the snake that is frogs and rats. So, it attracts a lot of snakes. Humans going into the field every morning and coming out in the evening, is just the time when the snakes are active. Thus, the chance of an encounter between farmer and snake is very high.

It is not correct to say that if a snake had bitten in the recent past, its poison is less in the subsequent bite. A snake never runs out of venom and it does not inject all the venom from the sac.

Status of venomous snakes in India

Tamil Nadu, Kerala, Rajesthan and West Bengal where the incidence of snakebite is high, where different snakes are responsible for the bites. In Rajesthan it was the Saw Scaled Viper, in northern Kerala, it was mainly the bite of Russell's viper and in Tamil Nadu, it is a mixture of Cobra and the Krait. In Bengal it was a mix of all of the "Big four" except Saw Scaled Viper.

Cobra flourish as long as there are rice fields. There they feed mainly on the mole rat. (Varapu eli – in Tamil). They live and lay their eggs in the rat burrow network, Kraits also get by very well in rice fields because they like the plentiful small rodents such as field mouse (sundeli –in Tamil) and rock mouse.(kallueli) We have found a lot of Kraits in the mounds of earth and rubble near wells .The Russell's Viper lives in the rocky outcrops and hedgerows of cactus and other bush.

There, on the high ground they have a plentiful supply of common gerbil (velleli –in Tamil)

CLINICAL MANIFESTATIONS

The clinical manifestations of snakebite occur in a wide spectrum with some bites resulting in minimal or no symptoms at all, while others are severe enough to result in systemic manifestations and even death.

1. SNAKE BITE WITH NO MANIFESTATIONS

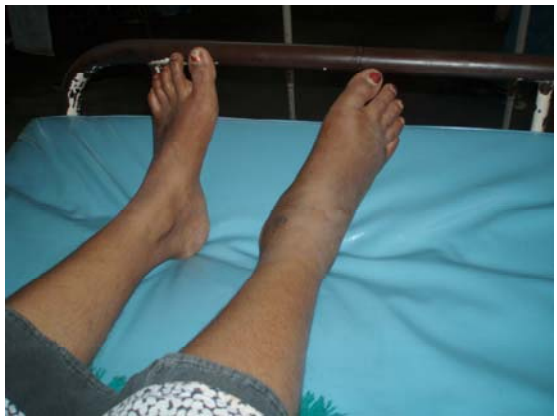
The most obvious explanation for a confirmed snakebite but no clinical manifestations is bite by a non-poisonous species. However, it is well documented that a large number of poisonous species also often do not cause symptoms.

In a study of 432 snakebites in North India, Banerjee noted that 80% of victims showed no evidence of envenomation (1). This figure correlates almost exactly with a more recent observation from Brazil (24). Reid also states that over 50% of individuals bitten by potentially lethal venomous snakes escape with hardly any features of poisoning.(22)This is corroborated by saini' s study of 200 cases in Jammu region in India, in which only 117 showed symptoms and signs of envenomation (19). From the relatively low frequency of poisoning following snakebites, it has been suggested that snakes are on the defensive when biting humans and seldom inject much venom (25). Other possible explanations include a bite without release of venom (dry bite). There are also cases wherein venom is spewed in to the victim`s body as the snake attempts to bite, there by reducing the overall quantity of venom in the blood stream. Other protective factors include the layers of clothing or boot leather through which the snake sometimes strikes.(27).

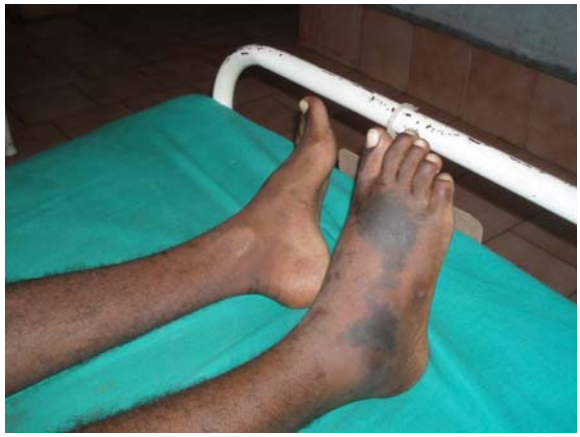
2. LOCAL MANIFESTATIONS

With the possible exception of the psychological trauma of being bitten, local changes are the earliest manifestations of snakebites (28). Features are noted with in 6-8 minutes but may have onset upto 30 minutes (21,29). Local pain with radiation and tenderness and the development of small reddish wheal are the first to occur. This is followed by oedema (16), swelling, (due to increased vascular permeability) appearance of bullae – all of which can progress quite quickly and extensively even involving the trunk (19). The factors responsible for increased vascular permeability are proteases,\ phopholipases,\ membrane damaging polypeptide toxin,\ hyaluronidase,\and endogenous autocoid (histamine, 5HT and kinin). In Viperbites due to increased vascular permeability leading to pulmonary edema, serous effusion, conjunctival and facial oedema, haemoconcentration are reported. Tingling and numbness over the tongue, mouth and scalp and paraesthesias around the wound occur mostly in viper bites. (21). Local bleeding including petechial and / or purpuric rash is also seen most commonly with this family. Regional lymphadenopathy has been reported as an early and reliable sign of systemic poisoning. (30) For local tissue necrosis, direct action of myotoxic, cytolytic factors possibly by polypeptide toxin, and ischaemia caused by thrombosis, external compression by tourniquet or compression of arteries by swollen muscle with in tight facial compartments also contribute. Generally Elapid bites result in early wet type gangrene whereas Vipers cause dry gangrene of slower onset; though one of the authors (JLM) has also seen the reverse pattern.

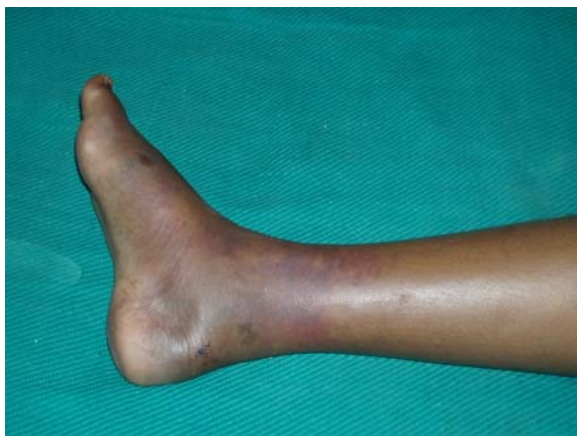
LOCAL MANIFESTATIONS



CELLULITIS



CELLULITIS WITH GANGRENE



CELLULITIS WITH ECCHYMOSIS

3. Systemic Manifestations

As mentioned previously, the most common and earliest symptom following snakebite (Poisonous or Non poisonous) is fright (28) particularly of rapid and unpleasant death.(21) Owing to fright, a victim attempts "flight" which unfortunately result in enhanced systemic absorption of venom. These emotional manifestations develop extremely rapidly and may produce psychological shock and even death. Fear may cause also transient pallor, sweating and vomiting.

Other systemic manifestations depend upon the pathophysiological changes induced by the venom of that particular species.

i) Hypotension and Shock

Profound hypotension is part of the acute pharmacological syndrome, which can occur within minutes in Viper bite. It may be due to (a) release of vasodilating autocoids, oligopeptides, inhibition of bradykinin deactivating enzymes and angio tensinogen converting enzymes. b) Leakage of plasma or blood in to the bitten limb and elsewhere (or) massive GI bleeding may cause hypovolaemia c) Vasodilatation especially of splanchnic vessels. d) Direct myocardial action may contribute to hypotension after viper bite.

ii) Bleeding and clotting disturbances

Snake venom can cause haemostatic defect in different ways. Its venom procoagulant can activate intravascular coagulation and produce consumption coagulopathy leading to incoagulable blood and thrombocytopenia. Venoms also can cause qualitative and quantitative defects in platelet function. (39) Spontaneous

systemic bleeding is attributable to distinct venom component, haemorrhagins that damage vascular endothelium.

iii) Intravascular haemolysis

The Russell's Viperbite may be associated with massive intravascular haemolysis (37). Evidence of mild microangiopathic haemolysis is sometimes found in patients with severe bleeding and clotting disturbances.

iv) Neurotoxicity

Neurological deficits can occur following Viperbites. It is usually due to intracerebral haemorrhage (6) and subarachnoid haemorrhage as a result of depletion of clotting factors.

v) Renal failure

It is one of the common complications of Viper bite and one of the major causes of death (41). The possible mechanisms of acute tubular necrosis are prolonged hypotension, DIC, direct nephrotoxic action of venom, haemoglobinuria, myoglobinuria and hyperkalemia. In a series of 40 viper bites, renal failure was documented in about a third. (42) The extent of renal abnormality in them correlated well with degree of the coagulation defect; however in a majority renal defects persisted for several days after the coagulation abnormalities normalized: Suggesting that multiple factors are involved in venom induced ARF.

vi) Cardiotoxicity

Cardiotoxic features include tachycardia, hypotension and ECG changes. Cardiotoxicity occurs in about 25% viperine bites and include rate, rhythm, and

blood pressure fluctuations. (32) In addition, sudden cardiac standstill may also occur owing to hyperkalemic arrest.

vii) Rhabdomyolysis

It is a feature of Sea Snakes and Srilankan Viper. The patient may die of bulbar and respiratory muscle weakness from acute hyperkalemia or later due to renal failure.

4.Rare Systemic Manifestations

Non- dyselectrolytemic acute myocardial infarction has been reported. (33) There is a single case report of non-bacterial thrombotic endocarditis following viper bite (35)(PGI chandigarh, 1998). One case of ventricular tachycardia following Russell's viper bite has been reported from Thailand (2005) and successfully treated with cardioversion and Amiodarone. (91) Snake bite induced ischaemic colitis with colonic stricture complicated by DIC has been reported from Japan 1995. (88) One case of snakebite presenting as acute myocardial infarction, ischaemic CVA, ARF and DIC has been reported from Nizam's Institute, Hyderabad 2000. (83) One patient had developed hypopituitarism after viperine envenomation. (75)

A healthy young male developed motor aphasia and right- sided hemiplegia within 2 hours of viper bite. CT brain revealed a left frontal lobe infarction (Panicker J.N. Kerala, JAPI 2000). (49) One patient had developed acute flaccid paraplegia as a result of dorsal spinal cord involvement following viper bite (Singh.S. PGI Chandigarh 2002)(34)

Dr. Rathod K, King Edward VII memorial hospital, Mumbai 2003(71) report the CT findings in a case of Russell's viper bite resulting in hemo peritoneum, which to the best of our knowledge has not been reported in the literature.

Multiple thrombotic occlusions of vessels in the form of multiple cerebal infarctions, digital gangrenes and ischaemic organs after Russell's viper envenoming has been reported. (79). Bilateral thalamic haematoma (45) and hysterical paralysis (46) have also been reported.

5.Unusual manifestations of ophitoxaemia

a. Delayed manifestations

Authors are all uniform in their opinion that delayed onset of signs is rare. In their series of 56 cases, Saini et al documented 4 patients who had normal clinical and laboratory coagulation profile at admission shortly following bite, but started bleeding as late as 4-6 days after the bite. (28)

The possible explanation for these manifestations is that local blebs constitute a venom depot, which is suddenly released into the blood stream, especially when the wound is handled surgically. (29) Further, these depots are generally inaccessible to antivenom. Reid has noted that haemorrhage in the brain may be delayed up to one week after bite. (28) Kumar et al have reported a singular occurrence of unconsciousness 6 days after an individual was bitten who remained symptom free for the first 5 days. (53)

b. Recurrent manifestations

Recurrent manifestations have not been discussed in most of the published literature. The only record is Warrell's assertion that signs of systemic

envenomation may recur hours or even days after initially good response to antivenom. This has been explained by ongoing absorption of venom from the blood, which has a half- life of 26-95 hrs. (17) He therefore suggests daily evaluation of patients for at least 3-4 days.

c. Manifestations of Snake bite not because of toxemia

Cases have been reported wherein the clinical manifestations of snakebite are not because of the poisoning, but due to hypersensitivity. (27) This has been noted, irrespective of a history of previous bite by the same or different species. Such patients may manifest with anxiety, cutaneous sensitivity or tightness in the throat. They may also present with features of anaphylactic shock.

d .Toxemia without bite

Naja Nigricollis (Spitting Cobra) is a species which can eject venom with considerable accuracy even from a distance of 6-12 feet.(17) The venom is aimed at the victim's eyes resulting in conjunctivitis and corneal ulceration.

e. Bite by a killed snake

There are instances on record where in a recently killed snake and even those with severed heads have ejected venom into those handling them. This is the basis for the absolute ban on handling and extreme caution in transportation, which is usually advocated for killed snakes. (17)

Factors affecting severity and outcome in Ophitoxaemia

There are several agent, host, and environmental factors that modify the clinical presentation and resultant mortality of ophitoxaemia.

Host factors

Children overall fare worse than adults owing to greater amount of toxin inj ected per unit body mass. (16) For the same age, individuals in a better state of health fare better than more debilited counter parts. (16) Patients bitten on the trunk face and directly in to the blood stream have a worse prognosis. (16) Reid however asserts that the age of the victim and part of body bitten have no relation to outcome.(29)

Exercise and exertion following bite may result in systemic absorption of venom. This is why individuals who panic and free from the scene of bite generally have a worse outcome. (57) The protection afforded by layers of clothing or shoes sometimes mitigates the effects of envenomation to a considerable extent. (27) Sensitivity of individuals to venom naturally modifies the clinical picture. Victims who develop secondary infection at the site of bite fare worse than those uninfected. (57)

Agent Factors

The number and depth of the bites inflicted by the Snake is a relative index of the amount of venom injected. (16) Indirect evidence for this is also available by studying the volume of venom remaining in the glands and fangs. The condition of fangs, intact or broken is also an indirect indicator of amount of envenomation. The

species of snake, which has bitten alters outcome since the amount of venom injected and the 'Lethal dose' varies with species. (21)

The length of time a snake clings to its victim and the presence or absence of pathogenic organisms in its mouth is two other agent factors affecting outcome.
The time of bite (day or night) and breeding habits of the snake are not related to outcome in anyway. (27) The size of snake does not appear to be related to the efficacy of envenomation since several small specimens also have lethal capacity.

Environmental Factors

The nature of first aid and the time elapsed before administration is perhaps the single most important factor- affecting outcome. (27)

Mortality

While there are many factors influencing the outcome in victims of snakebite, there is an over all agreement in the case fatality rate, generally varying from 2-10% (16, 47-51). The mortality rate is higher in children owing to larger amount of toxin per kg body weight absorbed. (27) There is significantly higher mortality among victims who develop neurotoxicity. (47,51) On an average – Cobras and Sea snakes result in about 10% mortality (28) ranging from 5-15 hours following bite. Vipers have a more variable mortality rate of 1-15% and generally more delayed. (Up to 48 hours.)(22)

Laboratory Aids in Ophitoxaemia

The laboratory serve rather poorly in the diagnosis of snakebite, with the exception of **ELISA** studies which are now available to identify the species involved, based on antigens in the venom. (22) These tests are expensive and not

freely available hence of limited value, except for epidemiological study. (16) Radio immune assay (**RIA**) has been developed for detection of Russell's viper venom in body fluids.

1.**Blood changes** include **anaemia,** leucocytosis of **neutrophils > 20,000** cells and thrombocytopenia among envenomation cases. 2.Peripheral smear may show **fragmented RBC's** evidence of haemolysis – particularly in viperine bites. 3**.Haematocrit** initially high because of haemoconcentration due to increased capillary permeability. Subsequently fall in haematocrit due to bleeding. 4.Plasma **fibrinogen** less than 200mg, (16) **FDP** level more than 80 ug/ml, clotting time of more than 20 mints, prolonged prothrombin time, thrombocytopenia are the abnormality found in DIC.

5**.**Among the metabolic changes, **hyperkalemia** and hypoxemia with respiratory acidosis, especially with neuroparalysis may be present. (16) In case of ARF, all features of **azotemia** are present. 6**.Quality of clot** formed may be a better indicator of coagulation capability than the actual time required for formation, since clot lysis has been observed in several patients who had normal clotting time. (19)

7**.Increased serum bilirubin** level**, urobilinogen** in urine, black coloured urine seen in intravascular haemolysis.8.Urine Examination could reveal **haematuria, proteinuria, haemoglobinuria, or myoglobinuria**. 9.Blood CPK, aspartate amino transferase, pottassium, myoglobin all are increased in rhabdomyolysis.10.Serum **cholesterol** at admission has been found to correlate negatively with severity of envenomation. It is more likely an indication of change in lipoprotein transport and metabolism as a result of phospholipase A2 in venom.

(59) 11.The measure of **urinary N – acetyl beta – D – glucosaminidase** is earlier indicator of renal failure, even with in 2 hours of bite.

12**.ECG changes** are generally non-specific and include alterations in rhythm (predominantly bradycardia) and atrioventricular block with ST segment elevation or depression. T wave inversion and QT prolongation (1) have also been noted. Tall T waves in lead V2 and patterns suggestive of acute myocardial infarction have been reported as well. (32) Cases who develop hyperkalemia manifest typical ECG changes.

13.**EEG changes** have been noted in upto 96% of patients bitten by snakes. Starting with in hours of the bite. Interestingly none of them showed any clinical features suggestive of encephalopathy. These abnormal EEG patterns were picked up mainly in the temporal lobes. 14.**USG abdomen** for size of kidney and to find out the existence of renal disease. 15.**CT brain** for infarction and haemorrhage.

Management of Ophitoxaemia

A review of literature pertaining to management of snakebite makes interesting reading, particularly with respect to traditional methods. (27) However even a brief review of these novel practices is beyond the scope of the present discussion. Owing to the variables involved in therapy, an ideal prospective clinical trial will likely never be done. (61)

1.First Aid

Most physicians are in disagreement with regard to nature, duration and even necessity of first aid. Russell advises minimal wastage of time with first aid measures which often end up doing more harm than good. (27)

It is felt that reassurance and immobilization of the affected limb with prompt transfer to a medical facility are the cornerstones of first aid care. (16,22) Most experts also advocate the application of a wide tourniquet or crepe bandage over the limb to retard the absorption and spread of venom. (16,28) The tourniquet should be tight enough to occlude the lymphatics, but not venous drainage. (1) Though some also prefer to occlude the veins. Enough space to allow one finger between the limb and bandage is most appropriate. Should the limb become edematous, the tourniquet should be advanced proximally. (16)

Tourniquets should never be left in place too long for fear of distal avascular necrosis. (27) In a recent repot from Brazil, two cases were reported to have increased local envenoming subsequent to a tourniquet. (62) Efficacy of compression immobilization technique was studied in Immunology Research division, Yangon Myanmar 1994. (87) This technique effectively retard the spread of radio labeled Russell's viper venom and Radioactive Na I 131 from the site of injection.

Efficacy of Tourniquet as a first aid measure was disagreed by immunology research division, Rangoon, Burma (1987)(89) and Dept. of medical research, Yangon, Myanmar 2000. (69)

It was formerly believed and therefore advocated that incision over the bite drains out venom. However, it has now been established from animal experiments that systemic venom absorption starts almost instantly; this form of 'therapy' is therefore being questioned. (27,28) Some experts suggest that longitudinal incision within fifteen minutes of the bite may be beneficial. (1) Suction of the local area, a staple of snakebite measurement in Indian Cinema, also has its advocates and

detractors, while most have rejected it for its questionable efficacy. (63) There are others who advice this method on the grounds of rapidly removing a large amount of venom. (64) There is patented device, the sawyer extractor available in the U.K. for this purpose. It's suggested use has generated controversy with a series of letters to the Editor of NEJM justifying or condemning its use. (63,64)

Reid has advised that the wound site be minimally handled. Most authors recommend saline cleaning and sterile dressing. (28) Some however advise that the wound be left open. (1,29) There is disagreement over the use of drugs as part of first aid care. It has been suggested that NSAID`S particularly aspirin may be beneficial to relieve local pain. Russell however dissuades use of analgesia and in particular aspirin for fear of precipitating bleeding. (27) In Reid's experience pain relief with placebo was as effective as NSAID`S. (22) Codeine may be useful in some cases. (1) Similarly there are proponents as well as opponents for use of sedatives. (27)

Almost all experts agree that the offending snake must not be provoked further by attempts to capture or kill it. (27) This is for fear of provoking an already enraged reptile to strike again.

2.Specific therapy – Antivenom

Antivenoms are prepared by immunizing horses with venom from poisonous snakes and extracting the serum and purifying it. Antivenoms may be species specific (monovalent) or effective against several species (polyvalent). Monovalent is ideal, but the cost and non-availability, besides the difficulty of accurately identifying the offending species – makes its use less common. (17)

a.Indication for use :

There are specific indications for use of antivenom. (11,17) Every bite even if poisonous species does not merit its use. This caution against the empirical use of antivenom is due to the risk of hypersensitivity reactions. (28,29) Therefore, antivenom is indicated only if serious manifestations of envenomation are evident viz coma, neurotoxicity, hypotension, shock, bleeding, DIC, ARF, Rhabdomyolysis and ECG changes. (16) In the absence of these systemic manifestations, swelling involving more than half the affected limb, (1) extensive bruising or blistering and progression of the local lesions with in 30-60 minutes, pregnancy and in children are other indications.

b.Dosage :

Despite widespread use of antivenom, there are virtually no clinical trials to determine the ideal dose. (68) The conventional practice is to base the initial dose on the severity of envenomation.

Approximate Initial dose of antivenom

Grade of severity	Initial dose
Minimal envenomation Mainly local effects No significant laboratory changes	50 ml
Moderate envenomation Signs of envenomation extend beyond bite site Significant systemic envenomation Moderate laboratory changes	100 ml
Severe envenomation Entire limb affected Serious systemic envenomation Very significant laboratory changes	150 ml

The antivenom is given intravenously; 5 ml / min, or diluted in isotonic fluid and infused over 30 to 60 minutes. Pregnancy is not a contraindication. Children require the same dose of antivenom (even more) as adults. Venepuncture sites must be dressed with pressure bandage. Repeat the initial dose of antivenom if, severe CVS or CNS symptoms, persists for more than ½ hour; or incoagulable blood persists for more than 6 hours after the first dose. It must be remembered that systemic envenoming can recur several days after an initial good response to antivenom. There is no fixed upper limit to the dose of antivenom to be administered. (14) Enormous doses have been given in some cases.

c. Administration :

The Freeze- dried powder is reconstituted with 10 ml of injection water or saline or dextrose. A test dose is administered on one forearm with 0.02 ml of 1:10

solution intradermally. Appearance of erythema or wheal greater than 10 mm within 30 min is taken as a positive test.(16)

Desensitization : Begin with subcutaneous administration of 0.1 ml of 1:100 solution, and increase the dose every 15 min as follows, 0.2 ml and 0.5 ml. Repeat the same regimen with 1:10 solution and finally with undiluted antivenom. Since desensitization is a time consuming and laborious procedure, some investigators recommend an alternative method; it consists of IV administration of anti histamine followed by an infusion of a dilute solution of adrenaline.

Antivenom is administered by the intravenous route (16) and never into finger or toes. (27) Some authors recommend that 1/3 to ½ the dose be given at the local site to neutralize venom there. (27) However animal experiments have established that absorption begins almost instantly from bite sites. Besides this, systemic administration of antivenom has been shown to be effective at the local site as well. Therefore most experts do not advise local injection of antivenin. (27)

Efficacy of **intramuscular** administration of antivenom followed by standard hospital management has also been evaluated and a definite reduction in the number of patient with systemic envenomation complications, and mortality from Russell's viper toxaemia has been noted. (71) This route of administration is likely to have value in a field setting prior to transfer to better facilities.

d. Timing :

There is no consensus as to the outer limit of time of administration of antivenom. Best effects are observed within four hours of bite. (16) It has been noted

to be effective in symptomatic patients even 6-7 days after the bite. (72) This is corroborated by Saini's observations also.(73)

e. Response :

Response to infusion of antivenom is often dramatic (16) with comatose patients sitting up and talking coherently with in minutes of administration. Normalization of blood pressure is another early response. (70) Within 15 to 30 minutes bleeding stops though coagulation disturbances may take upto 6 hours to normalize. If response to antivenom is not satisfactory use of additional doses is advocated. Normalization of clotting time has been taken as end point for therapy (In experimental settings) Infusion may be discontinued when satisfactory clinical improvement occur even if recommended dose have not been completed. (21)

f. Reactions :

i) **Early (analphylactic) reaction** : Hypersensitivity reactions including the full range of anaphylactic reactions may occur in 3-4 % of cases. Usually within 10 to 180 min after starting infusion. It begins with cough, urticaria, tachycardia, palpitations, nausea, vomiting, headache, and fever. The full blown anaphylactic reaction is characterized by hypotension, bronchospasm and angioedema. These usually respond to conventional management including adrenaline, anti histamines and corticosteroids. (17)

ii) **Pyrogenic reaction** : It is due to contamination of the antivenin by endotoxin like compounds. It is characterized by chills, goose fleshing, shivering, rise in temperature, sweating, vomiting and diarrhoea. Develops in 1 to 2 hours of

beginning of therapy. Treatment involves fanning, tepid sponging, and antipyretics.

iii) **Late (serum sickness) reaction** : Develops 5 – 24 (mean 7) days after treatment. The symptoms include fever, itching, urticaria, arthralgia, lymphadenopathy, periarticular swelling, mononeuritis multiplex, albuminuria and rarely, encephalopathy. It usually responds to antihistamines and corticosteroids.

g. Availability:

In India, polyvalent antivenom is commonly available which is effective against the "Big Four". It can be procured from Central Research Institute, Kasauli or Serum Institute of India, Pune. Antivenom produced at the Haffkine Corporation, Parel, Mumbai includes other species as well. It is however, much more expensive. The WHO has designated the Liver pool school of Tropical Medicine as the International collaborating centre for antivenom production or testing.

h. contraindications :

There are no absolute contraindications to antivenom in life threatening case of snakebite. Caution may be exercised in atopic and previously sensitized individuals.

3.Supportive Therapy

Clean the bite site with povidone - iodine, but do not apply dressings. Leave blisters alone. They will break spontaneously and heal. Alternatively, they can be aspirated to dryness with a fine sterile needle.

a. Intra compartmental syndrome :

This results from swelling of muscles within tight fascial compartments. It manifests as severe pain, weakness of compartmental muscles, resistance to passive stretching, hyperaesthesia of area of skin supplied by local nerves, and tenseness of the compartment. An intracompartmental pressure of more than 45mm Hg (60 cm of H2O) indicates risk of imminent necrosis. It is a strong indication for fasciotomy to relieve the pressure, but such a procedure must be embarked upon only after blood coagulability has been restored.

If coagulation abnormalities are not corrected by antivenom therapy, it may be necessary to administer fresh whole blood, fresh frozen plasma, cryoprecipitate or platelet concentrates. (Use of FFP and Fibrinogen are not recommended by some) Heparin and epsilon aminocaproic acid have not been found to be beneficial.

b. Hypotensive Shock :

Volume expanders including plasma and blood are recommended, but not crystalloids. (16) Persistent shock may require inotrope support under CVP monitoring (16).

c. Renal failure :

If urine output falls below 400 ml / 24 hours, insert urinary catheter and central venous catheter. If urine flow fails to improve after rehydration, diuretics (Frusemide upto 100 mg iv / mannitol) and dopamine (2.5ug / kg / min) should be given and patient placed on strict fluid balance. Established renal failure will have to be managed by dialysis. Routine antibiotic therapy is not must, (28) though most Indian authors recommend use of broadspectum antibiotics (16)

d. Snake venom opthalmia :

The spat venom washed from eye, topical anti microbial agent and closure of eye with dressing pad with 0.1% adrenaline eye drops relieves the pain.

Four cases of tetanus have been documented following snakebite, (27) hence tetanus toxoid is a must. Early surgical debridement is generally beneficial, (16, 70) though fasciotomy is usually more harmful than useful. (16, 70) There is no role for steroid therapy in acute snakebite. (27) Although it delays the appearance of necrosis, it does not lessen the severity of outcome (29).

Recent studies have reported the beneficial effects of intravenous immunoglobulin (IvIg) in ophitoxaemia. There are suggestions that its administration may improve coagulopathy, and eliminates the need to repeat antivenom for envenomation associated with coagulopathy. (76) A compound extracted from the Indian Medicinal plant Hemidesmus indicus R (2-hydroxy 4-methoxy benzoic acid) (77) has been noted to have potent anti-inflammatory, antipyretic and antioxidant properties particularly against Russell's viper venom (78).

Postmortem appearances

In India, a significant proportion of mediolegal autopsies comprise cases of alleged snakebite. Unfortunatelly, some of these are cover-ups for death caused by foulplay. (Poisoning, mechanical asphyxia, etc) Since physical signs of envenomation need not be present even in a case of genuine snakebite and chemical analysis frequently reveals nothing, the doctor doing autopsy in a case of alleged snakebite must always exercise great caution while giving an opinion. A careful

search must always be made from head to toe for evidence of fang marks. In case this is located, the skin and underlying tissues to a depth of a few centimeters must be cutout and submitted for analysis. In unequivocal cases there may be clearcut evidence of envenomation, the post mortem signs depending mainly on the nature of the snake.

Mediolegal Importance

The vast majority of snakebites are accidental in nature. Homicide may rarely be committed, for instance by throwing a venomous snake on a sleeping victim or slipping it under the bathroom door. Suicides are virtually unreported (with the famous exception of Queen Cleopatra who is reputed to have committed suicide by having a venomous snake, an asp bite her). Some times snake venom is used to kill cattle.

Prevention

The snakebite can be avoided by, carrying torch while walking in snake-infested areas. Wearing boots, shocks, and long trousers while working in field. Using a stick, which if tapped on the ground scares away the most of the snakes. Snakes never be disturbed or attacked or handled. The snake should not be indiscriminately destroyed since; they play a major role in keeping the rodent population under cheek. Potent antivenom in sufficient quantity should be ready in all hospital in snake- infested areas.

Capillary Leak Syndrome(105)

It is characterized by hypotension with haemoconcentration, hypoalbuminemia without albuminuria and generalized edema due to increased

capillary permeability. Inflammatory mediators play a key role in CLS. The **Etiology** of which is multiple, starting from snakebite and dengue fever to sepsis and drugs.

Typically the syndrome manifests in **two phases:** Initial capillary leak phase characterized by generalized edema, serous effusion and hypotension, which is followed by phase of volume overload or Recruitment phase.

Treatment :

It is in the form of fluid replacement to vasopressor therapy and inotropic support during capillary leak phase. Diuretics during volume overload phase. Specific treatment, in the form of ASV. Prognosis however is poor in most of the patients. **Disease modifying agents** like Theophylline, Terbutaline, Leucotrine inhibitors – Monteleukast, Zafarleukast have been shown to terminate an acute episode.

Plasmapheresis, steroids, prostacyclin have been tried in individual patients with variable success. Endothelial cell apoptosis has been shown to be increased in CLS and apoptosis is induced by reactive oxygen species (ROS). Studies have shown that antioxidants protect against endothelial cell apoptosis. Endothelium stabilizing agents may have a role in treatment.

Disseminated Intravascular coagulation (98)

It is characterized by Thrombo-haemorrhagic disorder, which includes a wide spectrum of coagulopathy ranging from subclinical bleeding diathesis to the most fulminant haemorrhagic emergencies. The basic pathology is wide spread thrombotic occlusion of many small vessels, lead to multiorgan failure, due to ischaemic necrosis.

Etiology :

It occurs in varied condition like gram (-ve) septicemia, malaria, and various obsteritical problems, following trauma, leukaemia, and snakebite, anaphylaxis and incompaitable blood transfusion.

Pathogenesis : It starts with (1) Damage to endothelium with activation of intrinsic pathway of coagulant cascade or, (2)Release of thromboplastin like materials from tissue with activation of extrinsic pathway or,(3)The injection of procoagulant of various snake venom -Russell's viper, saw – scaled viper, pit viper.In Viper bite two major procoagulant activate factor X and V.

These potent thrombogenic stimuli cause the deposition of small thrombi and emboli throughout microvasculature. This early thrombotic phase of DIC is then followed by a phase of procoagulant consumption and secondary fibrinolysis, deposition of fibrin in the kidney and other organs. With severe systemic envenomation there are wide spread spontaneous haemorrhage resulting from the coagulation factor and platelet depletion and the antihaemostatic effects of fibrin degradation products.

Clinical Features :

The clinical presentation varies with the stage and severity of the syndrome. Most patients have extensive skin and mucous membrane bleeding and haemorrhage from surgical incisions or venipuncture or catheter sites. Less often, patients may present with peripheral acrocyanosis, thrombosis, and pregangrenous changes in digits, genitalia and nose areas where blood flow is markedly reduced by vasospasm or microthrombi.

Cause of Death includes

Early shock from haemorrhage, vasodilatation and increased capillary permeability, intracerebral and subarachnoid haemorrhage, late shock from massive gastro intestinal haemorrhage, pituitary adrenal insufficiency following haemorrhage or infarction, and acute renal failure

Diagnosis :

The diagnosis is by clinical features and laboratory investigations. In DIC, the time of test is vital, since the pattern of abnormality is continuosly changing. Hence, sequential testing is necessary to judge improvement or deterioration over the period of time. The laboratory manifestations include, thrombocytopenia, and the presence of schistocytes or fragmented RBC's that arise from cell trapping and damage with in fibrin thrombi; prolonged PT and aPTT and thrombin time and a reduced fibrinogen level and elevated fibrin degradation products (FDP) from intense secondary fibrinolysis. The D – Dimer immuno assay, which measures cross – linked fibrin derivatives, is a more specific FDP assay. The simple test of whole blood clotting time > 20 minutes indicate coagulation abnormality.

Treatment :

DIC, although sometimes indolent, can cause life threatening haemorrhage and may require emergency treatment including correction of the underlying cause (with ASV), controlling the major symptom, either bleeding or thrombosis. Patients with bleeding should receive fresh frozen plasma to replace depleted clotting factors and platelet concentrates to correct thrombocytopenia. Those with acrocyanosis and incipient gangrene or other thrombotic problems need immediate anticoagulation with intravenous heparin. The use of heparin in the treatment of bleeding is still

controversial. Although it is a logical way to reduce thrombosis formation and prevent further consumption of clotting proteins, it should be reserved for patients with thrombosis or who continue to bleed despite vigorous treatment with plasma and platelets. So, the use of heparin should be weighed against risk of bleeding and hence caution is advocated. (1)

Antithrombin III : It's role is to neutralize excessively generated thrombin. The dose is 120-250 units / kg / day for 2-3 days. Clemens et al documented complementary effects between antivenom and AT III in controlling of both fibrinopeptide A (FPA) and platelet Factor 4 (PF-4) release induced by the venom. Further more, in this invitro experiment, AT III alone (high dose) when administered in a sufficient dose abolished the procoagulant effects of Russell's viper venom. (58)

The **human activated protein C** (APC) helps in amelioration of haemorrhage of DIC, more effective and cause less bleeding than heparin. The drug under trial are **Dx 9065 A** novel, synthetic, selective and orally active inhibitor of Factor X a.

Apoprotein can be used for hyper fibrinogenolysis. The DIC is the complication of haemotoxic snake envenomation. It is then responsible for many of the complication of snakebite such as renal failure, ICH, and hypotension and important cause of death among snake envenomation and it should be attempted promptly.

ACUTE RENAL FAILURE

Definition : Acute renal failure is a sudden decrease in the glomerular filtration rate (GFR) occuring over a period of hours to days and resulting in the failure of the

kidney to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis.

Recognition of acute renal failure :

Clinically, ARF is recognized by an increase in serum creatinine and blood urea nitrogen. Practically and in clinical trials of ARF, an increase in creatinine of 50% above baseline or an increase of 0.5 mg per dl are commonly used definitions of ARF.ARF may occur in patients with previously normal renal function or patients with chronic kidney disease (CKD); in either case, the clinical approach to find and treat the cause remain similar.

ARF is typically described as either oliguric or nonoliguric. Oliguria is defined as a urine output of less than 400 ml per day. 400 ml is the minimum amount of urine that a person in a normal metabolic state must excrete to get rid of the daily solute production. ARF is usually asymptomatic and diagnosed when biochemical monitoring of hospitalized patients reveals a recent increase in blood urea and creatinine concentrations. Oliguria is a frequent but not invariable clinical feature. Most ARF are reversible.

Classification of ARF :

Prerenal ARF: (55%) diseases that cause renal hypoperfusion without compromising the integrity of renal parenchyma. **Intrinsic renal ARF:** (40%) diseases that directly involve renal parenchyma. **Post renal AR**F: (5%), diseases associated with urinary tract obstruction.

ARF in Snake envenomation (94)

ARF is mainly observed following bites by the viperidae group, sea snakes, and the colubridae group, but substantial proportion of these cases do result from viper bites.

In India, particularly in the Ratnagiri district of Maharashtra, Punjab, Kashmir, Sandy deserts of Rajesthan and west coast upto Karwar, Echis carinatus or Saw Scaled Viper are found in incredible numbers. The incidence of ARF following poisonous snakebite varies from 13-22% following Echis carinatus or Russell's viper bite. (Mitral B.V. et al 1994)(8) According to chugh K.S. et al 1989. ARF incidence is 5% - 30%. (86) It may develop within hours to 4 days of the envenomation. A history of oliguria or anuria, loin pain and 50% of patients with history of cola coloured urine is commonly seen. In 6% of cases nonoliguric renal failure is seen.

Pathology :

On gross examination, the kidney size may be normal, or enlarged and the surface may show petechial haemorrhages. Light microscopy shows **acute tubular necrosis** in 70 to 80% of patients (chugh 1989). (86) Electron microscopy reveals dense intracytoplasmic bodies representing degenerated organlles in the proximal tubules.

Acute cortical necrosis carries the worst prognosis and is seen in about 20 to 25% of cases (Chugh et al 1984). (43)

Other lesions, which have been described in these patients, include

Acute interstitial nephritis with prolonged oliguria (Sit Prija et al 1982)(26); which may result from a hypersensitivity reaction to some component of the snake

venom. (Gundappa RK et al 2002)(84) **Ballooning** of glomerular capillaries, **thickening and splitting** of glomerular basement membrane, (Acharya V.N 1989) (Merchant MR 1989)(38)(52) swelling of endothelial cells, focal proliferation of measangial cells, tubular degeneration and glomerular changes, (Merchant MR, 1989). (52) Necrotizing vasculitis and nephrotic syndrome have also been reported. (Mittal B.V. 1994)(8) Occassionally, crescentric glomenulonephritis has been reported. (Seedat et al 1974, Sitprija et al 1982) Deposition of IgM and C3 in glomerular measangium with extension along the capillary walls, dense deposits of C3 in the arteriolar walls were noted in viperbite and cobra bite. (Sit prija .V)(92)

Pathogenesis :

A number of clinical and experimental studies have provided insights into the pathogenic mechanisms that lead to acute renal failure in snake envenomation patients.

Haemodynamic alterations induced by cytokines and vasoactive mediators leading to renal ischaemia are important in the pathogenesis of ARF. (Sitprija V et al)(85) Intravascular haemolysis and rhabdomyolysis are important contributing factors. (43) Metalloproteases and phospholipase A2 can induce direct nephrotoxicity. (31,107) Immunological mechanism plays a minor role in the pathogenic of renal lesion. (92)

1.Hypotension and circulatory collapse : It is resulting from massive bleeding (DIC), increased vascular permeability, release of kinins, and depression of the medullary vasomotor centre and myocardial depression. Hypotension and shock play a significant pathogenetic role in the causation of acute tubular necrosis.

(Minton 1971) Kinin-forming enzymes (kininogenases) are present in crotalid venom. (Mebs 1970). Vipera palastinae venom is thought to cause shock by depression of medullary vasomotor centre. Bitis ariefans venom causes hypotension through a combination of myocardial depression, arteriolar dilatation, and increased vascular permeability.

2.Intravascular Haemolysis :

The haemolysis results from the action of phospholipase A2 and a basic protein called 'direct lytic factor'. Phospholipase A2 present in venom of most of the snakes acts on plasma lecithin, leading to the production of haemolytic lysolecithin. (Condrea et al 1964, Chugh et al 1975) Microangiopathic haemolytic anaemia has been recorded following Russell Viper bites (Chugh et al 1975), which may be of pathogenetic importance in the development of acute renal failure.

3.Direct Nephrotoxicity :

Some investigators have produced evidence that the renal lesions are due to the direct cytotoxic effects of the snake venom on the kidney. (Harding and Welch 1980) The Kidney is particularly vulnerable to the effects of the toxins because of its high blood flow rate and capacity to concentrate these substances in the urine. Willinger et al 1995 have shown extensive destruction of the glomerular filter, lysis of vessel wall, and epithelial cell injury in all segments of the tubule in experiements with Russell's Viper venom.

A vasculotoxic factor has been isolated from the venoms of several snakes including E. Carinatus and viper palastinae. Win Aung et al 1998 described direct

toxic effect of Russell's Viper venom on the kidney in the absence of DIC.However the occurrence of these lesions has not been confirmed by all workers.

4.Disseminated intravascular coagulation :

One of the important findings observed in experimental animals as well as in patients bitten by Viper snakes is DIC.The Viper venom activates the coagulation cascade at a number of sites, leading to rapid thrombin formation. The presence of fibrin thrombi in the renal microvasculature in the histological specimens both in clinical and experimental studies points to the role of DIC in the genesis of renal lesions. (Chugh et al 1975, 1984)

Complications of Acute renal failure :

ARF **impairs renal excretion of sodium, potassium and water** and perturbs divalent cation homeostasis and urinary acidification mechanism. As a result, ARF is frequently complicated by intravascular volume overload, hyponatremia, hyperkalemia, hyperphosphatemia, hypocalcemia, hypermagnesemia, and metabolic acidosis. In addition, patients are unable to excrete nitrogenous waste products and are prone to develop the **uraemic** syndrome.

Expansion of extracellular fluid volume is an inevitable consequence of diminished salt and water excretion in oliguric or anuric individuals. Whereas milder forms are characterized by weight gain, bibasilar lung crackles, raised JVP, and dependent edema, continued volume expansion may precipitate life threatening pulmonary edema.

Hyperkalemia is a frequent complication of ARF, due to impaired excretion of ingested or infused potassium, and potassium releaed from injured tissues

(hemolysis, rhabdomyolysis and tumor lysis syndromes). Coexistent metabolic acidosis may exacerbate hyperkalemia by promoting potassium efflux from cells. Mild hyperkalemia (< 6 mmol / L) is usually asymptomatic, Higher levels may trigger ECG abnormalities or arrythmias.

ARF is typically complicated by **metabolic acidosis** since; metabolism of dietary proteins yields 50 and 100 mmol/d of fixed nonvolatile acids that are normally excreted by the kidneys. Mild **hyperphosphatemia** is an almost invariable complication of ARF. Severe hyperphosphatemia may develop in highly catabolic patients or following rhabdomyolysis, hemolyis, or tumour lysis. Hypocalcemia due to tissue resistance to the action of parathyroid hormone, and reduced levels of 1,25 dihydroxy vitamin D. **Hypocalcemia** is often asymptomatic but can cause perioral paresthesia, muscle cramps, seizures, hallucination, confusion, prolongation of QT interval and nonspecific T wave changes on ECG.

Anaemia develops rapidly in ARF and is usually mild and multi factorial in origin. Contributing factors include impaired erythropoiesis, hemolysis, bleeding, hemodilution, and reduced red cell survival time. Prolongation of bleeding time and leucocytosis are also common. Common contributors to the bleeding diasthesis include the thrombocytopenia (mild), platelet dysfunction, or clotting factor abnormalities. (Factor VII dysfunction) Leucocytosis usually reflects sepsis, a stress response.

Infection is a common and serious complication of ARF; occurring in 50 to 90% of cases and accounting for up to 75% deaths. It is unclear whether patients

with ARF have a clinically significant defect in host immune responses or breaches of mucocutaneous barriers.

Cardio pulmonary complications of ARF include arrythmias, myocardial infarction, pericarditis, and pericardial effusion, pulmonary edema, and pulmonary embolism. Mild **gastro intestinal bleeding** is common (10 to 30%) and is due to stress ulceration of gastric or small intestinal mucosa.

Vigorous diuresis during the recovery phase of ARF, which may on occasions, be inappropriate and lead to **intravascular volume depeletion** and secondary prerenal ARF, Hypernatremia, less commonly hypokalemia, hypomagnesemia, hypophosphatemia, and hypocalcemia.

Management of ARF in snakebite :

The therapeutic approach to renal failure following snakebite is the same that for ARF of any other cause. The additional problem like bleeding, shock, and sepsis are threat to patient life should be attended promptly. In addition to serotherapy with ASV the following measure should be done.

Fluid and Electrolytes Management :

1) Intravascular volume over load : Salt (1-2 g / day) and water (1L/d) restriction, diuretics (usually loop blockers + thiazide) and ultra filtration or dialysis.

2) Hyponatremia :Restriction of enteral free water intake (<1 L/d). Avoid hypotonic intravenous solution including dextrose.

3) Hyperkalemia : Restriction of dietary K+ intake (< 40 mmol / day),eliminate K+ supplements and K+ sparing diuretics,intake of potassium binding ion exchange resins (sodium polystyrene sulphonate),glucose (50 ml of 50% Dextrose) and Insulin

(10 units regular),sodium bicarbonate (50-100 mmol),calcium gluconate (10 ml of 10% solution over 5 minutes),and dialysis with low K+ dialysate.

4) Metabolic acidosis : Restriction of dietary proteins (0.6 g / kg / day of high biologic value),or use of sodium bicarbonate (maintain serum HCO3 > 15 mmol / L or arterial pH > 7.2) and dialysis.

5) Hyperphosphatemia : Restriction of dietary phosphate intake (<800 mg / day) and intake of Phosphate binding agents. (Calcium carbonate, aluminium hydroxide)

6) Hypocalcemia : Treated with Calcium carbonate (if symptomatic or if sodium bicarbonate to be administered), Calcium gluconate. (10 – 20 ml of 10% solution)

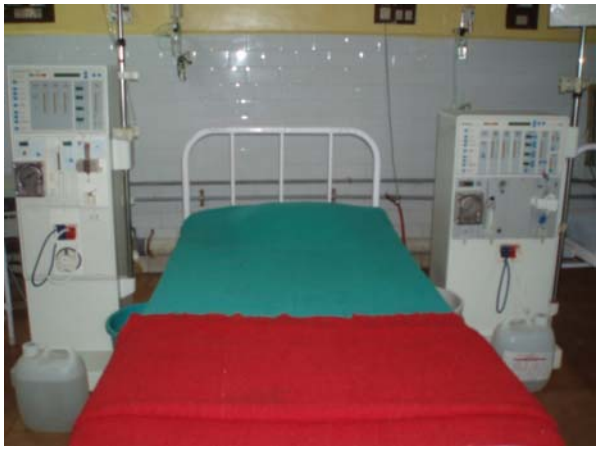
7) Nutrition : Restriction of dietary protein (0.6 g / kg / day), carbohydrate (100 g / day), enteral or parenteral nutrition .(if recovery prolonged or patient very catabolic)

8)Indication for dialysis : Clinical evidence (symptoms or signs) of uremia, intractable intravascular volume overload, hyperkalemia or severe acidosis resistant to conservative measures? Prophylactic dialysis when urea > 100 – 150 mg / dl, or creatinine > 8-10 mg / dl.

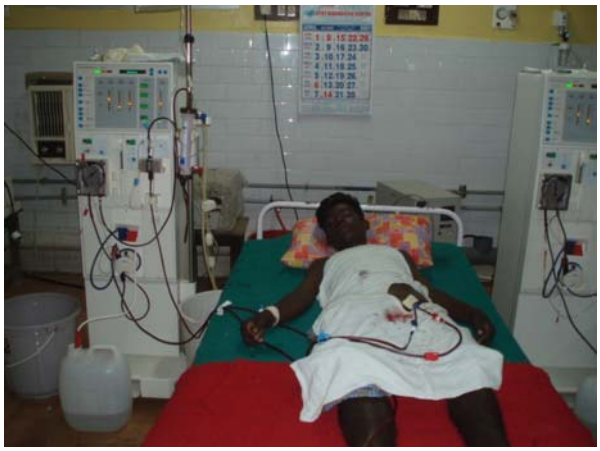
Severe hyperkalemia may be present in the course of renal failure in patients with intravascular haemolysis and may necessitate immediate dialysis. With effective management, oliguria resolves in 2-3 weeks but may be persist in patients with acute cortical necrosis. Early administration of ASV prevents renal damage however severe the coagulation abnormality (Vijeth. S.R. et al 1997). (107) In contrast, according to Chen J.B. et al 1997, (36) early administration of ASV cannot be too strongly emphasized to prevent development of ARF.

Newer agents under trial includes : Natriuretic peptides – in oliguric renal failure, omega –3 fathyacids,adhesin molecule,**growth factor** – Epidermal growth factor, hepatocyte growth factor and insulin growth factor – reduce the extent of renal dysfunction and accelerate the recovery of kidneys,**replacement therapy** in addition to hemodialysis, peritoneal dialysis, continous veno venous hemofiltration, continuous arterio venous hemofiltration may be advocated.

PERITONEAL DIALYSIS



HAEMODIALYSIS ROOM



HAEMODIALYSIS

Outcome and long term prognosis of ARF :

The mortality rate among patients with ARF approximates 50% and has changed little over the past 30 years, vary greatly depending on the cause of ARF.Oliguria at time of presentation and a rise in serum creatinine of > 3 mg / dl are associated with a poor prognosis and probably reflect the severity of renal injury and of the primary illness. Mortality rates are higher in older debilitated patients and in those with multiorgan failure. Most patients who survive an episode of ARF recover sufficient renal function to live normal lives. However, 50% have subclinical impairment of renal function or residual scarring on renal biopsy. Approximately 5% of patients never recover function and require long- term renal replacement with dialysis or transplantation.

MATERIALS AND METHODOLOGY

All patients admitted to the medial wards of Government Rajaji Hospital, with history of snakebite from July 2006 to June 2007 were included in this study. The study was a prospective one. The patients of both sexes of all age group excluding the paediatric group were included in this study.

Inclusion Criteria :

i) Patients with history of snake bite with cellulitis either with bleeding diathesis or with prolonged clotting time or both.

ii) Patients with history of snake bite with oliguria irrespective of the number of days since time of bite.

Exclusion Criteria :

i) Patients with history of snakebite with any neurological problems such as ptosis, respiratory failure etc.

ii) Patient without bite mark.

A detailed history was recorded from all patients, with special emphasis on the following points, 1.Snakebite in relation to time of bite, number and site of bite, whether tourniquet applied or not. 2.Any bleeding diathesis including bleeding from the bitten area/ bleeding gums/ haematamesis/ Malena/ haemoptysis/ haematuria/ epitaxis and their time of onset. 3.Pre existing illness if any, mainly history in relation to severe anaemia. 4.History in relation to urine output, colour of the urine, and the time of onset of oliguria or anuria if any, since time of bite.

Examination of the patients with special reference to :

1. Site of the bite, look for bite mark, any local incision, bleb, blisters, skin necrosis, sloughing and gangrene if any, and regional adenitis and cellulitis. 2. Vital signs – pulse, blood pressure, temperature, respiratory rate and the level of consciousness. 3.Look for anaemia, jaundice, pedal edema, priorbital edema and stigmata of renal failure.

Investigations :

Urine analysis for albumin, sugar, RBC's deposits, bilesalts, bile pigments. Blood – TC, DC, ESR, Hb%, bleeding time, clotting time, peripheral smear for

fragmented RBC's, platelet counts, fibrinogen and reticulocyte count. Blood urea, creatinine and electrolytes. ECG, USG abdomen, CT brain whenever needed. The investigations were done on the day of admission and whenever needed.

Management aspects : Focus on the following :

1.Onset of treatment since bite. 2.Total number of vials of antivenom used. 3.The supportive therapy for acute renal failure such as lasix, dopamine and its dose and days. 4.Avoidance of nephrotoxic drugs. 5.Blood transfusion and treatment for circulatory failure and hypotension. 6.Peritoneal and haemodialysis, number of cycles and days. 7.Outcome of medical management. 8.Any other complications noted other than renal failure. 9.If the outcome was fatal – time of death since time of bite, if possible trace out the probable cause of death.

CLINICAL OBSERVATION

This study was conducted on 107 patients admitted to medical wards of Madurai Government Rajaji Hospital during the period from July 2006 to June 2007.The study was a prospective one. Both male and female cases were taken for the study.

1.Renal failure – Incidence :

Totalno.of cases	Renal failure	Percentage
107	25	23.4

Incidence of renal failure	25/107	-	23.4%
Oliguric renal failure	20/25	-	80%
Non oliguric renal failure	5/25	-	20%

2.Sex Distribution :

A total of 107 cases were taken for study of which 75 cases were male and the remaining 32 were female.

i) Total Distribution :

Sex	No.of patients	Percentage
Male	75	70.1
Female	32	29.9
Total	107	100

ii) Sex – Renal failure :

Sex	Total no of patients	Renal failure	
		No.of patients	Percentage
Male	75	17	22.66
Female	32	8	25
Total	107	25	23.4

iii) Sex – Death :

Sex	Total no of patients	Death	
		No.of patients	Percentage
Male	75	3	4
Female	32	0	-
Total	107	3	2.8

The data shows that most of the snakebite victims were males.

The renal failure incidence

Total 25/107 - 23.4%

Male 17/75 - 22.66%

Female 8/32 - 25%

The Death Incidence

Total 3/107 - 2.8%

Male 3/75 - 4%

Female - 0

3.Age Distribution :

i)Total Distribution

Age (yrs)	Male		Female		Total	
	Envenomation	%	Envenomation	%	Total	%
14-30	35	46.7	18	56.3	53	49.5
31-40	14	18.7	4	12.5	18	16.9
41-50	11	14.7	4	12.5	15	14.0
51-60	11	14.7	6	18.7	17	15.9
> 60	4	5.2	0	-	4	3.7
Total	75	100	32	100	107	100

ii)**Age – Renal Failure** :

Age(yrs)	Male			Female			Total		
	Envenomation	Renal failure	%	Envenomation	Renal failure	%	Envenomation	Renal failure	%
14-30	35	9	25.7	18	3	16.7	53	12	22.6
31-40	14	2	14.3	4	1	25	18	3	16.7
41-50	11	2	18.2	4	1	25	15	3	20
51-60	11	2	18.2	6	3	50	17	5	29.4
> 60	4	2	50	-	-	-	4	2	50
Total	75	17	22.7	32	8	25	107	25	23.4

iii) Age - Death

Age (yrs)	Male			Female		
	Envenomation	Death	%	Envenomation	Death	%
14-30	35	2	5.7	18	-	-
31-40	14	1	7.1	4	-	-
41-50	11	-	-	4	-	-
51-60	11	-	-	6	-	-
> 60	4	-	-	-	-	-
Total	75	3	4	32	-	-

Age of study group ranged between 14-70 years

49.5% of them were below 30 years

80.4% of them were below 50 years

19.6% of them were above 50 years

Incidence of renal failure :

14-30 years of age 12/53 - 22.6%

14 – 50 yrs of age 18/86 - 20.9%

> 60 yrs of age 2/4 - 50%

4.Site of Bite :

Site of Bite	No.of cases	Percentage
Lower limb	88	82.25
Upper limb	18	16.82
Back	1	0.93
Total	107	100

5.Tourniquet Distribution :

No.of cases treated with tourniquet - 67/107 - 66.62%

No.of cases not treated with tourniquet - 40/107 - 37.38%

Tourniquet	Envenomation		Renal failure		Death	
	Total	%	Total	%	Total	%
Yes	67	66.62	16	23.9	1	1.5
No	40	37.38	9	22.5	2	5
Total	107	100	25	23.4	3	2.8

The Renal failure Incidence :

Tourniquet group - 16/67 - 23.9%

Non -tourniquet group - 9/40 - 22.5%

The Death Incidence :

Tourniquet group - 1/67 - 1.5%

Non -tourniquet group - 2/40 - 5%

6.Bleeding diathesis – Distribution :

Total number of cases presented with bleeding diathesis - 31 cases

i) Bleeding diathesis Incidence - 31/107 - 28.97%

Time interval since bite (hrs)	No.of cases	Percentage
0-2	10	32.26
3-6	11	35.48
7-24	9	29.03
25-48	1	3.23
Total	31	100

ii) **Time interval since bite** (hrs)

0 – 6 - 21 cases - 67.74 %

0 – 24 - 30 cases - 96.77 %

25-48 - 1 case - 3.23%

iii) **Type of bleeding – Distribution** (31/107)

Type	No.of cases	Percentage
Bleeding gums	14	45.16
Haematuria	2	06.45
Haematamesis	4	12.90
Haemoptysis	1	3.23
Malena	2	6.45
Multiple sites	8	25.81
Total	31	100

7.Bleeding diathesis and Renal failure :

Bleeding diathesis		Renal failure	
	No.of cases	Total cases	%
Yes	31	16	51.61
No	76	9	11.84
Total	107	25	23.4

Bleeding diathesis with renal failure - 16/31 - 51.61%

Bleeding diathesis without renal failure - 15/31 - 48.39 %

Prolonged clotting time and bleeding diathesis - 27/31 - 87.1%

Normal clotting time and bleeding diathesis - 4/31 - 12.9%

8.Clotting time distribution :

No.of cases with prolonged clotting time - 101/107 - 94.39%

No.of cases with normal clotting time - 6/107 - 5.61 %

i) **Clotting time and Renal failure** :

		Renal failure	
CT	No.of cases	No.of cases	%
Prolonged	101	21	20.8
Normal	6	4	66.7
Total	107	25	23.4

Prolonged CT with renal failure - 21 / 101 - 20.79%

Normal CT with renal failure - 4 / 6 - 66.66%

ii) **Number of ASV vials required for normalization of clotting time**

Range → 4- 25 vials

Mean → 13 vials

9.Distribution of onset of treatment (ASV) and Renal failure :

Time of onset of Treatment (hrs)	Envenomation		Renal failure	
	No.of cases	%	No.of cases	%
1 – 12	89	83.18	18	20.2
13 – 24	12	11.21	2	16.7
25 – 48	4	3.74	3	75
> 48	2	1.87	2	100
Total	107	100	25	23.4

Renal failure Incidence :

Onset of treatment (ASV) (1-24 hrs) - 20/101 - 36.9%

Onset of treatment (25-48 hrs) - 3 / 4 - 75%

Onset of treatment > 48 hrs - 2 / 2 - 100%

10.Distribution of Relationship between preexisting anaemia and Renal failure

Anaemia	Envenomation		Renal failure	
	No.of cases	%	No.of cases	%
Yes	11	10.28	10	90.91
No	96	89.72	15	15.63
Total	107	100	25	23.4

Renal failure Incidence :

Patients with pre existing anaemia - 10/11 - 90.91 %

Patients without preexisting anaemia- 15/96 - 15.63%

11.Distribution of time of onset of renal failure :

Time (hrs)	No.of cases	Percentage
< 12	5	20
13 – 24	11	44
25 – 36	4	16
37 – 48	3	12
> 48	2	8
Total	25	100

Time of onset of renal failure

Range - (1 ½ hrs-56 hrs)

Mean - 25hrs

Renal failure incidence

Within 24 hrs -16 cases -16/25 - 64%

After 24 hrs - 9 cases -9 / 25 - 36%

12.Distribution of probable etiology of renal failure :

S.No.	Probable etiology	No.of cases	%
1.	DIC	12	48
2.	DIC with hypotension	4	16
3.	DIC with shock and capillary leak syndrome	2	8
4.	DIC with shock and sepsis	1	4
5.	Direct nephrotoxicity	6	24
	Total	25	100

13.Distribution of management of renal Failure :

No.of renal failure cases	Supportive treatment	Outcome	
		Improved	Not improved
25	25	14(56%)	11(44%)

Outcome of supportive therapy for renal failure :

Total no.of renal failure cases - 25

All 25 cases treated with supportive therapy

Outcome : Improved - 14/25 - 56%

Not improved- 11/25 - 44%

Total no.of cases not improved with supportive treatment – 11 cases

No.of cases treated with hemodialysis - 7 cases

No.of cases treated with peritoneal dialysis- 4 cases

14.Outcome of hemodialysis :

Total No.of cases	Improved	Not improved
7	5 (71.43%)	2 (28.57%)

Total No.of cases treated with hemodialysis - 7 cases

Improved - 5/7 - 71.43%

Notimproved - 2/7 - 28.57%

Total no.of cycles (Hemodialysis)

Range - 2 – 12

Mean - 6 cycles

15.Outcome of peritoneal dialysis :

Total No.of cases	Improved	Not improved
4	-	4 (100%)

Total no.of cases treated with peritoneal dialysis - 4 cases

Improved - Nil

Not improved - 4/4 - 100%

16.Complications of Snake envenomation :

S.No.	Complications	No.of cases	%
1.	ARF	25	23.36
2.	Bleeding diathesis	31	28.97
3.	Anaemia	11	10.28
4.	Hypotension / shock	8	7.48
5.	Compartment syndrome	5	4.67
6.	Gangrene	2	1.87
7.	ICH	1	0.93
8.	Sepsis	1	0.93
9.	Jaundice	1	0.93
10.	Stroke (unusual)	1	0.93
11.	Vitreoushaemorrhage(unusual)	1	0.93

17.Distribution of death due to envenomation in relation to cause, time, and interval since bite .

The study of 107 cases of snakebite envenomation, death occurred in 3 cases - 3/107 - 2.8% .

Analysis of death and it`s distribution

S.No.	Cause	Death – time interval since bite (hrs)	Time interval for onset of treatment (hrs)
1.	DIC with ICH, ARF	72hrs	4 hrs
2.	DIC, circulatory failure, ARF and sepsis	36hrs	5 hrs
3.	DIC, circulatory failure, ARF and capillary leak syndrome	84hrs	3 hrs

Analysis of cause of death in snake envenomation :

i) DIC with ICH / ARF - 1 case

ii) DIC, circulatory failure, ARF and sepsis - 1 case

iii) DIC, circulatory failure, ARF and capillary leak syndrome – 1case

Analysis of time interval of death since bite

Range - 36hrs - 84hrs

Mean - 64hrs

Analysis of time interval for onset of treatment :

Range - 3 – 5 hrs

Mean - 4hrs

DISCUSSION

Of the 107 patients included in this study with haemotoxic snake envenomation acute renal failure occurred in 25 patients. While analysis, multiple factors were found responsible for the onset of renal failure.

Incidence of renal failure

In this study, it was found to be 23.4% (25/107). The incidence of oliguric renal failure was 80% (20/25) and nonoliguric renal failure was 20% (5/25). A study in PGI Medical science chandigarh by Dr. Chugh et al 1984 it was 28.6% (45/157), 1989 it was 5% - 30%. A study in Sardarjang hospital in New Delhi by Banerjee and Siddiqui 1976, it was observed 16.9%. The study by Verma et al 1982, Chugh et al 1984, Mather and Raja Rathinam 1987, it was 13-32%. A study from JIPMER by Vijeth, Dutta 1997 it was observed 32.5%. A study in Seth G.S. Medical College by Mitral B.V. 1994 it was 16.2% and the incidence of oliguric renal failure was 100%.

So the incidence of renal failure in our hospital in this study was 23.4% and when compared to other studies was neither very high nor low.

Sex and Renal failure

In this study of 107 cases 70.1 % (75/107) were males and 29.9 % (32/107) were females. Among them the percentage of renal failure was 22.7% (17/75), 25% (8/32) respectively. A study in sardajang hospital (1970-74) showed that 75% were male and 25% were female.

It was observed from both the studies that males are affected more and was mainly attributed to outdoor nature of work. Regarding the incidence of renal failure

in male and female 22.7 and 25% respectively, there was no obvious reason and again information of previous study related to sex is not available.

Incidence of Death

In this study, it was observed as 2.8% (3 / 107). In a study from JIPMER by Vijeth, 1996, it was noted as 5%. A study from Saudi Arabia by Hisham and Mahaba the case fatality rate was 2.9%. According to study by Kulkarni 1981, it was reported as 5.2%. According to WHO the global annual mortality of 40,000 of which 10% is from India. A study in Chennai Medical College, the death rate was 10% (1989).

The study of our hospital mortality showed close relation to other previous studies.

Age and renal failure

From this study, it was observed that the percentage of envenomation decreases with increase in age. ie. Below 30 years it was 49.5% and below 50 years it was 80.4% and above 50 years it was 19.6%. The renal failure incidence increase with increase in age i.e. age less than 30 years it was 22.6% and age less than 50 years it was 20.9% whereas in more than 60 years of age it was 50%.

The high incidence of renal failure noted in elderly patients, may be attributed to anatomical and physiological changes occurring due to ageing process. The snake venom, as it passes through the renal tubules may produce direct nephrotoxic effect.

Site of Bite

From this study it was observed that the most frequent site of bite was the lower extremity 82.25% (88/107) and suggests that in most cases the snake is inadvertently trodden upon.

Tourniquet and renal failure

The tourniquet is usually applied in order to prevent the spread of venom following snakebites. In this study 67 out of 107 cases (66.62%) used tourniquet as a first aid measure. In this evaluation of renal failure in relation to tourniquet are 23.9% whereas in the cases without tourniquet it was 22.5% and hence, no difference between tourniquet group and non-tourniquet group was noted. The death incidence in relation to tourniquet, it was observed that the death incidence was more with non-tourniquet group (5%) when compared with the tourniquet group (1.5%).

The study of Amaral CF, Toxicon 1998, in 97 cases stated that there was no difference between tourniquet group and non-tourniquet group in the frequency of renal failure and other complications, number of deaths and their study stress the ineffectiveness of tourniquet. The above study was controversial to the present study.

A case report from Department of clinical sciences, University of papua, New Guinea showed tourniquet induced ischaemic damage and rhabdomyolysis causing acute renal failure and highlights the danger of tourniquet use and sudden release of tourniquet.

The other consequences of tourniquet are damage to peripheral nerve, (Lateral popliteal nerve) increased fibrinolytic activity, congestion, swelling, increased bleeding and increased local effect of venom. (Stewart et al 1981). The subsequent release of tourniquet leads to sudden flooding of accumulated venom from bitten site to systemic circulation. (Robert Otten et al 1986).

Because of the dangers associated, general concensus is against the application of tourniquet except in certain conditions like bitten by neurotoxic snakes or if medical attention is delayed for 1-2 hrs enroute to hospital (Warrell et al 1996).

Bleeding diathesis

In this study, it was noted that bleeding diathesis rate was 28.97% (31/107). It was also noted in this 31 cases, 67.7% of cases bleeding occurred with in 6 hrs and 96.8% of cases bleeding occurred with in first 24 hrs. The onset of bleeding ranges from 30 minutes to 40 hours and so observation for bleeding diathesis is essential from the beginning.

The common type of bleeding noted according to this study was bleeding gums 45.16%. Next to this, haematamesis 12.9%, haematuria 6.45%, malena 6.45%, and haemoptysis 3.23%. The incidence of multiple bleeding sites was 25.81%. Haematamesis and bleeding gums were the commonest types of systemic bleeding following viperine bite. (Mahasundanas et al 1980).

It was also observed that the Incidence of renal failure in the cases with bleeding diathesis was 51.61% (16/31) and cases without bleeding diathesis was 11.84% (9/76). According to present study bleeding diathesis secondary to disseminated Intra vascular coagulation is enough to produce hypotension and it is the important cause of acute renal failure in haemotoxic snake envenomation.

A study by Chen JB et al 1997, Factors contributing to acute renal failure following viperine bite are haemorrhage, hypotension, DIC, hemolysis and Rhabdomyolysis.Intravascular hemolysis and DIC contributed to the development of acute Renal failure. (chugh KS et al 1975) DIC is the important cause of renal

dysfunction in most of the cases of ARF. (Vijeth ST et al 1997). Acute Renal failure often associated with haemorrhagic diathesis, intravascular hemolysis and Rhabdomyolysis. (Sitprija V et al 2006).

The above studies strongly support our present study.

Clotting Time

In our study it was observed that prolonged clotting time was noted in 94.39% of cases. (101/107). The incidence of renal failure in the cases with prolonged clotting time was 20.8% (21/101) where as, in cases with normal clotting time it was 66.7% (4/6). According to present study, the acute renal failure occurred in these cases in the absence of DIC, which might be due to direct nephrotoxic action of venom.

Direct toxicity caused by venom could be responsible for renal dysfunction in certain cases. (Vijeth SR et al 1997) (Win-Aung 1998). Although hypotension, hemolysis and DIC are likely to be important pathogenetic factors, a direct nephrotoxic effect of the venom on the kidney in producing ARF cannot be excluded. (Chugh KS et al 1984).

The above studies strongly supports direct nephrotoxic action of venom and also supports present study.

The study by Bhat 1974 in India, it was observed that 60-270 ml (average of 12vials) needed to resume the clotting time normal .In the present study, the dose of ASV used among envenomation cases for normalization of clotting time was 40 ml – 250 ml. The mean was 13vials. When compared with Bhat study of ASV requirement, not of much difference in the dose utilization.

Onset of Treatment since Bite

ASV should be given with same sense of urgency as one shown while using streptokinase in acute infarction. When the onset of treatment with ASV was within 24 hrs, the incidence of renal failure observed was 36.9% (20/101). In cases with onset of treatment with ASV after 48 hrs, the incidence of renal failure was 100% (2/2). So, delay in onset of treatment since bite resulted in renal failure. In patients with early treatment with ASV if renal failure develops, it may be due to either severe envenomation or inadequate dose of ASV.

The study of renal failure in 40 cases of Viper envenomation by Vijeth ST et al, the use of ASV with in 8 hrs, no renal abnormality occurred. The study by Narvencar K. et al 2006 stated that early administration of ASV is beneficial in preventing complications however severe is the systemic envenomation.

Pre existing anaemia and renal failure

The preexisting anaemia was noted in 11 out of 107 cases. The study of renal failure in cases without anaemia (96/107) was 15.6% and in cases with anaemia (11/107) was 90.9%. So the presence of severe anaemia may aggravate the process of ongoing renal failure. The renal ischaemia is a consequence of envenomation. The presence of anaemia may worsen the hypoxia and persistent hypoxia in outer medulla ended in acute tubular necrosis. (The kidney by Brenner).

Time of onset of renal failure since bite

The present study showed that the range of time of onset of renal failure was 1 ½ hrs – 56 hrs. The mean was 25hrs. It occurred with in 24 hrs in 64% of cases and after 24 hrs in 36% of cases. The previous study it was found that the renal

failure occurred within 24 hrs and lasted for 17-26 hrs. (Chen JB et al 1997) The range of time of onset of renal failure according to Sit prija et al 1974 was few hours to 96 hours. According to Chugh et al 1984 it was with in hours to 3 days.

The Disseminated intravascular coagulation, the complication of envenomation, can occur as early as with in 2 hours. In DIC there is activation of coagulation cascade, which leads to microthrombi in number of sites including renal vasculature. So it is possible for renal failure to occur earlier. (Chugh et al 1984, Warrell et al 1977, Sitprija et al 1974)

Etiology of Renal failure

In this study, the etiology of renal failure was multifactorial. In 48% of cases (12/25) DIC play a role in the genesis of renal failure and in 16% (4/25) of cases the etiology was DIC with hypotension and in 8% (2/25) was DIC with shock and capillary leak syndrome and in 4% (1/25) was DIC, shock and sepsis and in 24% (6/25) the etiology of renal failure was possible direct nephrotoxic action of venom.

A study of 8 cases of renal failure by Chugh KS, Bket BK and others regarding the etiology, Intravascular hemolysis and DIC contribute to 75% (6/8) and direct nephrotoxicity in 25% (2/8). Studies of 45 cases of renal failure, by Chugh KS et al in 1984, the etiology of renal failure was multifactorial. (Hypotension, DIC, hemolysis and direct nephrotoxicity) A study of 13 cases in JIPMER, 61.35% (8/13) DIC with fibrinolysis was the etiological factor.

Management aspects of renal failure

The supportive therapy in the form of careful rehydration, Inj. lasix, Inj. dopamine and blood transfusion were attempted. From the present study, it was

observed that 14 cases out of 25 (56%) improved from renal failure by supportive therapy alone. The patients not improved with supportive therapy were 11. The hemodialysis was attempted in 7 out of 11 cases. 5 cases (71.4%) improved and 2 cases (28.6%) not improved. The above 2 cases was diagnosed as acute on CRF with the help of other investigations.

The peritoneal dialysis was attempted in 4 out of 11 cases. One case not improved and diagnosed as acute on CRF with the help of other investigations. 3 cases died of renal failure with other complications of envenomation.

It was observed by a study of 8 renal failure cases by Chugh et al 1975, by histopathologically, acute tubular necrosis in 52.5% (5/8) and bilateral acute cortical necrosis in 37.5% (3/8). The (2/5) cases with ATN improved with conservative treatment and (3/5) improved with dialysis. In bilateral ACN inspite of dialysis all 3 cases died. By effective treatment oliguria resolved in 4-5 days. (chugh et al 1986)

Complications of Haemotoxic envenomation

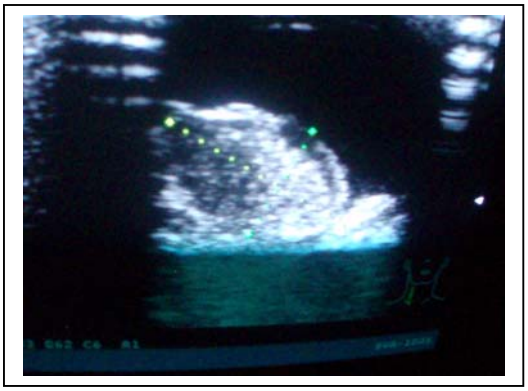
The study of the complications in 107 cases, it was found that ARF in 25 cases (23.6%), hypotension and shock in 8 cases (7.48%), anaemia in 11 cases (10.28%). bleeding diathesis in 31 cases (28.97%), compartment syndrome in 5 cases (4.67%), gangrene in 2 cases (1.87%) and sepsis, jaundice, stroke, ICH and vitreous haemorrhage in 1 case each (0.93%).

Unusual complications of haemotoxic envenomation

In this study, there were 2 cases presented with unusual complications. One case presented with ARF and left vitreous haemorrhage and intra retinal haematoma with probable etiology of DIC. The second case presented with right hemiparasis

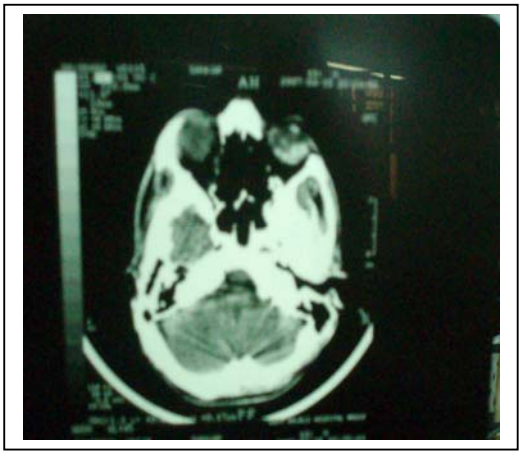
UNUSUAL MANIFESTATION
LEFT VITREOUS HAEMORRHAGE

SUBCONJUNCTIVAL HAEMORRHAGE



'B' SCAN (USG-LEFT EYE) SHOWS VITREOUS HAEMORRHAGE

HAEMATURIA

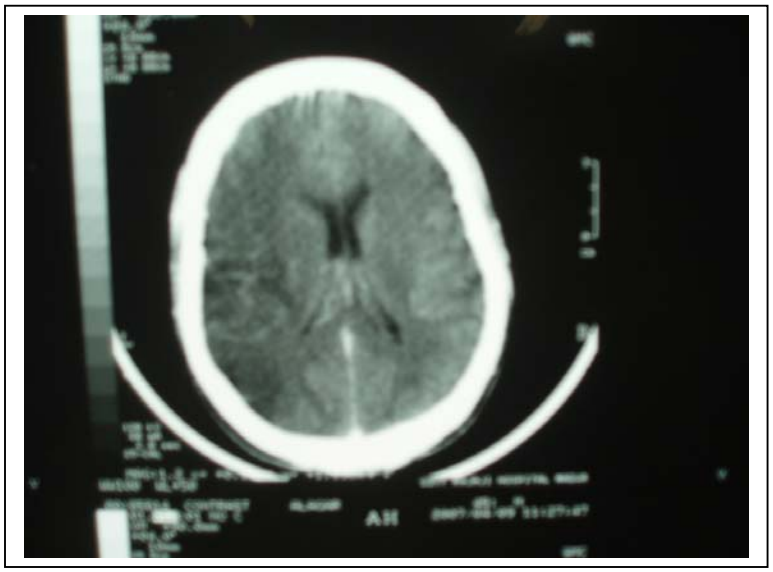


CT BRAIN SHOWS LEFT EYE VITREOUS HAEMORRHAGE

18- Year -old Shankar, presented with bleeding from multiple sites including Left Vitreous haemorrhage, and ARF. He was treated with ASV, HD, his renal function recovered completely with partial recovery of left eye vision.

UNUSUAL MANIFESTATIONS (STROKE)

Right UMN Facial palsy – Deviation angle of mouth to left



CT brain shows – left temparo parietal infarct

and right UMN facial palsy with in 4 hrs of viper bite with wernick's aphasia and normal renal function, CT brain showed left temparo parietal infarct.

Analysis of Death :

Analysis of cause of death in Snake envenomation :

In this study of 107 cases, death occurred in 3 cases ie. 2.8%. Renal failure occurred in all the 3. One case died due to ICH and one case died of circulatory failure and sepsis and one died due to circulatory failure and capillary leak syndrome.

A study of cause of death in 9 cases by Haudy DC 1986, there was prolonged hypotension and multiorgan failure in (5/9), Intestinal haemorrhage in (1/9) and unknown cause. (3/9) Another study showed that the distribution of cause of death by Aebuqueoge, Reberio (1988-93), it was acute renal failure (34-79%), shock (18-41%) and sepsis. (18-41%) Among the renal failure of 23 cases, the incidence of death in ATN was 17.4% and bilateral ACN was 37.9% (Chugh and Chakaravarthi1984)

Analysis of time interval of Death since bite

In this study, the time interval of death since bite ranges from 36hrs to 84hrs. Mean was 64hrs. The onset of death in viper bite occurs in a day to 3 days of bite.

The previous study available in relation with onset of death since bite was range from 1-6 days.(Banarji 1976) 29.4% death occurred in first 2 days. 67.6% of death occurred with in 5 days. (Aebuqueoge, Reberio 1988-93).

Analysis of Time interval for onset of treatment

In the death cases, the time interval for onset of treatment observed by present study ranges from 3-5 hrs. The mean was 4hrs. A study of 9 death cases by Haudy DL 1986, the serotherapy (ASV) was administered within 4 hours.

CONCLUSION

1. In this study, the incidence of acute renal failure was 23.4% among the 107 cases of snake envenomation (25/107). The etiology of renal failure was multifactorial. The DIC and circulatory failure were the common etiological factors. DIC with capillary leak syndrome, DIC with sepsis and direct nephrotoxicity were considered as the other main etiological factors.
2. The Incidence of renal failure was observed more with increase in the age of the victims and it was more in patients with delayed onset of treatment. There was no difference in the incidence of renal failure among both sexes and tourniquet group and non-tourniquet group. But, according to present study tourniquet application reduce the incidence of death.
3. The Incidence of renal failure was more in the cases with preexisting severe anaemia (Hb < 8 g%)
4. The incidence of renal failure was more in the cases with delayed onset of treatment with ASV since bite. The optimum dose of ASV used for normalization of clotting time from this study was 13 vials.
5. Bleeding tendency occurred in 28.97% (31/107) cases. In 96.8% of cases bleeding occurred within first 24 hours. From this study, the commonest type of bleeding observed was bleeding gums. The haematamesis and haematuria were next common type of bleeding.
6. The incidence of renal failure was more in the cases with bleeding diathesis (DIC and circulatory failure were the common etiological factors.)

7. The incidence of renal failure was more in the cases with normal clotting time. (Indicates the direct toxic effect of venom on the kidney).
8. 64% of cases (16/25) the onset of renal failure was before 24 hrs. Only in 36% of cases (9/25) the onset was beyond 24 hrs. DIC with microthrombi in multiple sites including renal vasculature was the possible explanation for the early onset of renal failure.
9. The supportive therapy with careful rehydration, and drugs such as lasix, dopamine and blood transfusion help in the recovery of renal failure in 56% of patients. (14/25). Patients not improved with supportive therapy were 11. Hemodialysis was attempted in 7 out of 11 cases. 5/7 recovered and 2/7 not recovered and diagnosed as acute on CRF. Peritoneal dialysis was attempted in 4 out of 11 cases. 1/4not recovered and diagnosed as acute on CRF. 3 / 4 died of ARF with other complications of snakebite envenomation.
10. The complications other than renal failure and hypotension were also noted. ICH, compartment syndrome, Jaundice, gangrene, sepsis also were observed in few cases. Unusual complications like vitreous haemorrhage and stroke were observed in this study.
11. The incidence of death was 2.8% among 107 cases. The probable cause of death were DIC/ ARF/ ICH in one case, ARF / DIC / circulatory failure / sepsis in 2nd case and ARF / DIC / circulatory failure / capillary leak syndrome in 3rd case. Thus, more than one etiological factor was observed. The death occurred within 84hrs. In all 3 cases ASV administered within 5 hours of bite.

SUMMARY

The snakebite envenomation is preventable by the measure discussed earlier. The acute renal failure in snakebite is preventable to a certain extent. The onset of renal failure in haemotoxic envenomation depends upon the factors like the severity of envenomation, the time of onset of serotherapy since bite, initial maximum and optimum dose of antisnake venom, degree of bleeding diathesis, degree of DIC and presence or absence of circulatory failure.

The correction of preexisting severe anaemia by blood transfusion, avoidance of nephrotoxic drugs, early normalization of clotting time is helpful in the prevention of onset and retard renal failure. The role of heparin is still controversial. The supportive therapy, haemodialysis help to reduce mortality in renal failure among snake envenomation cases.

SUGGESTIONS

Snakebite is more common in rural and semi urban areas than in urban areas where snakes are more prevalent. The areas should be kept clean to prevent infiltration by snakes and rodents. Anti rodent measures should be vigorously carried out in all newly developing areas.

Avoid nocturnal activity in the snake prevalent areas. No attempt should be made to kill the snakes on seeing them. With improving economic standard, farmers should be encouraged and motivated to use low cost foot wears and gloves and carry torch light while walking in snake infested areas. Piles of rubble, stones, bricks, termite mounds,deep vegetations thick foliage must be approached causiously specially more so after rains. Every effort should be made to prevent and treat anaemia.

Dissemination of information regarding readily available effective treatment may drastically prevent the morbidity and mortality. Over emphasis on first aid can be dangerous because it`s value is debatable and too much valuable time is wasted in it`s administration. All primary health centers (PHC`s) should be provided with adequate anti snake venom and drugs for anti allergic measures. Species identification is not necessary since we are using polyvalent antivenom. ‘Snakebite is not synonymous with snakebite poisoning and all poisoning does not end in death if properly treated.’

BIBLIOGRAPHY

1. Philip E. Snake Bite and Scorpion sting. Chapter 28 in Paediatric and Neonatal emergency care. Ed. RN. Srivatava 1994. PP 227-234.
2. Bhetwal BB, et al, Snakes and Snake bite in Nepal, Tropical Doctor, 1998 ; 28 (4) : 193-195.
3. Chippaux JP, Snakebites : appraisal of the global situation Bull. WHO 1998 ; 76(5) : 515-524.
4. Chippaux JP, Snake Bite Epidemiology in Benin (West Africa), Toxicon 1998 ; 27 : 37.
5. Snow RW, The prevalence and morbidity of snakebite and Treatment seeking behaviour among a rural Kenyan population Ann. Trop Med Parasitol 1994 ; 88 : 665-671.
6. Swaroops, Grab B, Snake Bite mortality in the World Bull. WHO, 1954 ; 10 : 35-76.
7. Hati aK, et al, Epidemiology of Snake bite in the district of Burdwan, West Bengal. J. Indian Med. Assoc. 1992 ; 90(6) : 145-147.
8. Mittal BV, Acute Renal failure following Poionous Snake Bite, J PGH 1994 : 40 (3) ; 123-126.
9. K.S. Girish et al – Snake Venom hyaluronidse – AR evidence for isoforms and extracellular matrix degradation. Molecular and cellular Biochem. 2004 ; 240 (2) : 105-110.
10. N. Sharma et al. Snake envenomation in a North Indian Hospital. Emerg. Med J. 2005 ; 22 : 118-120.

11. Kingston ME. Management of Snake bite in Saudi Arabi, King Fascial Spcl. Hospital Med. J. 1981 ; 1 : 87-94.

12. Priya Sexena – Snake venom could ease arthritis pain. Treatement PG News 2007.

13. Joseph.L. Mathew et al – Ophitoxaemia – Delhi 2006.

14. Hansdak SG et al, A clinico epidemiological study of Snake bite in Nepal. Tropical Doctor. 1998 ; 28 : 223-226.

15. When a Cobra strikes, The Hindu Magazine 2004

16. Paul VK. Animal and Insect bites. In Singh M (Ed) Medical emergencies in children. 2nd Ed. NewDelhi. Sagar Pulications, 1993.

17. Warrel DA et al Venoms and Toxins – Poisons of animals and plants. Oxford Text book of Medicine, 3rd Ed. Vol I 1996.

18. Romano E et al – Clinical course and histopathology of Acute oliguric and non oliguric renal in sufficiency. Minerva med 1985 ; 76 (21) : 985-992.

19. Saini RK et al, Snake bite poisoning. JA PI 1984 ; 32 (2) : 195-197.

20. Pukrittayakamee S. et al. A competitive Radio immuno assay using a monoclonal antibody to detect factor X activator of Russell's viper venom. Toxicon 1987 ; 25 (7) : 721-729.

21. Reddy KS. Essentials of forensic Medicine and Toxicology.

22. Reid HA. Animal poisons. Manson's Tropical diseases 1982 ; 544 – 546.

23. Ari aratnam CA et al. A new monospecific ovine Fab Fragment antivenom for Treatment of envenoming Am I Trop Med Mgg 1999 ; 61 (2) : 259-265.

24. Silveria PV et al. Nonvenomous Snakebite and snakebite without envenoming in a Brazilian Teaching Hospital. Rev. Inst. Med. Trop Sao Pauto 1992 ; 34 (6) : 499-503

25. Haywood BJ et al, Investigation and Treatment of snake bite toxicon, 1998 ; 36(3) : 431 – 446.

26. SitPrija V et al Acute interstitial nephritis in Snak bite Am J Trop Med Hyg 1982 ; 31 (2) : 408-410.

27. Russell FE. Snake venom poisoning philadelphia JB Lippin ott company 1980 ; 235 – 285.

28. Reid HA, Venomous bites and stings, 1979

29. Reid HA et al. The management of snake bite,Bull WHO 1983; 63 : 885-895

30. Trevett AJ et al. Analysis of referral letters to assess the management of poisonous snakebite in rural population. Trans R soc Trop Med Hug 1994 ; 88 (5) : 572 – 574.

31. Sathyanathan VP et al. Raynaud's phenomenon and gangrene following snake envenomation JAPI 1993 ; 41 (2) : 122-123.

32. Nayak Kc et al, Profile of cardiac complications of Snake bite. Indian Heart J 1990 ; 42 (3) : 185-188.

33. Tony JC et al. Acute myocardial infarctions following snake bite. Trop. Doct. 1995 ; 25(3) : 137.

34. Singh S et al, Acute paraplegia following viper bite. JAPI 2002 ; 50 : 1427-1429.

35. Budzynski AZ et al. Fibrogenolytic afibrinogenaemia after envenomation by Western diamond black rattle snak. 1984 ; 63 : 1-14.

36. Chen JB et al. ARF after snake bite. Zhonghua Yi Xue Za zhi, 1997 ; 59(1) : 65-69.

37. Hatton RA et al. Arboreal pituipers of South east Asia, Trans R soc Trop Med Hyg 1990 ; 84 : 866-874.

38. Acharya VN et al. ARF due to viperine snakebite as seen Tropical Western India. Fail 1989 ; 11(1) : 33-35.

39. Mirtschin PF. Fatal cerebral haemorrhage after snak bite. Med. J Aust. 1991 ; 155 (11-12) : 850 851.

40. Kouyou rndjian JA et al, Fatal extradural haematoma after snake bite. Trans R coc Trop Med Hyg 1991 ; 85 (4) : 552.

41. Myint – Lwin et al Bites by Russell's viper in Burma Lancet 1985. (ii) 1259-1264

42. Vijeth SR et al Correlation of renal status with haematologic profile in viperine bite. Am J Trop Med. Hyg. 1997 ; 56(2) : 168-170.

43. Chugh KS et al. ARF following poisonous snake bite Am J Kidney Dis 1984 ; 4 (1) : 30-38.

44. Chugh KS et al, ARF following snake bite, Am J Trop Med Hyg. 1975 ; 24(4) : 692-697.

45. Gupta PK. Bilateral thalamic haematoma following snakebite. J Asso phy India 1992 ; 40 (8) : 549-550.

46. Adogu AA et al. Hysterical paralysis as a complication of snakebite. Trop geogr Med. 1992 ; 44 (1-2) : 167 – 169.

47. Ariarantham CA et al A Open, randomized comparative trial of two antivenoms for the treatement of envenoming by Srilankan Russell's viper, Trans R soc Trop Med Hyg 2001 ; 95(1) : 74-80.

48. Hung Dz et al. Antivenom treatment and renal dysfunctions in Russell's viper snake bite in Taivan. Trans R Soc Trop Med Hyg 2006 ; 100 (5) : 489 – 494.

49. Panicker JN. Cerebral infarction in a young male following vipr envenomation. JAPI 2000 ; 48 (7) : 744-745.

50. Deva Raj. T. Bleeding manifestations in Snake bite. South East Asian J Trop Med Public Health 1979 ; 10(2) : 255-257.

51. Win – Aung et al, Clinical trial of intramuscular ASV administration as a first aid measure in the field in the management of Russell's viper bite patients. South Asian J Trop Med. Public health 1996 ; 27(3) : 494 – 497.

52. Merchant MR et al. Clinico pathological study of ARF following viper snake bite. JAPI 1989 ; 37 (7) : 430 – 433.

53. Kumar PD et al. Unconsciousness following Snake bite J. Ind. Med. Assoc. 1995 ; 93 (10) : 397-398.

54. Mahapatra BN et al coagulation disorders following viper bite in Orissa. J Indian Med. Assoc. 1992 ; 90 (1) : 12-14.

55. Narvencar K. Correlation between timing of ASV administration and complications in snake bites. JAPI 2006 ; 54 : 717-719.

56. Warrell DA et al, Snake venom opthalmia and blindness caused by the splitting cobra in Nigeria. Am J Trop. Med Hyg 1976 ; 25 : 525-529.

57. Russell FE, Snake venom poisoning, Philadelphia JB Lippincott company 1980 ; 291-350.

58. Clemons R. et al Effects of anti thrombin III and antivenom on procoagulant activity of Russell's viper venom, South East Asia J Trop Med. Publich Health 1995 ; 26(1) : 143-148.

59. Winkler E et al. Decreased serum cholesterol level after snake bite as a measure of severity of envenomation J Lab clin Med 1993 ; 121(6) : 774-778.

60. Ramachandran S et al. EEG abnormalities in patients with snake bites. Am J Trop Med. Hyg 1995 ; 52(1) 25-28.

61. Seiler JG et al Venomous snakebite current concepts of treatment. 1994 : 17 (18) : 707-714.

62. Jorge MT et al, Aeromonas hydrophila soft tissue infection as a complication of snakebite. Ann Trop Med Parasitol 1998 ; 92 (2) : 213 – 217.

63. Gellert GA. Snake venom and insect venom extractor N Engl J Med 1993 ; 329 : 13-22.

64. Forgey WW. More on snake venom and insect venom extractors N. Engl J Med 1993 ; 328 : 516-517.

65. Hayee A. Effect of prolonged poisoning by Russell's vipr venom on blood coagulation, platelets, Fibrinolysis, J pn J Med Sci Biol. 1984 ; 37 (1) : 1-7.

66. Napathorn S et al. Effects of Russell's viper venom on human erythrocyes in vitro, J Nat Toxins 1998 ; 7 (1) : 73-85.

67. Singh S et al Fatal non bacterial thrombotic endocarditis following viperine bite. Intern Med. 1998 ; 37 (3) : 342-344.

68. Thomas PP et al. Randomized trial of antivenom in snake envenomation with prolonged clotting time. Brit Med J. 1985 ; 291 : 177-178.

69. Pe T. et al Field trial of efficacy of local technique in Russell' viper bite patients – South East Asia J Trop Med Publich Health 2000 ; 31(2) : 346 – 348.

70. Russell FE, Snake venom poisoning, Philadelphic JB Lippincott company, 1980 ; 325 – 350.

71. Sheth et al Haemoperitoneum complicating snake bite – rare CT features. Abdom. Imaging 2003 ; 28(6) : 320-321.

72. Reid HA et al, Clinical effect of bites by Malayan viper. Lancet 1983 ; 1 : 617-621.

73. Myint – Lwin et al. Heparin therapy in Russell's viper bite victims with impending DIC. South Asian J Trop Med. Publich health 1989 ; 20 (2) : 271-277.

74. Paul V. Trial of heparin in Viper bites. JAPI 2003.

75. Uberoi HS et al. Hypo pituitarism following snakebite JAPI 1991 ; 39(7) : 579-580.

76. Sellahuva KH et al. Intravenous Ig in the treatment of snake bite envenoming Ceylon Med J 1994 ; 39 (4) : 173-175.

77. Alarn MI et al. Adjuvant effect and antiserum action potentiation by a compound 2 – hydroxyl 4-mythoxy benzoic acid. Isolated from the root extract of the Indian medicinal plant 'Sarsa Parilla'. Toxicon 1998 ; 36 (10) : 1423 – 1431.

78. Alarn MI et al. Vipervenom induced inflammation and Inhibition of free radical formation by pure compound 2 hydroxy 4 methyl benzoic acid : Toxicon : 1998 ;36 (1) : 207-215

79. Hung DZ et al. multiple thrombotic occlusions of vessels after Russell's viper envenoming. Pharmacol Toxicol 2002 ; 91 (3) : 106-110.

80. Shastry JC. Renal failure following snakebite. Am J Trop Med Hyg. 1977 ; 26 : 1032-1038.

81. Win-Aung et al. Renal involvement in Russell's viper bite. Patients without DIC. Trans R SOC Trop Med Hyg 1998 ; 92 (3) : 322-324.

82. Jones Psy et al. Russell's viper venom Stimulater Insulin, Secretion from rat islet of Langerhans. J. Endocrinol. 1993 ; 136 (1) 27-33.

83. Upadyyaya AC et al. Snake bite presenting as acute MI, ischeamic CVA, ARF and DIC. JAPI 2000 ; 48 (11) : 1109-1110.

84. Gundappa RK. Snake Bite induced AIN, Ren fail 2002 ; 24(3) : 369-372.

85. SitPrija V. Snake bite nephropathy. Nephrol (Carlton) 2006 ; 11 (5) : 442-448.

86. Chugh KS. Snake bite induced ARF in India Kidney Int. 1989 ; 35 (3) : 891-907.

87. Tun – Pe et al. Efficacy of compression Immobilisation in retarding spread of Radio labeled venom. South East Asia J Trop Med. Public health. 1994 ; 25(2) ; 344-353

88. Iwakiri R et al. Snake strikes induced ischaemic colitis with colonic stricture complicated by DIC. South Med J. 1995 ; 88 (10) : 1084 – 1085.

89. Tun-po et al. The efficacy of Tourniquets as a First Aid measure for Russell's viper bites in Burma. Trna R SOC Trop Med Hyg. 1987 ; 81(3) : 403-405.

90. Clemens R et al. Antivenom supplementary by Anti thrombin III, in rats experimentally envenomated with Russell's viper venom 1995.

91. Thewjitcharoen et al. Ventricular Tachycardia, rare manifestations of Russell's viper bite. J. Med. Ass. Thai 2005 ; 88 (12) : 1931 – 1933.

92. Sit Prija V et al. The Kidney in Tropical Snake Bite, Clin Nephro 1977 ; 8 (3) : 377-383.

93. Oxford Text Book of Clinical Nephrology

94. API Text book of Medicine (7th edition)

95. The kidneys – Brenner and Rector (1996 edition)

96. Manson's Tropical disease

97. Oxford Text book of Medicine – Venom, Toxin and Poisonous animal, 4th edition.

98. Harrison's principles of Internal Medicine (16th edition)

99. De Gruchy's clinical haematology in Medical Practice (DIC)

100. Manual of clinical haematology (DIC)

101. MKR. Krishnan Forensic Medicine by Patnaik

102. Principles of Forensic Medicine by Apurba Nandy

103. Manual of Clinical Nephrology (6th Edition)

104. Parikh's Text book of Medical Jurisprudence and Toxicology (5th edition)

105. Postgraduate Medicine – Recent advances in Medicine volume XXI, 2007.

106. W Pillay, Modern Medical Toxicology 3 rd edition.

107. Vijeth SR. Correlation of renal status with haematologic. Profile in viperine bite. Am J Trop Med. Hyg 1997 ; 56 (2) : 168-170.

ACUTE RENAL FAILURE IN HAEMOTOXIC SNAKE ENVENOMATION PROFORMA

1.	Name	:	6.	Case No.	:
2.	Age	:	7.	I.P.No.	:
3.	Sex	:	8.	Date of admission	:
4.	Occupation	:	9.	Date of Discharge	:
5.	Address	:	10.	Pre existing illness (if any)	:

11. General condition (Admission)

Vomiting	Abdominal colic	Seizure	Consciousness

12. Vital signs (Admission)

PR	BP	RR	TEMP	URINE	
				COLOR	OUTPUT

Color : N – Normal R – Red B – Brown BL – Black

13. Local examination

i) Bite mark

Yes / No	Site	No.of fang mark	Time

ii) Tourniquet Yes / No

iii)

Cellulitis	Blisters	Reginal adenitis

14. Bleeding diathesis

Onset bleeding (hrs)	Type of bleeding

Type of bleeding

1. Bleeding gums
2. Haematuria
3. Hae matamesis
4. Malena
5. Epitaxis
6. Haemoptsis
7. Rectal bleeding
8. Multiple sites

15. Clotting N – Normal P - Prolonged

On admission	On Treatment
I N / P	1. N/P
II if P – (time interval since bite)	II If N – time interval since tmt start

Day	1st	2nd	3rd	4th	5th	Subsequently
Intake						
Output						

16. Investigations

1. Urine

Albumin	Sugar	Deposits	RBC's	Bs / Bp	Others

2. Blood

TC	DC	ESR	BT	HB %

3.

Blood	On Admission	On set of Renal failure			
		1st day	2nd day	3rd	4th
Urea					
Creatinine					
RBS					
Electrolytes					

4)

Peripheral smear (RBC – fragment)	Platelet count	Reticulocyte count

5. Serum Fibrinogen
6. LFT
7. ECG
8. Ultra sound Abdomen
9. Others

17. Treatment : Onset of Treatment (hrs) :

Anti snake venom (dose)	Stratum (Vials)			Total dosage (Vials)
		2nd	3rd	

No. Of vials for CT to become Normal : How long :

18. Renal failure

1) Time interval since bite to onset of renal failure (hrs)

2)

Renal failure (cause)	DIC	Hypotension	Direct Nephrotoxicity	Intravascular Haemolysis

3)Medical Treatment

Inj. Lasix		Inj. Dopamine		Blood Transfusion	Outcome	
Dose	Days	Dose	Days		Improved	Not improved

3) Dialysis

Peritoneal Dialysis		
No.of cycles	How long	Outcome

Hemodialysis		
No.of cycles	How long	Outcome

19. Other complication (if any)

(Compartment syndrome ICH, Sheehan's syndrome cardio toxicity)

20. Period of Hospital stay :

21.

Final Outcome	Recovered	Morbidity	Mortality

22.

Cause of death date	Renal failure	Other cause

KEY NOTES FOR MASTER CHART

1.	Serial No.	13.	Urine output - UO Normal - N Bile salt - BS Oliguria ↓ Bile pigment - BP Positive +
2.	Name	14.	Haemoglobin in g %
3.	Age / Sex - Male - M Female - F	15.	Urea / Creatinine (mg / dl) Normal - N Increased - ↑
4.	Site of Bite - Foot - F Hand - H Back - B	16.	Platelet count - Normal - N Decreased - ↓
5.	Tourniquet Yes - Y No - N	17.	Reticulocye count - Normal – N
6.	Clotting time Prolonged - P Normal - N	18.	Fibrinogen (mg %)
7.	Bleeding Diathesis Yes - Y No - N	19.	Peripheral smear - Fragmented RBC's Nil Present +
8.	Time of onset of bleeding (hours)	20.	Complete haemogram (CH) Neutrophilia - Neu Normal - N
9.	Type of bleeding Bleeding gums - BG Haematamesis - HE Haemoptysis - HU Multiple sites - MS Malena - M	21.	Electro cardiogram (ECG) Normal - N Sinus bradycardia - SB Sinus tachycardia - ST Left bundle branch block - LBBB Left ventricular hypertrophy – LVH Left anterior hemi block - LAHB
10.	Onset of Treatment with ASV (hrs)	22.	Onset of Renal failure since bite (hours)
11.	Total vials used	23.	Cause of Renal failure DIC – Disseminated intravascular coagulation AOC- Acute on chronic renal failure SS - Septic shock DT - Direct Toxicity CS – Capillary leak syndrome
12.	Blood pressure in mm Hg Normal - N Decreased – ↓ Increased - ↑		

24.	Supportive Treatment Lasix Dopamine DOP Blood transfusion BT	28.	Period of hospital stay (days)
25	Dialysis Peritoneal dialysis- PD Hemodialysis - HD	29.	Cause of death
26	No.of cycles	30.	Time since bite (hours).
27.	Other complications Compartment syndrome – CS Gangrene Stroke Vitreous haemorrhage		

40 Year old Alagar, presented with right hemiparesis, right UMN facial palsy, Wernick's aphasia with normal renal function

MASTER CHART

S.No. (1)	Name (2)	Age/Sex (3)	Site of Bite (4)	Tourniquet (Yes/No) (5)	CT (P/N) (6)	Bleeding diathesis (Y/N) (7)	Time of onset (hrs) (8)	Type of bleed (9)	ASV onset of treatment(hrs) (10)	Total vials used (11)	BP (12)	UO / BS / BP (13)	Hb (g%) (14)	Urea / creatinine (15)	Platelet count (16)	Reticulocyte count (17)	Fibrinogen (mg%)(18)	PS – Fragment RBC's (19)	CH (20)	ECG (21)	Onset of RF since bite (hrs) (22)	Cause of RF (23)	Supportive Treatment (24)	Dialysis PD / HD(25)	No.of cycles(26)	Other complications(27)	Period of stay (days)(28)	Death Cause (29)	Time since bite (days)(30)
1	Mahalingam	35 M	F	N	P	Y	6	BG	16 ½	25	N	N	9.6	N	N	N	100	Nil	Neu	T↓ V1-V4	-	-	Nil	-	-	Nil	5	-	-
2	Chittammal	40 F	F	Y	N	Y	9	HE	8	10	N	N	13.6	N	N	N	125	Nil	Neu	T↓ V1-V4	-	-	Nil	-	-	C.S	12	-	-
3	Guru samy	25 M	F	Y	P	-	-	-	4 ½	25	N	N	10.2	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-
4	Rogu mani	28 F	F	Y	P	-	-	-	5	15	N	N	9.6	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-
5	Bala murugan	35 M	F	Y	P	-	-	-	2 ¼	15	N	N	13.4	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-
6	Santhanam	55 M	F	N	P	-	-	-	7	15	N	N	10	N	N	N	150	Nil	Neu	ST↑ V1-V4	-	-	Nil	-	-	Nil	4	-	-
7	**Selva mani**	**27 F**	**F**	**Y**	**P**	**Y**	**1**	BG	**33 ½**	**4**	**N**	**N**	**8.4**	↑	↓	**N**	**100**	**+**	**N**	**SB**	**48**	**DIC**	**Lasix**	**-**	**-**	**Nil**	**5**	**-**	**-**
8	**Shankar**	**30 M**	**F**	**Y**	**P**	**Y**	**½**	BG	**1 ½**	**23**	**N**	**N**	**9.6**	↑	↓	**N**	**115**	**Nil**	**Neu**	**N**	**1 ½**	**DIC**	**-**	**-**	**-**	**Nil**	**6**	**-**	**-**
9	Karuppaiya	37 M	F	Y	P	-			5 ½	9	N	N	9.4	N	N	N	75	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
10	Mayandi	42 M	F	Y	P	-			15	5	N	N	14.2	N	N	N	100	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
11	Karuppan	33 M	H	Y	P	Y	4 ½	BG	6	15	N	N	13.4	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	2	-	-
12	Periya samy	57 M	F	Y	N	-			7 ½	10	N	↓	13.4	N	N	N	150	Nil	N	N	-	-	Nil	-	-	Gan grene	7	-	-
13	Sathiya	23 F	H	N	P	Y	7 ½	HO	5	10	N	N	10	N	N	N	75	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
14	Rajagam	45 M	F	Y	P	-			6	10	N	N	11.4	N	N	N	150	Nil	Neu	SB	-	-	Nil	-	-	Nil	5	-	-
15	Ravi	30 M	H	N	P	-			6	10	N	N	13.6	N	N	N	110	Nil	N	ST↓ V1-V6	-	-	Nil	-	-	Nil	3	-	-
16	Suresh	13 M	F	Y	P	-			4	5	N	N	12.4	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
17	**Ramayee**	**50 F**	**H**	**Y**	**P**	**Y**	**12**	**BG**	**5**	**5**	↑	↓	**10.2**	↑	**N**	**N**	**125**	**Nil**	**N**	**ST**	**10**	**DIC AOC**	**Lasix**	**PD HD**	**30 12**	**Nil**	**36**	**-**	**-**
18	Aru mugam	35 M	F	N	P	-			3	10	N	N	11.8	N	N	N	150	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-

S.No.	Name	Age/Sex	Site of Bite	Tourniquet (Yes/No)	CT (P/N)	Bleeding diathesis (Y/N)	Time of onset (hrs)	Type of bleed	ASV onset of treatment(hrs)	Total vials used	BP	UO / BS / BP	Hb % (g%)	Urea / creatinine	Platelet count	Reticulocyte count	Fibrinogen (mg%)	PS – Fragment RBC's	CH	ECG	Onset of RF since bite (hrs)	Cause of RF	Supportive Treatment	Dialysis PD / HD	No.of cycles	Other complications	Period of stay (days)	Death Cause	Time since bite (days)
19	**Ramar**	**13 M**	**F**	**N**	**P**	**-**			**5**	**5**	↓	↓	**8**	↑	↓	**N**	**125**	**Nil**	**N**	**S.T**	**16**	**DIC S S**	**DOP**	**PD**	**30**	**CS**	**-**	**DIC SS**	**36**
20	Thiru mathi	17 F	F	N	P	-			9	5	N	N	10.8	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
21	Selva rani	19 F	F	Y	P	Y	½	MS	2 ½	15	N	N	3.2	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	5	-	-
22	Kantha mmal	20 F	F	N	P	-			4	5	↑	N	9.8	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
23	**Devayee**	**55 F**	**F**	**Y**	**P**	**Y**	**½**	**BG**	**2**	**15**	↓	↓	**7**	↑	↓	**N**	**150**	**Nil**	**N**	**ST**	**28**	**DIC**	**Nil**	**HD**	**4**	**Nil**	**20**	**-**	**-**
24	Alagu	25 M	F	Y	P	Y	10 ½	BG	3	13	N	N	14.6	N	N	N	150	Nil	Neu	ST	-	-	Nil	-	-	Nil	6	-	-
25	Ramasamy	20 M	F	N	P	-			2	10	N	N	13.4	N	N	N	100	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-
26	Via kulam	37 M	H	Y	P	-			6	10	N	N	12.6	N	N	N	127	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
27	Periya samy	42 M	F	N	P	-			4 ½	20	N	N	12.8	N	N	N	150	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
28	Pakiri	43 M	H	N	P	-			5	10	N	N	10.6	N	N	N	125	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
29	**Janaki raman**	**30 M**	**F**	**N**	**N**	**Y**	**6**	**HE**	**2 ½**	**15**	↑	↓	**14.8**	↑	**N**	**N**	**225**	**Nil**	**Neu**	**N**	**28**	**DT**	**Nil**	**-**	**-**	**Nil**	**6**	**-**	**-**
30	Christober Muthiah	26 M	F	Y	P	-	-	-	3 ½	5	N	N	13.2	N	N	N	125	Nil	N	N	-	-	Nil	-	-	Nil	4	-	-
31	Muthu raman	22 M	H	Y	P	-	-	-	2 ½	5	N	N	12.8	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-
32	Kannan	32 M	H	Y	P	-	-	-	2 ¼	20	N	N	13.6	N	N	N	125	Nil	Neu	ST↑ Vi-V4	-	-	Nil	-	-	Nil	4	-	-
33	**Sang Ammal**	**55 F**	**F**	**N**	**N**	**Y**	**2**	**HU**	**2 ¼**	**10**	**N**	↓	**11.4**	↑	**N**	**N**	**250**	**Nil**	**N**	**QS V1-V4**	**18**	**DT**	**Nil**	**-**	**-**	**Nil**	**3**	**-**	**-**
34	Thanga natchiyar	55 F	F	N	P	Y	4	BG	6	20	N	N	7.4	N	N	N	150	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
35	Chell ammal	20 F	F	Y	P	-	-	-	11	10	N	N	8.5	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
36	Arumugam	50 F	H	Y	P	-	-	-	4	15	N	N	11.4	N	N	N	150	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
37	Vellimalai	18 M	F	Y	P	-	-	-	2 ½	15	N	N	10.4	N	N	N	160	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
38	Dhanus kodi	24 M	F	Y	P	-	-	-	8	15	N	N	10.4	N	N	N	125	Nil	Neu	SB	-	-	Nil	-	-	Nil	4	-	-

S.No.	Name	Age/Sex	Site of Bite	Tourniquet (Yes/No)	CT (P/N)	Bleeding diathesis (Y/N)	Time of onset (hrs)	Type of bleed	ASV onset of treatment(hrs)	Total vials used	BP	UO / BS / BP	Hb % (g%)	Urea / creatinine	Platelet count	Reticulocyte count	Fibrinogen (mg%)	PS – Fragment RBC's	CH	ECG	Onset of RF since bite (hrs)	Cause of RF	Supportive Treatment	Dialysis PD / HD	No.of cycles	Other complications	Period of stay (days)	Death Cause	Time since bite (days)
39	Backiya Nathan	75 M	H	Y	P	-	-	-	11	15	↑	N	10.2	N	N	N	150	Nil	N	LVHC	-	-	Nil	-	-	Nil	4	-	-
40	Muthu Krishnan	14 M	F	Y	P	-	-	-	10	15	N	N	11.2	N	N	N	75	Nil	Neu	T ↓ V1-V3	-	-	Nil	-	-	Nil	2	-	-
41	Vellaiyan	60 M	F	Y	P	-	-	-	4	10	N	N	10.2	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
42	Selvam	25 M	F	N	P	-	-	-	8	10	N	N	10.6	N	N	N	125	Nil	Neu	ST	-	-	Nil	-	-	Nil	3	-	-
43	Muruga eswari	19 F	F	Y	P	-	-	-	8	15	N	N	6.2	N	N	N	125	Nil	N	T ↓ V1-V6	-	-	Nil	-	-	CS	7	-	-
44	Rackkayee	60 F	F	N	P	-	-	-	19	10	N	N	11	N	N	N	150	Nil	N	ST	-	-	Nil	-	-	Nil	3	-	-
45	**Priya**	**13 F**	**F**	**Y**	**P**	**Y**	**12**	**BG**	**4**	**12**	↑	↓	**7.2**	↑	↓	**N**	**125**	**Nil**	**Neu**	**SB**	**14**	**DIC**	**Lasix**	**HD**	**4**	**Nil**	**14**	**-**	**-**
46	Bala murugan	14 M	F	Y	P	Y	19	M	7	5	N	N	11.8	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
47	Venkatesh	21 M	F	Y	P	-	-	-	1	14	↑	N	13.2	N	N	N	75	Nil	Neu	Tall T V1-V6	-	-	Nil	-	-	Nil	3	-	-
48	Chinna adaikkan	50 M	H	Y	P	-	-	-	8	20	N	N	11.2	N	N	N	75	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
49	Balu	40 M	F	N	P	-	-	-	8	10	↑	N	11.2	N	N	N	50	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
50	Chitra	25 F	F	Y	P	-	-	-	7 ½	5	N	N	9.4	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-
51	Muniyandi	60 M	F	N	P	-	-	-	10	15	N	N	11.4	N	N	N	125	Nil	Neu	SB	-	-	Nil	-	-	Nil	4	-	-
52	Meena	22 F	F	Y	P	-	-	-	5	10	N	N	8.8	N	N	N	100	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
53	Krishna mmal	55 F	F	Y	P	-	-	-	26	10	N	N	8.4	N	N	N	75	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
54	**Velammal**	**55 F**	**F**	**N**	**P**	**Y**	**40**	**MS**	**60**	**15**	**N**	↓	**5**	↑	↓	**N**	**75**	**+**	**Neu**	**LBBB**	**40**	**DIC**	**BT**	**-**	**-**	**Nil**	**5**	**-**	**-**
55	Naina Mohamed	42 M	F	N	P	-	-	-	16	10	N	N	13.6	N	N	N	100	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
56	Perumal	70 M	F	N	P	Y	1	MS	8 ½	10	N	↓	11.6	N	N	N	100	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-
57	**Chandra sekar**	**25 M**	**F**	**Y**	**P**	**-**	**-**	**-**	**1 ½**	**15**	↑	↓	**13**	↑	↓	**N**	**75**	**Nil**	**Neu**	**N**	**54**	**DIC**	**Lasix**	**-**	**-**	**Nil**	**7**	**-**	**-**
58	**Jegadees waran**	**20 M**	**F**	**N**	**P**	**Y**	**4**	**HU**	**16**	**10**	**N**	↓	**10.6**	↑	↓	**N**	**125**	**Nil**	**Neu**	**LAHB ST**	**12**	**DIC**	**Lasix**	**-**	**-**	**Nil**	**5**	**-**	**-**

S.No.	Name	Age/Sex	Site of Bite	Tourniquet (Yes/No)	CT (P/N)	Bleeding diathesis (Y/N)	Time of onset (hrs)	Type of bleed	ASV onset of treatment(hrs)	Total vials used	BP	UO / BS / BP	Hb % (g%)	Urea / creatinine	Platelet count	Reticulocyte count	Fibrinogen (mg%)	PS – Fragment RBC's	CH	ECG	Onset of RF since bite (hrs)	Cause of RF	Supportive Treatment	Dialysis PD / HD	No.of cycles	Other complications	Period of stay (days)	Death Cause	Time since bite (days)
59	Pandi	45 M	F	Y	P	-	-	-	2 ½	22	N	↓	11.8	N	N	N	175	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
60	Chitra	30 F	F	N	P	-	-	-	14	10	N	N	10.4	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-
61	Saravana kumar	15 M	F	Y	P	-	-	-	3	25	N	N	8.8	N	N	N	150	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
62	**Pandi**	**30 M**	**F**	**Y**	**P**	**Y**	**5**	**HE**	**10**	**25**	↓	↓	**10.8**	↑	↓	**N**	**100**	**Nil**	**Neu**	**N**	**48**	**DIC shock CLS**	**DOP BT**	**-**	**-**	**Nil**	**8**	**-**	**-**
63	Gomathy	50 F	H	Y	P	-	-	-	24	10	N	↓	10.2	N	N	N	75	Nil	Neu	N	-	-	BT	-	-	Nil	5	-	-
64	**Pappa**	**35 F**	**F**	**Y**	**P**	**Y**	**2**	**MS**	**3**	**35**	↓	↓	**6.8**	↑	↓	**N**	**100**	**Nil**	**N**	**N**	**6**	**DIC shock**	**BT**	**-**	**-**	**Nil**	**12**	**-**	**-**
65	Ravi	30 M	F	Y	P	Y	2	MS	4	10	N	↓	10.8	N	N	N	125	Nil	N	SB	-	-	Nil	-	-	Nil	2	-	-
66	Adham	40 M	H	Y	P	-	-	-	3	10	↑	N	10.2	N	N	N	175	Nil	N	SB	-	-	Nil	-	-	Gan grene	6	-	-
67	Chinna raja	15 M	F	Y	P	-	-	-	5	10	N	N	10.6	N	N	N	150	Nil	N	N	-	-	Nil	-	-	Nil	2	-	-
68	Pandiya ammal	30 F	F	Y	P	-	-	-	4	20	N	↓	9.8	N	N	N	150	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-
69	**Kannnan**	**32 M**	**F**	**N**	**P**	**-**	**-**	**-**	**4**	**10**	**N**	↓	**10.2**	↑	↓	**N**	**75**	**Nil**	**N**	**N**	**24**	**DIC**	**DOP**	**PD**	**20**	**ICH**	**-**	**DIC ICH**	**72**
70	**Chinnavar**	**31 M**	**F**	**Y**	**P**	**Y**	**1**	**MS**	**5 ½**	**15**	↑	↓	**5.6**	↑	↓	**N**	**75**	**Nil**	**Neu**	**LAHB**	**36**	**DIC**	**Lasix**	**HD**	**2**	**CS**	**5**	**-**	**-**
71	**Amburose**	**70 M**	**F**	**Y**	**P**	**Y**	**8**	**MS**	**3**	**11**	↑	↓/+	**6**	↑	**N**	**N**	**125**	**Nil**	**Neu**	**SB LVH**	**24**	**DIC AOC**	**Lasix**	**PD HD**	**12 7**	**Nil**	**26**	**-**	**-**
72	Rathina mala	42 F	H	Y	P	-	-	-	3 ½	5	N	N	10.8	N	N	N	100	Nil	Neu	ST	-	-	Nil	-	-	Nil	3	-	-
73	Rajendran	49 M	H	Y	P	-	-	-	4	15	N	N	11.2	N	N	N	75	Nil	Neu	Tall T V2-V6	-	-	Nil	-	-	Nil	3	-	-
74	**Lakshmanan**	**65 M**	**H**	**Y**	**P**	**-**	**-**	**-**	**4**	**15**	↓	↓	**7.4**	↑	↓	**N**	**75**	**Nil**	**Neu**	**S B**	**56**	**DIC Shock**	**BT**	**-**	**-**	**Nil**	**6**	**-**	**-**
75	Anand	17 M	F	N	P	Y	17	BG	4	15	N	N	12.6	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	2	-	-
76	Mookkan	60 M	F	N	P	-	-	-	6 ½	15	↓	↓	6.8	N	N	N	100	Nil	Neu	N	-	-	DOP	-	-	Nil	4	-	-
77	Ismail	29 M	F	Y	P	-	-	-	4	10	N	N	11.8	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	4	-	-

S.No.	Name	Age/Sex	Site of Bite	Tourniquet (Yes/No)	CT (P/N)	Bleeding diathesis (Y/N)	Time of onset (hrs)	Type of bleed	ASV onset of treatment(hrs)	Total vials used	BP	UO / BS / BP	Hb % (g%)	Urea / creatinine	Platelet count	Reticulocyte count	Fibrinogen (mg%)	PS – Fragment RBC's	CH	ECG	Onset of RF since bite (hrs)	Cause of RF	Supportive Treatment	Dialysis PD / HD	No.of cycles	Other complications	Period of stay (days)	Death Cause	Time since bite (days)
78	Krishnan	51 M	F	Y	P	Y	3	BG	9 ½	15	N	N	11.6	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	3	-	-
79	Rama lingam	57 M	F	Y	P	-	-	-	4 ½	25	N	N	15.2	N	N	N	100	Nil	Neu	SB	-	-	Nil	-	-	Nil	4	-	-
80	Vellaiy ammal	23 F	F	Y	P	-	-	-	20	10	N	N	8.2	N	N	N	175	Nil	Neu	N	-	-	Nil	-	-	Nil	7	-	-
81	Mokka pillai	35 F	F	Y	P	Y	6	BG	6	10	N	↓	9.2	N	N	N	125	Nil	Neu	N	-	-	Nil	-	-	Nil	5	-	-
82	Mani kandan	22 M	F	N	P	-	-	-	10 ½	10	N	N	12.4	N	N	N	250	Nil	Neu	N	-	-	Nil	-	-	Nil	5	-	-
83	Raman	55 M	F	N	P	-	-	-	22	10	↑	N	12.8	N	N	N	225	Nil	N	N	-	-	Nil	-	-	Nil	4	-	-
84	**Perumal**	**17 M**	**F**	**N**	**P**	**-**	**-**	**-**	**35**	**20**	**N**	↓	**9.8**	↑	**N**	**N**	**200**	**Nil**	**N**	**N**	**24**	**DT**	**Lasix**	**-**	**-**	**Nil**	**5**	**-**	**-**
85	Muthu Krishnan	55 M	H	Y	P	-	-	-	9 ½	20	N	↓	13.2	N	N	N	175	Nil	N	N	-	-	Lasix	-	-	Nil	5	-	-
86	**Muthu**	**55 M**	**F**	**Y**	**P**	**-**	**-**	**-**	**7**	**10**	**N**	↓	**13.2**	↑	**N**	**N**	**225**	**Nil**	**Neu**	**N**	**24**	**DT**	**Lasix**	**-**	**-**	**Nil**	**5**	**-**	**-**
87	Sathiya	24 F	F	N	P	-	-	-	4	10	N	N	10.2	N	N	N	175	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
88	Lakshmi	16 F	F	N	P	-	-	-	6	15	N	N	11.6	N	N	N	175	Nil	N	ST	-	-	Nil	-	-	Nil	2	-	-
89	**Bala murugan**	**13 M**	**F**	**Y**	**P**	**-**	**-**	**-**	**3**	**9**	**N**	↓	**9.2**	↑	↓	**N**	**75**	**Nil**	**N**	**N**	**16**	**DIC shock CLS**	**DOP PT**	**PD**	**24**	**Nil**	**-**	**DIC shock CLS**	**84**
90	**Ganapathy**	**60 M**	**F**	**N**	**P**	**Y**	**4**	**HE**	**6**	**10**	↓	↓	**10**	↑	↓	**N**	**100**	**Nil**	**Neu**	**SB**	**6**	**DIC Shock**	**DOP**	**-**	**-**	**Nil**	**4**	**-**	**-**
91	Alagar samy	29 M	F	N	P	-	-	-	2 ½	9	N	N	10.2	N	N	N	100	Nil	N	ST	-	-	Nil	-	-	Nil	3	-	-
92	Mani	37 M	F	Y	P	-	-	-	6 ½	5	N	N	11.2	N	N	N	75	Nil	N	SB	-	-	Nil	-	-	Nil	3	-	-
93	**Sahaya Raja**	**45 M**	**H**	**N**	**N**	**-**	**-**	**-**	**51**	**5**	↑	↓	**7.8**	↑	**N**	**N**	**220**	**Nil**	**N**	**N**	**24**	**DT**	**Lasix**	**HD**	**4**	**Nil**	**30**	**-**	**-**
94	**Bala Krishnan**	**50 M**	**F**	**Y**	**N**	**-**	**-**	**-**	**27**	**5**	**N**	↓	**9.4**	↑	**N**	**N**	**225**	**Nil**	**N**	**N**	**26**	**DT**	**Lasix**	**-**	**-**	**Nil**	**8**	**-**	**-**
95	Guna sekaran	46 M	Ba	N	P	-	-	-	5 ½	10	N	N	10	N	N	N	100	Nil	N	ST	-	-	Nil	-	-	Nil	3	-	-
96	Mani kandan	25 M	F	N	P	-	-	-	12	10	N	N	9.8	N	N	N	75	Nil	N	SB	-	-	Nil	-	-	Nil	2	-	-

S.No.	Name	Age/Sex	Site of Bite	Tourniquet (Yes/No)	CT (P/N)	Bleeding diathesis (Y/N)	Time of onset (hrs)	Type of bleed	ASV onset of treatment(hrs)	Total vials used	BP	UO / BS / BP	Hb % (g%)	Urea / creatinine	Platelet count	Reticulocyte count	Fibrinogen (mg%)	PS – Fragment RBC's	CH	ECG	Onset of RF since bite (hrs)	Cause of RF	Supportive Treatment	Dialysis PD / HD	No.of cycles	Other complications	Period of stay (days)	Death Cause	Time since bite (days)
97	Asaiyan	16 M	F	Y	P	-	-	-	6	10	N	N	10.1	N	N	N	75	Nil	N	N	-	-	Nil	-	-	Nil	2	-	-
98	Kousalya	18 F	F	Y	P	-	-	-	2 ½	15	N	N	8.8	N	N	N	50	Nil	N	N	-	-	Nil	-	-	Nil	4	-	-
99	Pappathy	32 F	F	Y	P	Y	1	BG	2 ½	20	N	N	9.7	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
100	Dhava pandi	24 M	H	N	P	-	-	-	7 ½	10	N	N	9.2	N	N	N	125	Nil	N	SB	-	-	Nil	-	-	Nil	2	-	-
101	Bala murugan	32 M	F	Y	P	-	-	-	8 ½	15	N	N	10.6	N	N	N	100	Nil	N	Tall T V2-V4	-	-	Nil	-	-	Nil	2	-	-
102	**Tamilarasi**	**17 F**	**F**	**Y**	**P**	**Y**	**12**	**M**	**4 ½**	**10**	↑	↓	**6**	↑	**N**	**N**	**125**	**Nil**	**N**	**ST**	**16**	**DIC AOC**	**Lasix**	**PD**	**24**	**C.S.**	**13**	**-**	**-**
103	Sandana karuppu	27 M	F	N	P	-	-	-	6	10	N	N	10.2	N	N	N	100	Nil	N	N	-	-	Nil	-	-	Nil	3	-	-
104	Mani kandan	24 M	F	N	P	-	-	-	6 ½	10	N	N	11.2	N	N	N	125	Nil	N	N	-	-	Nil	-	-	Nil	5	-	-
105	Alagar	40 M	F	N	P	Y	3	BG	15 ½	15	N	N	10.6	N	↓	N	125	Nil	Neu	N	-	-	BT	-	-	Stroke	12	-	-
106	**Shankar**	**18 M**	**F**	**Y**	**P**	**Y**	**4**	**MS**	**12**	**20**	↓	↓	**10.2**	↑	↓	**N**	**125**	**Nil**	**N**	**N**	**16**	**DIC Shock**	**DOP BT**	**HD**	**6**	**Vit.Hge**	**14**	**-**	**-**
107	Karthick	21 M	F	Y	P	-	-	-	5	10	N	N	10.6	N	N	N	150	Nil	N	N	-	-	Nil	-	-	Nil	4	-	-