"VALIDATION OF 20 MINUTE WHOLE BLOOD CLOTTING TIME AFTER THE INITIATION OF ANTI SNAKE VENOM FOR COAGULOPATHY INDUCED BY HEMOTOXIC SNAKE BITE"

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

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IN

GENERAL MEDICINE

GUDIE:

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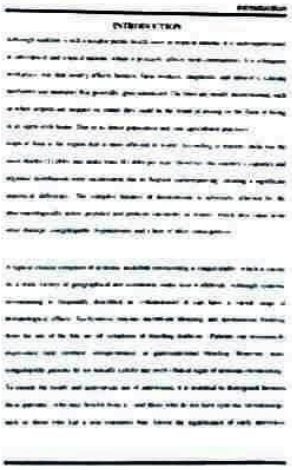

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VALIDATION OF 20 MINUTE WHOLE BLOOD CLOTTING TIME AFTER THE INITIATION OF ANTI SNAKE VENOM FOR COAGULOPATHY INDUCED BY HEMOTOXIC SNAKE BITE.

ABSTRACT

BACKGROUND: In this observational study, we have evaluated the validity of whole blood clotting time (WBCT) for the continuation of ASV treatment up to 18 hours by comparing PT/INR at baseline and at 12 hours and 18 hours for patients who have been initiated on ASV with the corresponding WBCT in patients with venom-induced coagulopathy.

METHODS: We prospectively included 46 patients with VIC received with ASV are included in the study who are eligible as inclusion and exclusion criteria and data regarding with WBCT20 , PT/INR results are collected.

RESULTS: To validate WBCT as a marker for the resolution of VIC and continuation of ASV for VICC WBCT-20 doesn't seem to be a good test. In our study Sensitivity of WBCT20 for coagulopathy (INR>1.4) at Baseline, 12h, and 18h was found to be 66.6%, 28.5%, and 18.1% respectively. Specificity of WBCT-20 for coagulopathy (INR>1.4) at Baseline, 12h, and 18h was found to be 28%, 72.70%, and 100% respectively. It showed that the sensitivity of WBCT-20 was coming down after ASV administration at 12 hours and 18 hours and the specificity of WBCT-20 was increasing progressively up to 18 hours after ASV administration. Because of the very poor sensitivity and the negative predictive value (NPV) of the test is poor WBCT is not an ideal test during the treatment phase of VICC with ASV PT/INR being a better indicator than WBCT during the treatment continuation phase**.**

CONCLUSION: WBC20 is a simple cost-effective and reliable test that can be performed at both primary and secondary/tertiary levels for the initiation of ASV. However, because of significant false negative and false positive results, INR is to be used wherever there is discordance between clinical evaluation and WBCT20. While WBCT20 is the only alternative is a resource-limited setting for monitoring treatment, in secondary/tertiary hospitals where INR measurement facilities are organized quickly with easier and fast access to reports monitoring, is better done by INR. Because of the good correlation between INR and ASV vials, further studies can explore the possibility of deciding the dose of founded ASV on quantitative report the of INR.

ABBREVATIONS

VICC	:	Venom induced Consumption coagulopathy.
RBC	:	Red blood cells
Ach	:	Acetylcholine
PPV	:	Positive predictive value
NPV	:	Negative predictive value
WBCT20	:	Whole blood clotting time at 20 minutes
30WBCT	:	30-minute whole blood clotting test
VeMac	:	Vellore manual activated clotting time
PT	:	Prothrombin time
INR	:	International normalized ratio
APTT	:	activated partial thromboplastin time
VCT	:	Venous Clotting time
TT	:	Thrombin time
ASV	:	Anti-snake venom
RV	:	Russell's viper
GPV	:	Green pit viper
FFP	:	Fresh frozen plasma
FDP	:	Fibrin degradation products

TABLE OFCONTENTS

INTRODUCTION

INTRODUCTION

Although snake bite is still a notable public health issue in tropical nations, it is underappreciated in subtropical and tropical nations, where it primarily affects rural communities. It is a frequent workplace risk that mostly affects farmers, farm workers, shepherds, and laborer's, causing morbidity and mortality that generally, goes unnoticed. The bites are mostly unintentional, such as when serpent are stepped on, either they could be the result of resting on the floor or living in an open-style home. Due to its dense population and vast agricultural practices, tropical Asia is the region that is most affected in world. According to reports, India has the most deaths (11,000) and snake bites (81,000) per year.[1]However, the country's statistics and regional distribution were inconsistent due to flagrant underreporting, creating a significant statistical difference. The complex balance of homeostasis is adversely affected by the pharmacologically active peptides and proteins encounter in venom, which also cause acute renal damage, coagulopathy, hypotension, and a host of other consequences.[2]

A typical clinical symptom of systemic snakebite envenoming is coagulopathy, which is caused by a wide variety of geographical and taxonomic snake taxa worldwide. Although systemic envenoming is frequently described as ―hemotoxic‖ it can have a varied range of hematological effects. Ecchymosis, mucous membrane bleeding, and spontaneous bleeding from the site of the bite are all symptoms of bleeding diathesis.[3] Patients can occasionally experience fatal cerebral, retroperitoneal, or gastrointestinal bleeding. However, many coagulopathy patients do not initially exhibit any overt clinical signs of systemic envenoming.[4]To ensure the timely and appropriate use of anti-venom,it is essential to distinguish between these patients who may benefit from it and those who do not have systemic envenoming, such as those who had a non-venomous bite. Given the

significance of early anti venom administration.[5,6] expensive of antivenom,[7] the high frequency of major adverse events with inferior antivenom,[8] and the anti venom scarcity,[7] are especially pertinent.

PT time and fibrin 1 assays have shown sensitive for diagnosing coagulopathy in range of diverse snake group in standardized laboratory settings.[9,10] despite the variations in the pathophysiology of snakebites, leading to problems of hemostasis. Unfortunately, traditional clotting assays are not frequently available because the majority of snake bites happen in isolated geographic regions. 20WBCT,[6] 30WBCT,[11] the capillary clotting time, the Lee-White clottingtest,[12] and the Vellore manual activated clottingtime(VeMac) are a few bedside tests that can identify clotting abnormalities as a result.

Two WHO snakebite management guidelines[1314]advocate 20WBCT as most used bedside clotting test in snakebite. Additionally, WBCT 20 used to monitor therapy response and the following doses as per government of India standards. The literature does not, however, validate whole blood clotting time for monitoring. Even in clinical settings, the role of WBCT20 as a tool for monitoring treatment response and deciding further management after the initial dosing of ASV remains skeptical remains even when the patient‘s health is improving or in cases when there is no clinical sign of coagulopathy.

Therefore, it is necessary to validate Whole Blood Clotting Time to continue or monitor the coagulopathy caused by snake envenoming. To confirm the effectiveness of the 20-minute WBCT-20 following the administration of Anti Snake Venom in patients with hemotoxic envenomation, the current hospital-based study set out to do so.

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

AIM

To validate the efficacy of WBCT after initiating Anti-Snake Venom in patients with hemotoxic envenomation.

OBJECTIVES

- To evaluate the efficacy of WBCT20 after initiating Anti Snake Venom in patients suffering from coagulopathy due to hemotoxic envenomation by comparing Whole blood clotting time to PT/INR.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

SNAKES BITE IN INDIA [15]

In South Asia, snakes have long been objects of devotion, aversion, or loathing. Both Hindus and Buddhists hold cobras in high regard and they frequently feature in stories and mythology. Around 270 family of poisonous and non-poisonous snakes may be found in India, where they thrive in the greatest environments in the densest forest, mangroves, water bodies, trees, and rain forests. Six species of the most poisonous snakes are known to exist in India; 4 of them are known as the big IV, and the other two are the most stunning King Cobra and disguised Pit Vipers. The most common causes of snake bites on the Indian Subcontinent are members of the big four.

One of the precarious snakes, found throughout the Bharat subcontinent, is the king cobra. The magnificent King Cobras are snake eaters, with rat snakes making up the majority of their diet. The most poisonous snake in India is the Indian Krait, primarily found in that country's jungles. This species is nocturnal and feeds on several snake species, such as kraits and blind worms. The most poisonous and lethal snake in Asia is the daboia, often known as Russell‘s viper. The Indian Russell‘s viper is to blame for the majority of snakebites in the country. The smallest but most deadly snake is a Saw-scaled viper of Indian, which is only found in arid areas. The Indian Cobra, commonly known as Spectacled Cobra, is one of India‘s most attractive and deadly snake species. The most common snake to bite a person in India was *Naja Naja*, which is glorified in Indian mythology. The Malabar Pit Viper is a venomous pit viper snake that is found in India‘s Western Ghats. It blends in nicely with its surroundings. This species is found in the Western Ghats rainforest and is reported to come in a variety of colors and patterns, including green, orange, brown, and yellow. Only in southern India can one find bamboo

pit vipers, which are typically found in bamboo forests next to streams of water. A common cause of snakebites in southern India is the venomous pit viper species known as hump-nosed pit viper. South India‘s coffee plantations, mountainous terrain, and lush jungle are all home to this exceedingly venomous snake. The banded sea krait, one of the worlds most poisonous and venomous snakes, inhabits India‘s coral reefs and spends most of its time submerged. One of the three largest non-venomous python species found in the Indian Subcontinent, together with the reticulated and Burmese pythons, is the Indian Rock Python.

SNAKE VENOM

The primary classifications of snake venoms are neurotoxic and hemotoxic. While hemotoxic venoms, in addition to their effects on the circulatory system, also induce tissue death in other body systems, neurotoxic venoms disrupt neuromuscular connections at the molecular level, reducing muscle action. Hydrolases, hyaluronidase, and kininogenase are venom enzymes. The 5‘nucleotidase, NAD-nucleosidase, DNAase, l-amino acid oxidase, peptidases, phospholipase A2 (PLA2), and zinc metalloproteinase. haemorrhagins are among the additional enzymes. Serineproteases and other pro-coagulant enzymes found in Elapid and Viper venoms may increase blood coagulation. Some venom (Such as that of Russell viper) contain toxins that trigger’s aggregation of platelets, fibrinolysis, protein C, anticoagulation, and bleeding. The most prevalent enzyme in the venom, phospholipase A2, causes extensive harm to mitochondria, RBC, peripheral nerve terminals, leucocytes, platelets, vascular endothelium,skeletal muscle, and other membranes. Hyaluronidase facilitates the spread of venom via tissues from bite site. Acetyl cholinesterase is present in the majority of elapid venoms, which can result in tetanic paralysis. Postsynaptic neurotoxins (α), which binds to Ach receptors at the motor endplate, are polypeptide toxins.

Acetylcholine is released at the nerve terminals at NMJ by Presynaptic (β) neurotoxins, which also injure the endings and prevent the release of acetylcholine.[14]

SNAKE BITE EPIDEMIOLOGY

Despite numerous attempts to estimate it, a precise assessment of world wide load of snakebite poisoning remain vague, and except for a few nations, good data on incidence, morbidity, and mortality are hard to come by[1] The most affected region is unquestionably South Asia.[14,16] According to WHO death estimates 35,000–50,000 worldwide each year due to bites, with India having greatest rate.[14,16] Every year in Pakistan 40000 bites are reported, and up to 8,200 of them might be fatal. Each year, there are more than 20,000 cases of envenoming in Nepal, and there are 1,000 reported fatalities. Every year, government hospitals in Sri Lanka report thirty three thousand envenomed snake bite patients.[1,16]

A significant occupational injury that affects farmers, farm workers and fishermen is a snake bite. Living in an open-style home and sleeping on the floor both put people at risk of getting bitten by nocturnal snakes in the area. In young men, bites are more common, and they typically affect the lower limbs. When there is a lot of agricultural activity and during the wet season, snake bites are more common.[17,18] The incidence and death of snake bites also rise significantly during severe meteorological conditions, such as floods.

According to reports, India has the most snakebites (81,000) and deaths(11,000) / year. However, the country‘s statistics, regional distribution are inconsistent due to flagrant underreporting, creating a significant statistical difference. The range of estimated deaths from snake bites is 1,300 to 50,000. In 2006, there were 61,507 snake bites, and 1124 people died as a result. In 2007, there were 76,948 bites, and 1359 people died. Additionally, a high mortality rate of 50,000 deaths per year has been documented.

Between 1974 and 1978, 1,224 deaths (or 2.43 deaths per 100,000) were recorded annually in the state of Maharashtra. In some West Bengali regions, community-based surveys conducted at random have revealed substantially higher yearly mortality rates of 16.4 fatalities per 100,000 people. Only 1,364 snakebite deaths were reported in 2008 by the hospitals under government of India, except for six states, which is thought to be a significant undercount because rural victims seek out traditional medicine. In India, a nationally representative study on snake bite deaths from 2001 to 2003 found that the state of Andhra Pradesh had the highest mortality rate at 45,900 per year.[1,16,19,20]

CLINICAL SNAKEBITE FEATURES[21]

- **Dry bites:**

No venom bites for at-least 20% of pit viper and a higher percentage seen in Elapid and sea snake bites.

- **Local examination:**

Fang marks: In most cases, the presence of two puncture wounds signifies snake bite that was lethal. Small puncture wounds organized in an arc are typical of a nonvenomous snakebite.

Pain: Immediately following the bite, bursting, burning or throbbing pain may start to appear and may advance proximally up the affected limb. Painful lymph node drainage rapidly sets in. Sea snakes and krait bites could be almost painless .

Local swelling: Viperbites result in a more severe local reaction than bites from other snakes. Within 15 minutes, swelling may be noticeable, and it might become huge within two to three days. It could last for as long as three weeks. From the bite site, the swelling spreads quickly and can affect the entire limb and nearby trunk. There could be regional lymphadenopathy. If the envenomed tissue is trapped in small fascia chamber, such as the

anterior tibial compartment or the pulp space between the fingers, ischemia will form.If no swelling for two hours at bite site then we can conclude that there has not been envenoming following viper-bite.

Local necrosis: A few days after a viper bite, bruising, blistering, and necrosis may develop. Following bites from some rattlesnakes and Asian pit vipers, necrosis is noticeable. Asian cobra bites can sometimes result in painful localized swelling and burning. Krait bites typically have no local effects.

General Features

Flushing, dyspnea, palpitations, disorientation, chest tightness, sweating, and acroparaesthesia are all common symptoms, even in people with ―dry bites‖. These are brought on by sympathetic overactivity and anxiousness. The early signs of elapid bites also include vomiting, heavy eyelids, blurred vision, hyper salivation, congested conjunctivae, and ‗gooseflesh; In addition to these, when a krait bites a person, cramping stomach pain, and diarrhea may follow. Envenomation by a sea snake results in nausea, vomiting, thirst, a thick tongue sensation, and headaches. It is crucial to keep in mind that severe envenomation frequently causes nausea and vomiting.

Systemic Features [22–24]

Clotting problems and hemolysis: Viperidae envenomation is characterised by hemostasis abnormalities. Blood is thought to be incoagulable if it bleeds continuously from fang mark wounds, injection sites, or other fresh and imperfectly healed wounds. The gingival sulci are where spontaneous systemic haemorrhage is most frequently found. There have also been reports of epistaxis, hemoptysis, hematemesis, ecchymoses,

subconjunctival ,retroperitoneal, and cerebral hemorrhages. Intravascular hemolysis can also be caused by sea snakes and viper venom.

Neurotoxicity: sea snake and Elapid venoms both have considerable neurotoxic properties. The initial signs of paralysis after an elapid bite are ptosis and external ophthalmoplegia, which can emerge within 15 min from the time of attack. The onset can occasionally be delayed by up to 10 hours. Later, paralysis develops in the neck muscles, deglutition muscles, vocal cords, facial muscles, palatal, jaws, tongue, and vocal cords. Respiratory failure is brought on by airway blockage or paralysis of diaphragm and intercostal muscles. The effects of neurotoxin are fully reversible, either immediately in response to ASV or anticholinesterases or they may disappear on their own in 1–7 days. It is significant to remember that these neurotoxins do not affect consciousness or pass blood-brain barrier.

Myotoxicity: Myotoxins found in sea snake venom produce myalgias, rhabdomyolysis. Aching, stiffness, myopathy, and tenderness of the muscles spread throughout the body between 0.5 and 3.5 hours after the bite. 3 to 8 hours after the bite, myoglobinuria owing to rhabdomyolysis manifests.

Cardio toxicity: Venom from vipers and elapids can directly harm the myocardium, resulting in arrhythmias, tachycardia, bradycardia, or hypotension.

Nephrotoxicity: Renal failure results from ischemia after viper bites, particularly those from Russell‘s viper. Shock is a result of several factors. Fear, hypovolemia (caused by fluid and blood loss extravasation into the body), cardiac depression, hemorrhage into the adrenal and pituitary glands and enhanced kinin production are a few of them (as in Viper bite).

VENOM INDUCED CONSUMPTIONCOAGULOPATHY:

The primary mechanism in hemotoxic bite is venom induced consumption coagulopathy (VICC). Toxins found in venom cause coagulation in vitro but factor activation and coagulopathy in vivo. Thus, they known as procoagulant toxins. The severity and progressive VICC are dependent on number and type of activators present in the venom. The next paragraphs provide a detailed description of how hemotoxic venom works.

ProthrombinActivators.[25,26]

Prothrombin activators come in four main varieties, which are described in research to date. Groups A through D. They are a member of the family of serine proteases. Structure, function, and the presence of cofactors are the basis for this classification.

Group:	Mechanism of act:
A- (Echis)	**Activating Thrombin to Meizothrombin**
B -(Russell's viper,Echis)	**Activating Thrombin to Meizothrombin**
C -(Elapids)	**Similar factor Xa-Va complex**
D- (Elapids)	**Similar Factor Xa**

Factor X and V activators [25]

The Prothombinase complex is produced when Factor X is activated, and this leads to the start ofdownstream coagulation flow.

Fibrinogenases, or thrombin like enzyme[25]

They are a member of the zinc metalloproteinase family. These enzymes break the fibrinogen component chains (alpha or beta), resulting in the creation of a degraded, non-functional protein. There is no creation of a functioning fibrin molecule as a result of this inactivation mechanism.

Haemorrhagins

They perform additional activities in addition to being prothrombin activators from Group A and B in the venom of Echis spp. Damage to the basement membrane causes shear stress injury, which in turn causes a capillary leak and a propensity for bleeding.[25]

In haemotoxic envenomation, low fibrinogen levels have been shown to correlate with the initiation of (V, X factors) and the spread of cascade downstream to prothrombin.[27]

The following variables seem to be linked to the risk of bleeding in VICC:[27]

1) The coagulation cascade is activated.

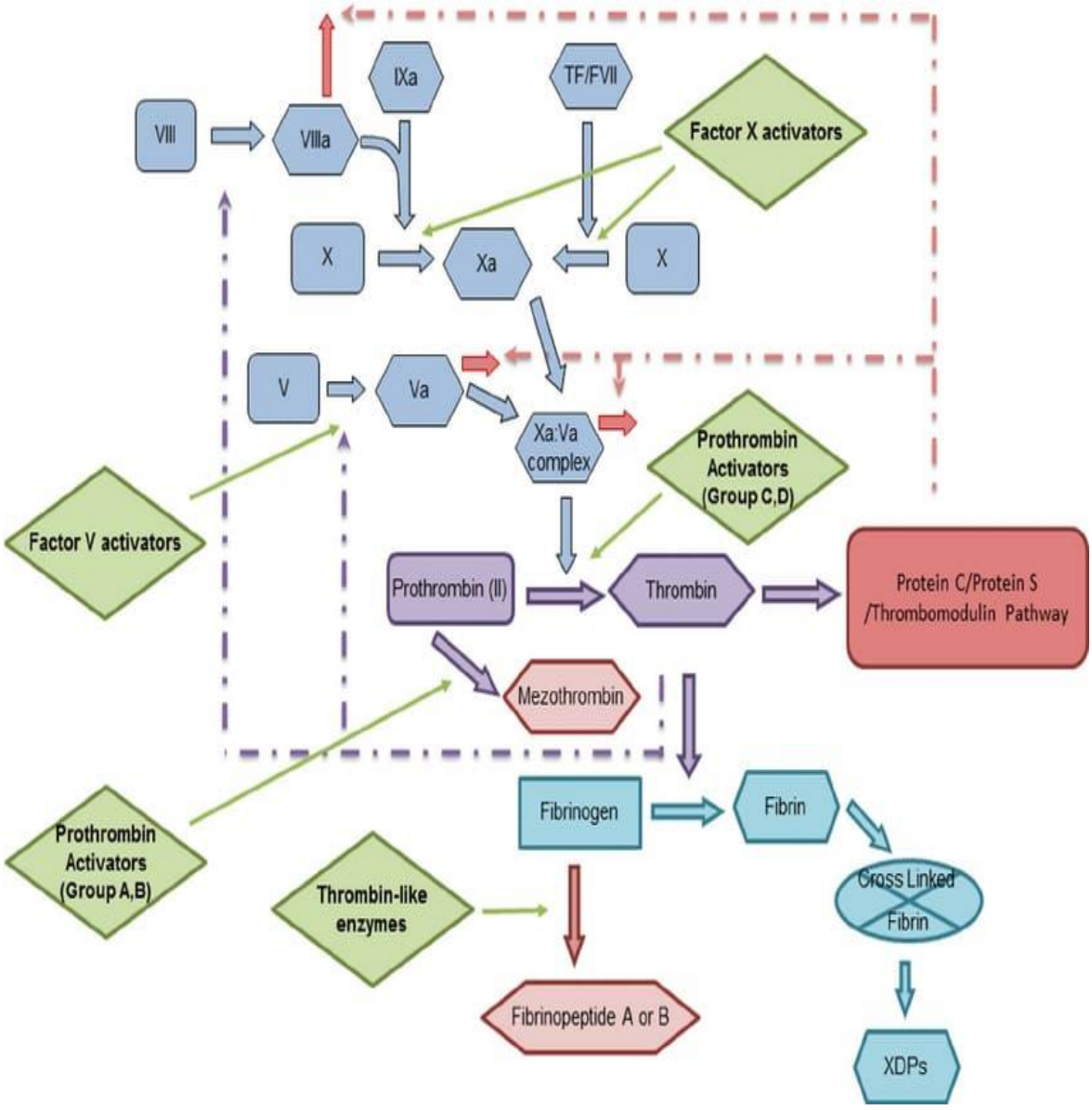
2) Deterioration of the vessel integrity

3) Platelet quantity and activity

4) Local effects

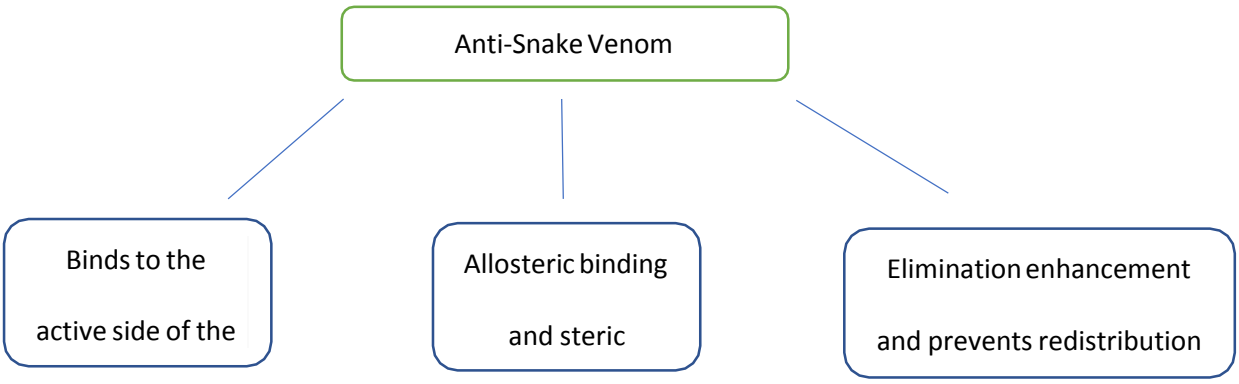
Similar to DIC, local bleeding symptoms are how VICC typically manifests. Systemic haemorrhage is less frequent, though. The more severe hemorrhagic symptoms are linked to bites caused by Echis spp.[28]

Pathogenesis of VICC (Figure 1)



In terms of treating VICC, ASV has endured the test of time. The four snakes *E.carinatus, N.naja*, *B.caeruleus*and *D.russelii*are all covered by antibodies in the polyvalent ASV that is offered in India. India does not have access to monovalent ASV.[29]Antivenoms are the suggested treatment for envenomation, according to a 2014 comprehensive review by Isbister to develop a treatment plan for hemotoxic snakbite.[30] They have polyclonal antibodies that can attach to various venom components and bind to the poisons found in venom.[30]

Mechanism of Action of ASV (Figure 2)



At the initial point contact between patient and the primary physician, the grade and severity of envenomation are evaluated, along with dosage ASV. The potency of venom, the effectiveness of the bite, and host parameters all play a part in establishing the dose of ASV. All patients should be administered 10 ASV vials at presentation under the Indian snake bite protocol. On the precise dosage of ASV and recommendations for monitoring that is tailored to hemotoxic snake bite, there is no consensus, though Repeat Dosing.[31]

The initial ASV dose will be administered over the course of an hour if initial blood test reveals a coagulation problem. The 6-hour time frame is the plan followed for repeat dosing. ASV won‘t be administered again until the subsequent clotting test has been completed. This is because liver fails to replenish clotting factors in less than 6 hours.

After six hours, another coagulation test should be done, and if the coagulation deficiency persists, another dosage of ASV should be given for one hour. Until the restoration of coagulation or unless species is recognized against polyvalent ASV is ineffective, repeat Clotting tests and dosages of ASV should be administered every six hours. One full dose of the initial dosage, or 10 vials of ASV, should be administered as the repeat dose.

20_MINUTE WHOLE BLOOD CLOTTING TEST (20 WBCT)

The 20_WBCT, by Warrell and colleagues are described in 1977 as adding a few milliliters of blood to dry test tube, untouched for 20 min, andengage it to see if the blood has clotted.[32] If clotted it is reflectedas negative and not suggestive of coagulopathy, but the blood that has not clotted after 20 minutes was reflectedas positive and symptomatic of coagulopathy and consequently systemic envenoming.

The 20WBCT was developed with consideration for the following factors:1) cost, 2) speed, 3) limited lab facilities and 4) reproducibility in location with limited access to ASV, which desired to be saved for patients with the high risk of consequences.[32] The most popular methodhas been adopted in national snake_bite guidelines by WHO[20] despite the usage of small variances in methodology. The 20WBCT has changed over time from its original purpose of recognizing patients are most at risk of serious blood loss.[32] Guidelines are increasingly including the 20WBCT as a test for spotting systemic hemotoxic envenoming.[20]

Epidemiological Studies: Diagnostic Accuracy of 20-WBCT

Sano-Martins etal.[33]investigated the validity of straightforward WBCT20 , as marker of low fibrinogen absorption in individuals exposed to Bothrops snakes. In 85 moderately envenomed patients, the findings of WBCT20 and plasma fibrinogen levels showed a strong correlation. The WBCT20 has several advantages over patient plasma fibrinogen concentration estimations, including being easier, quicker, and more accurate. It is also helpful in determining how well antivenom therapy works in terms of restoring blood Coagulability.[33]

PT and APTT were investigated for their diagnostic efficacy in snake bites by Pongpit J et al.[10] Enrolled were adult patients who ostensibly bitten by Cryptelytops sp. (greenpit vipers). APTT, PT with INR, 20WBCT, and conventional venous clotting time (VCT) were measured. The ideal fibrinogen concentration was less than 1.0 g/l. 97 patients were present. 49.5% were men and 46.1 years old was the average age. In 10.3,9.3and 7.2% of cases, respectively fibrinogen level < 1.0g/liter, INR>1.2and VCT>30min were discovered.

VCT >30 min, INRAPTT and 20WBCTsensitivities were 57.0%, 85.7%,57.1% and 85.7%, respectively. They were 94.4%, 95.6%, 95.8%, and 72.4%, respectively. Three hypo fibrinogenemic individuals who received no anti venom since their VCT was under 30 minutes and had persistently normal VCT and were able to return home without experiencing any clinical bleeding. Conclusion, PT/INR may be a more reliable test for patients who have been bitten by a green pit viper and as a result, inter laboratory standardization.

To evaluate the effectiveness of WBCT20 in the diagnosis of VICC in envenomation patients by Russell's viper, Ratnayake et al.[9]two hospitals were used to gather elder patients with suspected snake bites. On admission, the WBCT20 and PT tests were tested. Clinical research assistants who have received training performed the WBCT20 test by 1 ml blood in 5 ml borosilicate test tube with a 10mm internal diameter. A semi-automated coagulation system was used to measure the PT and calculate the INR. Having VICC was indicated by an INR >1.4. By evaluating the specificity and sensitivity of the WBCT20 for detecting VICC on admission, the diagnostic value of the test was obtained. Both the WBCT20 and PT were performed on admission from 987 snake bites. 79 patients (8%) with VICC were included in this. The WBCT20 was false positive in 13/908 participants with no coagulopathy and was positive in 65 out of 79 of VICC patients. The WBCT20 was false negative in 14/79 cases and negative in 895 out of 908 snake bites without coagulopathy. The WBCT20 test, when administered by competent clinical staff, had a fair amount of sensitivity for the diagnosis of VICC but missed about 1/5th of cases where anti-snake venom may have been necessary.[9]

Dsilva AA etal.[34] prospectively studied 60 patients who had a history of snake bites.[34] The presence of envenomation was determined by clinical and analytical standards. WBCT20 was performed using a standardized methodology at 0, 4, and 12 hours. To identify venom induced consumption coagulopathy, PT and INR estimates were made at comparable intervals. Envenomation criteria were used as the gold standard to assess the WBCT20's sensitivity, specificity, and likelihood ratios (LR). WBCT20 was compared to cut-off levels of INR ≥1.4 and ≥1.2. To investigate the inter observer variability of the WBCT20, two observers performed a test-retest correlation. Of the 60 patients, 17 showed signs of hemotoxic envenomation. Neurotoxicity and hemotoxicity were reported in four cases. WBCT20 had a 94 and 76% sensitivity and specificity, with a negative and

positive LR of 0.08 and 3.9 respectively. There was no inter_observer variability found. WBCT_20 is a very delicate test with outstanding reliability for envenomation detection, according to the study‘s findings. However, in this study, the false positive rate was 24%. To avoid wasting unnecessary anti-venom, PT/INR testing should be performed on snake bite patients who have positive WBCT20 but no associated clinical indications of envenomation prior to running ASV.

To ascertain the relationship among clotting tests (20WBCT, PT, INR, platelets and APTT)1) serum fibrinogen of below 100 mg/dL and 2) systemic bleeding in patients bitten by either Russell‘s viper (RV) or green pit viper (GPV), Saengnoi T et al.[35] conducted a study. There were 30 patients; 21 of them had GPV bites, and 9 had RV bites. Blood samples totaling 166 different sets were gathered. four cases had widespread bleeding in total. Unclotted 20WBCT (p=0.01), PT >13 seconds, and INR of ≥1.2 were all linked with fibrinogen levels of <100 mg/dL. Systemic bleeding was more likely to occur in people with unclotted 20WBCTs, INR ≥ 1.2 , and Se.fibrinogen levels below 100 mg/dL. The study concluded that systemic bleeding in GPV and RV envenomation is linked with serum fibrinogen levels <100 mg/dL, unclotted 20WBCT, and INR of ≥1.2.

Patients with Bothrops snakebite who received anti venom therapy were evaluated by Oliveira SS et al.[32] for their progress in recovering from hemostatic diseases. 14% of the patients had systemic bleeding when they were admitted. 10% of the patients showed signs of thrombocytopenia. A total of 54 percent of the patient’s blood has not clotted with high values of fibrin/fibrinogen-degradation product (FDP) and D_dimers and low levels of α 2antiplasmin and fibrinogen. 12 hours after receiving anti venom medication, the majority were free of un clottable blood and systemic bleeding. 48 hours after receiving anti venom medication, systemic hemorrhage occurred in three patients. Around 48 hours after the treatment or when the patient was discharged, the levels of

FDP, D_dimer ,fibrinogen and α 2-antiplasminreverted to normal. In the first 24 hours following anti venom medication, the incidence of thrombocytopenia is increased, then it decreased upon discharge. The patient‘s Bothrops venom levels were reduced 12 hours after receiving anti venom medication, and these levels were unrelated to coagulation or fibrinolytic measures. Deaths weren‘t reported. The study concluded that 48 hours after receiving anti venom medication until discharge, the laboratory parameters of coagulopathy were restored to normal values. A few patients continued to exhibit bleeding symptoms 48 hours after starting anti venom medication.

The 20WBCT was the subject of a thorough study and meta-analysis by Lamb T. et al.[32]Click here to enter text.to see how well it might identify coagulopathy, a sign of systemic envenoming. 3,599 studies were found through the searches; 15 of those matched the requirements for inclusion, and 12 were used in the meta-analysis. A entire of 2,270 patients were involved in the data from 6 different nations. The 20WBCT had an overall weighted sensitivity of 0.84, specificity of 0.91 and SROC AUC of 0.94 for detecting INR >1.4. The 20WBCT had overall weighted sensitivity was 0.72,specificity was 0.94 , and AUC was 0.93 for identifying fibrinogen below 100 mg/dL. (0.91 to 0.95). There was a lot of variability in both studies that employed fibrinogen and INR as the reference test. According to the study findings, the 20WBCT is still a highly sensitive and specific bedside diagnostic for identifying coagulopathy in absence of laboratory resources. Although the 20_WBCT has a poorer sensitivity for diagnosing minor coagulopathy and the remission of coagulopathy after anti venom. In the meta-analysis it was noted that Patients with false negative 20WBCT had a median INR of 1.9, compared to a true positive group where it was 12, suggesting that milder coagulopathy could be missed with WBCT.[32]

Diagnostic accuracy of 20WBCT for coagulopathy resolution has been done only in a small number of studies. Results of these studies indicate a very poor sensitivity of 20WBCT for coagulation resolution at 6-12 hrs.[32]

Resolution of VICC

The resolution of VICC is broadly divided into two: neutralizing the venom-causing VICC and coagulation factors replacement. ASV is the recommended treatment for snake envenoming. ASV binds to the pro coagulants of the toxin and prevents its effect. However, for this to happen the ASV has to be administered as early as possible which again varies from species to species. A model of the coagulation pathway was used to feign the effect of venom of Australian elapids and it showed that ASV needs to be given almost immediately (within 15-30min) to completely or at least partially prevent VICC.[36]

Knowledge gap:

Based on these studies it is evident that WBCT is a fairly good test for initiating the treatment with ASV. However, for monitoring of resolution or continuation of treatment, there have been not many studies present and studies have been there with a limited number of patients.

There seems to be heterogeneity in the results obtained for the continuation of ASV based on WBCT. Most of the studies had a follow-up for only 12 hours. There is a need for validation of Whole blood clotting time for further administration of ASV and also for monitoring for follow-up for a longer duration (18 hours).

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY SETTING: SRI DEVRAJ URS MEDICAL COLLEGE, kolar, India.

STUDY DURATION: 2022 for 18 months.

STUDY TYPE: Observational Study.

SELECTIONMETHOD: Non-probability, Convenient selection.

SAMPLE SIZE:

Estimated is based on the sensitivity of WBCT20 was 94% in detecting envenomation as reported by study done by Dsilvaet al using below formula $n=Z_{\alpha 2)}{}^2P\hat{}(1-P\hat{})/d^2$

Where P^ is pre-determined value of sensitivity (or specificity) that is ascertained by previous published data or clinician experience and for $\alpha = 0.05$, Zα2 is inserted by 1.96. P^ = 94% or 0.94 d = 7.5% or 0.075.

Using the above values at 95% Confidence level a sample size of 39 subjects will be included in trate a sample size of 39+ 3.9 = 43 subjects minimum to be included in the study.

Considering 10% Non-response.

Data Analysis: The agreement between PT/INR and WBCT20 was calculated by Kappa Statistics.

Data Analysis: P value less than 0.05 was measured as significant.

STUDY POPULATION: Adults hospitalized with Snake envenoming with prolonged

WBCT at the time of admission and initiated on ASV.

- Inclusion criteria:

1. Adult patients (more than or equal to 18 years)
2. Patients willing to give informed agreement

- Rejection criteria:

1. Patients with a known history of bleeding diathesis /coagulation disorders
2. With decompensated liver disease.

WBCT20 and PT/INR

- Method of WBCT20:
- WBCT20 was done as per the treating doctors‘ orders.
- WBCT 20 was performed by residents.
- A bedside test in which 2 ml (venous blood) was placed in a test tube and left for 20 minutes at room temperature.
  - The tube should be tilted if blood is in liquid form which implies that blood is **—not clotted**, means VICC.

- Prothrombin time:
- Prothrombin time was done at the SDUMC laboratory

- Principle and Method: Semi-automated. Detection of fibrin formation utilizing the mechanical clot method (Ball Method).

- 2.7ml Blood was collected in vacutainer (3.2% sodium citrate)maintaining 9:1 ratio of whole-blood and anticoagulant . PT can be find out by using blood coagulation analyzers

- Equipment and Reagents required: KC-4 TriniClot PT excel S KC-4 test cuvettes with magnetic ball

- Procedure: Citrated blood is centrifuged at 4000 rpm for 20 minutes. Citrate plasma is then separated.

- Cuvette was placed in the cuvette position and 50 microliter of plasma was added and incubated for 120 seconds. once the incubation was completed 100 microlitre PT reagent was added
- Instrument displays the test reading once the clot is formed and the test is repeated to confirm.
- **An INR>1.4 was considered as coagulopathy in snake bites.**

Data Collection Method

- Study was started after obtaining permission from the research committee and institutional ethics committee.
- Study-related procedures and enrolment of eligible subjects were done after obtaining informed consent. The confidentiality of patients was maintained at all levels.
- Subjects fitting inclusion and rejection criteria were enrolled in the study. Demographic data, the presence of co-morbid conditions along with treatment history. Data regarding the ASV treatment (including the number of vials) and clinical outcome and data regarding the WBCT20, and PT/INR results were collected.

RESULTS

RESULTS

Of all the snake envenomation patients who presented who were eligible and consented, were studied during the period 46 patients received ASV.

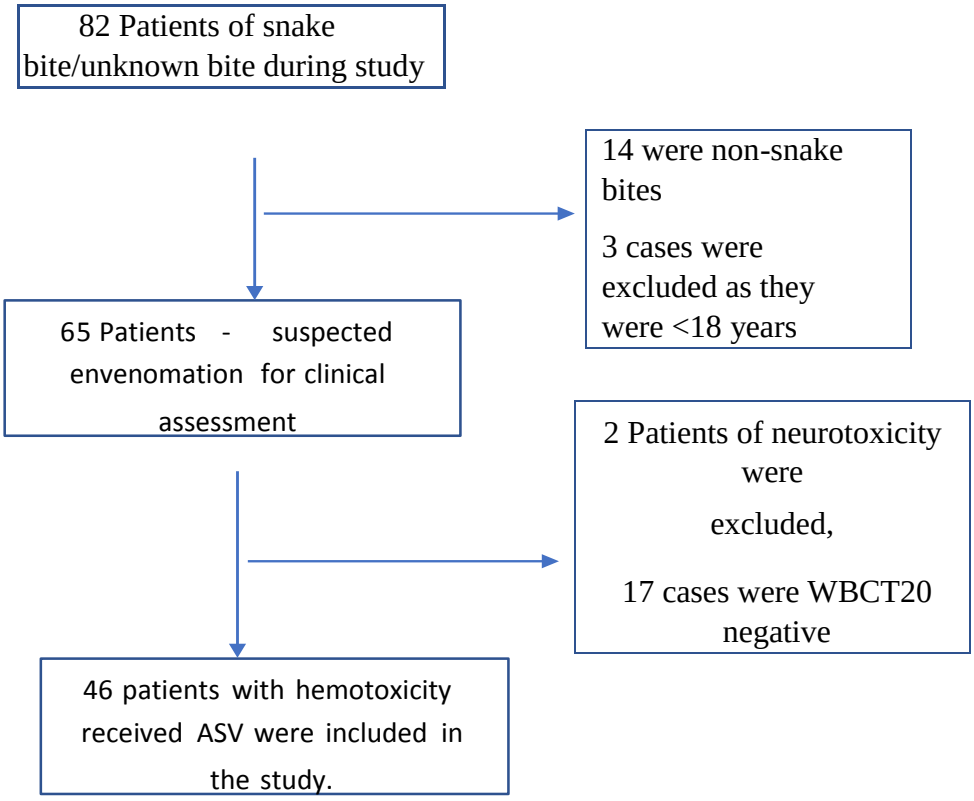


Figure-3

Of all the snake envenomation patients with hemotoxic manifestations who received ASV, the mean age was found to be 43.25; the median was 45.00 with a standard deviation of 13.40. 30 males were admitted and 16 were females and the average of the males was 33.47 years. (IQR 25-36). and females were 47.09 years (IQR 45-52)

Age distribution:

Age	Frequency	Percentage
18-30years	17	37.5
31-50 years	17	37.5
>50 years	12	25

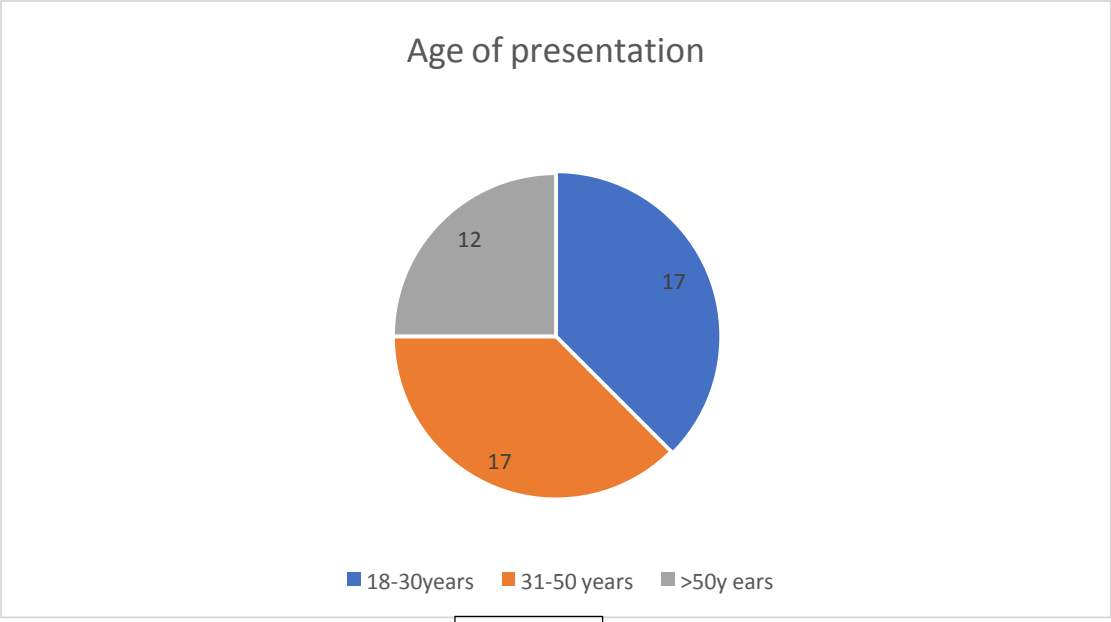


Figure 4

Gender distribution: Of the 46 patients 30 were males and 16 were females.

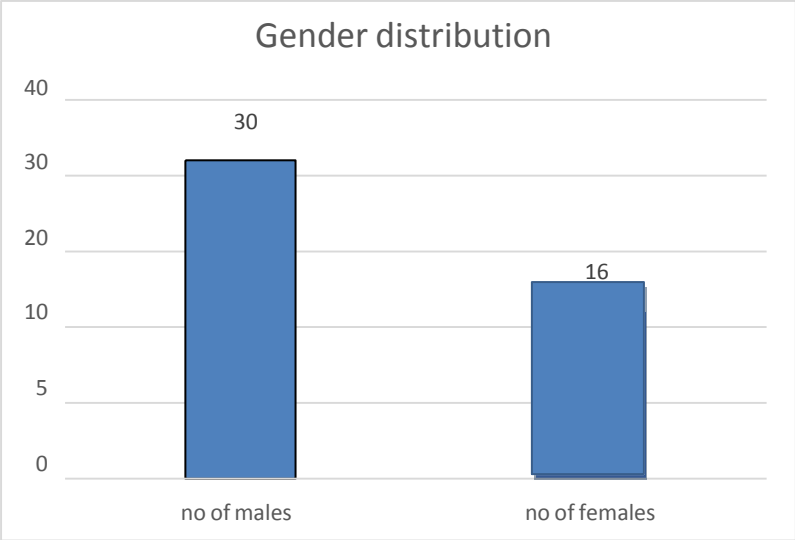


Figure 5

ASV vials given per patient: The average number of ASV given per patient is 10.94. The Median (IQR) is 10 and the standard deviation was 5.579. The correlation between Baseline INR and ASV vials given was 0.384 p-value 0.006

Whole blood clotting time (WBCT_20)

The **Baseline** WBCT at 20 minutes did not clot (WBCT20 Positive) in 32 patients and Whole blood did clot at 20 minutes (WBCT20 Negative) in 14 patients.WBCT_20MIN at **12 hours** was positive in 10 patients and found negative in 26 patients.

WBCT_20 at **18 hours** was positive in 2 patient and found negative in 26 patients.

Figure 6

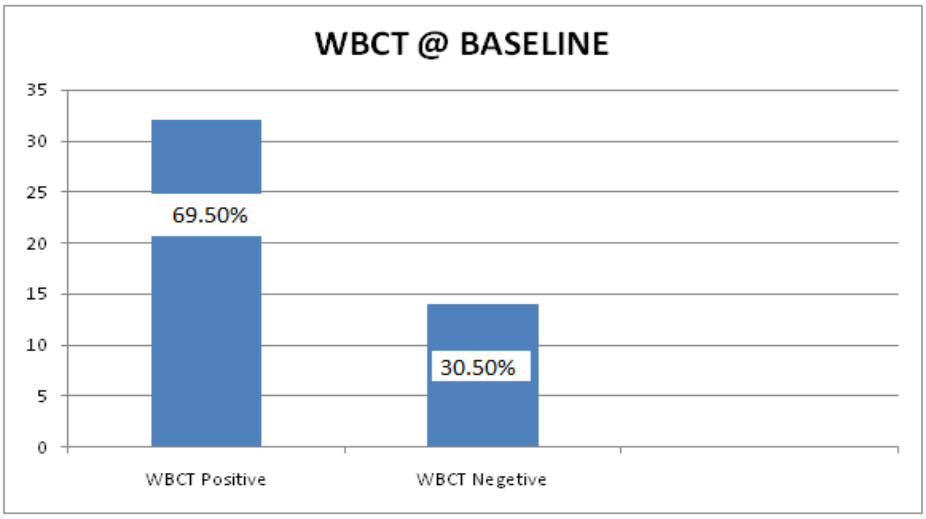


Figure 7

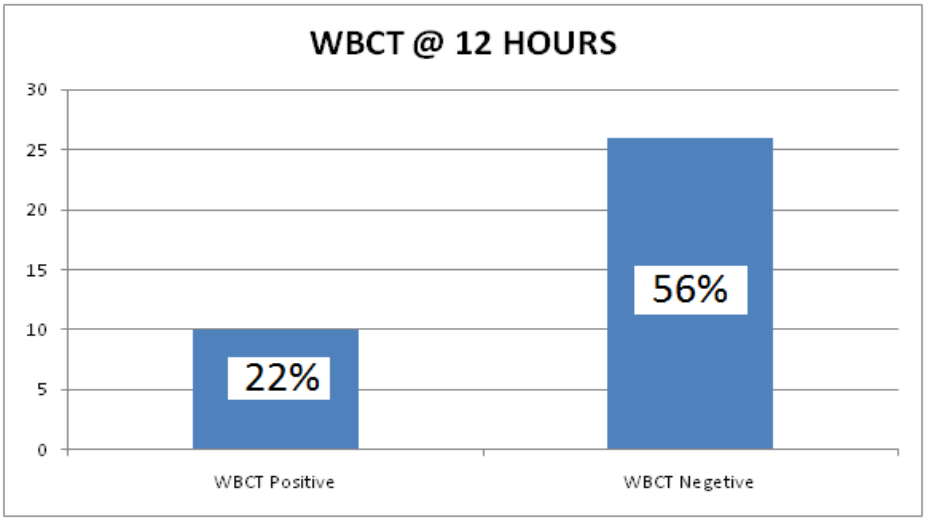


Figure 8

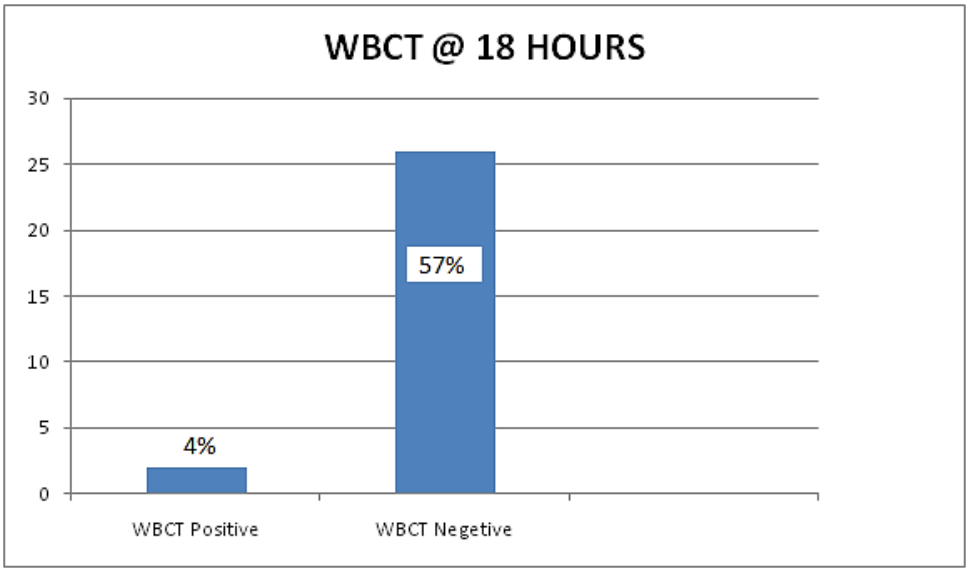
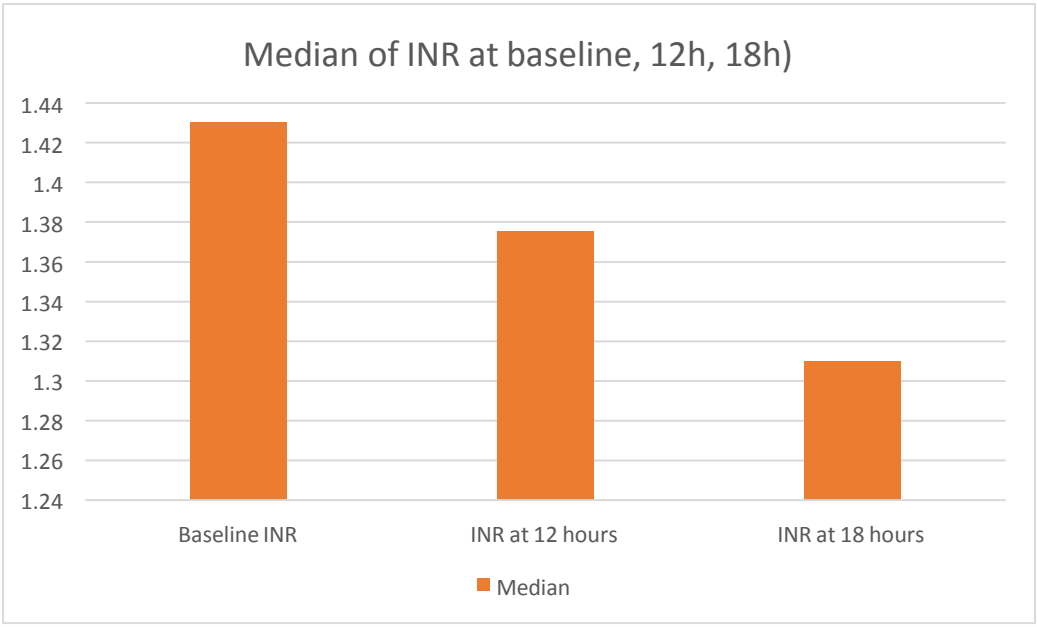


Figure 9



INR:

The Median Baseline INR in patients who received ASV was 1.430.

The Median of the repeat INR at 12 hours was 1.3750.

The Median of the repeat INR at 18 hours was 1.3100.

	Median	Interquartile range
Baseline INR	1.430	2.89
INR at 12 hours	1.3750	0.54
INR at 18 hours	1.3100	0.80

- **Validation of WBCT20@baseline**

INR Vs WBCT20 baseline – 46 patients: kappa 0.103

	High INR	Normal INR
WBCT Positive	14	18
WBCT Negative	7	7

In patients who received ASV the Baseline Whole blood clotting time at 20 minutes did not clot **(WBCT-20 Positive) in 22 patients** and Whole blood did clot at 20 minutes **(WBCT-20 Negative) in 10 patients**. The sensitivity of WBCT-20 for coagulopathy (INR >1.4) was 66.6 % and the specificity was found to be 28%. **Kappa measure of agreement for WBCT and PT/INR at baseline was found to be 0.103**

- **Validation of WBCT20 at 12 hours**

The sensitivity and specificity of WBCT at 20 minutes (WBCT20) at 12 hours were 28.5% and 72.70% respectively

Kappa measure of agreement for WBCT and PT/INR at 12 hours was found to be 0.161 (p-value 0.321)

INR VS WBCT20 12 hrs – 36 patients: kappa value 0.161

	High INR	Normal INR
WBCT Positive	4	6
WBCT Negative	10	16

- **Validation of WBCT20 at 18 hours**

  At 18 hours sensitivity of WBCT-20 was noted to be 18.12% and the specificity was found to be 100%. The Kappa coefficient was found to be 0.185 (p-value 0.134)

INR vs WBCT20 18 hrs – 28 patients: Kappa 0.185

	High INR	Normal INR
WBCT Positive	2	0
WBCT Negative	9	17

The sensitivity of WBCT20 for coagulopathy (INR>1.4) at 0h, 12h, and 18h was found to be66.6%, 28.5 %, and 18.1% respectively. The specificity of WBCT20 for coagulopathy (INR>1.4) at 0h, 12h, and 18h was found to be 28%, 72.70%, and 100% respectively. It was found that the sensitivity of WBCT20 progressively comes down and the specificity of WBCT20 increases during the course of treatment with ASV.

Correlation between baseline INR and repeat INR at 12 hours and 18 hours

The correlation coefficient (r) between the baseline INR and the repeat INR at 12 hours was found to be 0.752 with a p-value <0.001. The correlation coefficient (r) between the baseline INR and the repeat INR at 18 hours was found to be 0.555 with a p-value of 0.007. these values indicate that with a baseline INR we can fairly predict the repeat INR at 12 hours and 18 hours.

The area under ROC curve for Baseline INR and persistent coagulopathy at 18 hours (INR >1.4) was 0.730 with a p-value of 0.125 (95% CI 0.4730.987). The area under ROC curve for repeat INR at 12 hours and persistent coagulopathy at 18 hours (INR >1.4) was 1.000 with (95% CI 1.00-1.00).

-Test Result Variable(s)	Std. Error	Area	Asymptotic Sig.	Asymptotic95% CI:	
				Lower Bound	Upper Bound
Baseline INR	. 131	.730	.125	.473	.987
Repeat INR at 12h	.000	1.000	.001	1.000	1.000

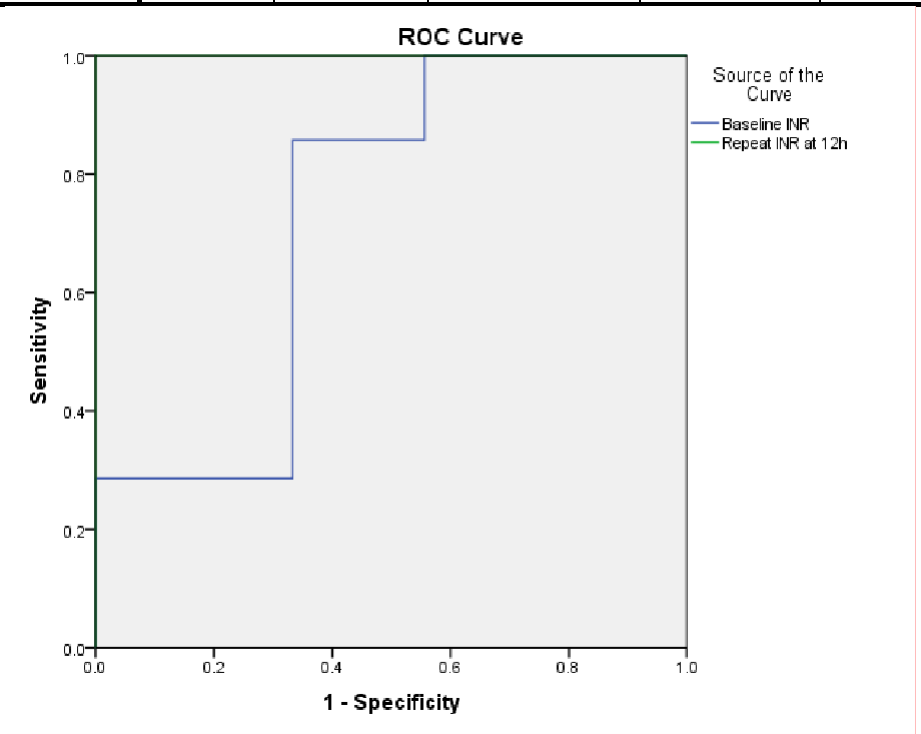


Figure 10

Correlation between the number of vials of ASV received and the INR

The number of vials received by the patient was correlating well with baseline INR and INR at 12 hours. The correlation coefficient (r) was 0.384 (p-value 0.006) for the Baseline INR and number of ASV vials given. The correlation coefficient (r) was 0.584 (p-value <0.001) for the number of vials given and Repeat INR at 12 hours. These values give us an indication regarding the number of ASV vials patients are likely to receive based on INR at baseline and 12 hours.

INR and its role in the prediction of VICC

A Baseline INR of >1.43 predicted the possibility of persistent VICC at the end of 18 hours with a sensitivity of 71.4% and specificity of 67%. INR 1.41 @ 12 hours had a sensitivity and specificity is 100% for VICC @ 18 hours.

DISCUSSION

DISCUSSION

In this observational study, we have evaluated the validity of whole blood clotting time (WBCT) for the continuation of ASV treatment up to 18 hours by comparing PT/INR at baseline and at 12 hours and 18 hours for patients who have been initiated on ASV with the corresponding WBCT in patients with venom-induced coagulopathy. We found that WBCT can be used as a typical diagnostic tool for the initiation of treatment of ASV with snake envenomation and it has been consistent with the other studies. However, to validate WBCT as a marker for the resolution of VIC and continuation of ASV for VICC WBCT-20 doesn‘t seem to be a good test. In our study Sensitivity of WBCT-20 for coagulopathy (INR>1.4) at Baseline, 12h, and 18h was found to be 66.6%, 28.5%, and 18.1% respectively. Specificity of WBCT-20 for coagulopathy (INR>1.4) at Baseline, 12h, and 18h was found to be 28%, 72.70%, and 100% respectively. It showed that the sensitivity of WBCT-20 was coming down after ASV administration at 12 hours and 18 hours and the specificity of WBCT-20 was increasing progressively up to 18 hours after ASV administration. Because of the very poor sensitivity and the negative predictive value (NPV) of the test is poor WBCT is not an ideal test during the treatment phase of VICC with ASV PT/INR being a better indicator than WBCT during the treatment continuation phase. For patients who are being treated with ASV, PT/INR has to be done, and then decide further management wherever facilities are available. In a resource-poor setting further management of high-risk patients can be decided by WBCT. The nature of WBCT20 is that it follows an all-or-none phenomenon. The subtle improvements during the resolution phase of VICC cannot be made even if clinical improvement is evident as it tells only if blood is clotted or not, whereas INR is a quantitative measure and clinical

improvement can be made by INR monitoring. The importance of this study suggests that performing WBCT is a good test for initiating ASV whereas PT/INR is a better test for continuing treatment.

17 patients among the initially screened patients were negative by WBCT and hence were not given ASV. 3 out of those 17 patients (3/17= 17.6%) had INR>1.4 suggesting that WBCT-20 has significant false negatives. In a meta-analysis it was noted that Patients with false negative 20WBCT had a median INR of 1.9, compared to the true positive group where it was 12, suggesting that milder coagulopathy could be missed with WBCT.[32]Previous studies have reported the accuracy of 20 WBCT up to 12 hours whereas our study has compared up to 18 hours. Decreasing sensitivity and improved specificity were observed for coagulopathy resolution up to 12 hours in previous studies[32] and our study confirms that the same trend continues up to 18 hours also.

The number of vials of ASV received by the patient was correlating well with baseline INR and INR at 12 hours. The correlation coefficient (r) was 0.384 (p-value 0.006) for the baseline INR and the number of ASV vials given. The correlation coefficient (r) was 0.584 (p-value <0.001) for the number of vials given and Repeat INR at 12 hours. These values give us an indication regarding the number of ASV vials patients might need for the resolution of VICC based on INR at baseline and 12 hours. The correlation is stronger for INR at 12 hours.

A Baseline INR of > 1.43 predicted the possibility of persistent VICC at the end of 18 hours with a sensitivity 71.4% and Specificity 67%. INR at 12 hours was a strong predictor of VICC status at 18 hrs. INR of 1.41 at 12 hours had 100% sensitivity and 100% specificity for VICC at 18 hrs. Patients with INR >1.41 at 12 hours should be

monitored and treated aggressively since they are likely to remain in a state of VICC. This could also indicate the need for FFP transfusion since the depleted and consumed coagulation factors need to be regenerated to effectively reduce VICC and this process can be facilitated by FFP transfusion.

Whole blood clotting time (WBCT-20):

The 20WBCT —a few ml (venous blood) in a test tube that is left untouched for 20-minutes and look for blood has clotted‖ or not.[4] However, in the original study, the reason for the validity and 20-min time period were not discussed. WBCT was only validated for the detection of VICC and initiation of ASV in VICC patients. WBCT was not validated for continuing the treatment with ASV. Also, there was heterogeneity in the methodology of performing WBCT including the type of the tube in which blood was collected, the volume, the width of tube, and other factors which effect WBCT. There is even heterogeneity in the time duration for which the test has to be performed. There is a meta-analysis that evaluated the efficacy of WBCT concluded that it is a fairly good test for initiating ASV but the analysis observed that limited number of small studies were existing for VICC resolution and hence the continuation of treatment with ASV.

WBCT-20 and PT/INR Comparison

Based on our literature review and our observations we have a comparison between WBCT and PT/INR the following points can be derived: WBCT is a qualitative measure of binary nature which tells that it is either positive or negative whereas INR is both qualitative and quantitative measure which helps us to measure the subtle improvement in VICC during the treatment phase. WBCT is a simple bedside test that can be performed by anyone ranging from a medical student to a professional and is cost-effective PT/INR is a lab-based test that requires trained personnel to handle the equipment and procedure

and is expensive. Both these tests can have an inter-operable variability. PT/INR can be performed only in large health-care facilities where INR measurement facilities are organized quickly with easier and fast access to reports monitoring while WBCT is done in both primary and secondary/tertiary care.

TREND of SENSITIVITY and SPECIFICITY of WBCT-20 for VICC:

The sensitivity of WBCT20 for VICC at baseline and after 12 hours of ASV running was found to be 67%, and 42% respectively (Shenoy et al) and 92%, and 67% respectively (D'Silva et al). In our study Sensitivity at baseline, 12h, and 18h after ASV administration was found to be 66.6%, 28.5%, and 18.1% respectively (refer to figure 11). In comparison to other studies, a similar trend of declining sensitivity of WBCT20 has been noted at 12 hours and our study showed a further drop in sensitivity at 18 hours. However, the specificity of WBCT increases at 12h (similar to other studies), and this study showed specificity further increases at 18 hours.

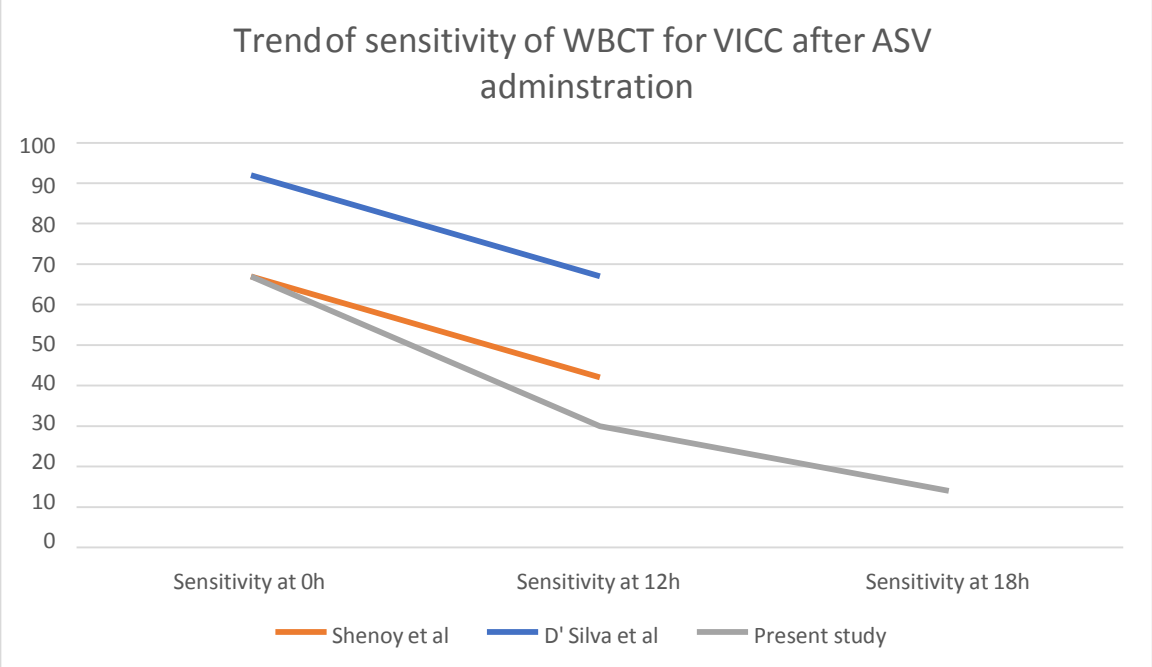


Figure 11

The specificity of WBCT20 for VICC at baseline and after 12 hours of ASV running was found to be 78%, and 84% respectively (Shenoy et al) and 70%, and 80% respectively (D'Silva et al) (refer to Figure 12). In our study Specificity at baseline, 12h, and 18h after ASV administration was found to be 28%, 72.7%, and 100% respectively. In comparison to other studies, a similar trend of increasing specificity of WBCT20 was noted at 12 hours and our study showed a further increase in specificity at 18 hours.

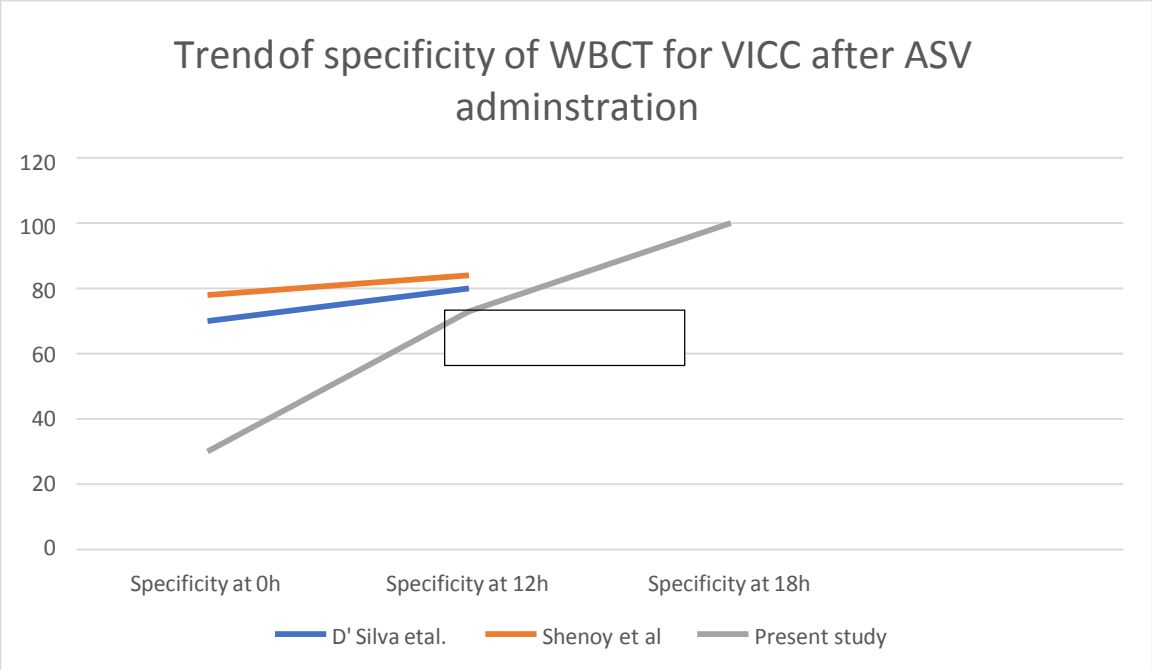


Figure 12

LIMITATIONS

LIMITATIONS

The limitations of our study include a small sample size, done in a single hospital setting, correlation of whole blood clotting with the severity of the envenomation was not done, species of the snake was not included and a non-randomized study. Also, time from the snake bite to the index test is not included which can be another probable confounding variable while evaluating the efficacy of WBCT. A larger study with a higher sample size is required to find the validation of Whole blood clotting time and PT/INR following administration of ASV.

CONCLUSIONS

CONCLUSIONS

Based on our study and the literature reviewed these are the following conclusions are arrived at as depicted in the flow chart. WBCT20 is a simple cost-effective and reliable test that can be performed at both primary and secondary/tertiary levels for the initiation of ASV. However, because of significant false negative and false positive results INR is to be used wherever there is discordance between clinical evaluation and WBCT20.

While WBCT20 is the only alternative is a resource-limited setting for monitoring treatment, in secondary/tertiary hospitals where INR measurement facilities are organized quickly with easier and fast access to reports monitoring, is better done by INR. Because of the good correlation between INR and ASV vials, further studies can explore the possibility of deciding the dose of ASV founded on the quantitative report of INR.

These are our recommendations for a patient with suspected envenomation when presented to primary v/s secondary/tertiary hospital settings as depicted (figure 13):

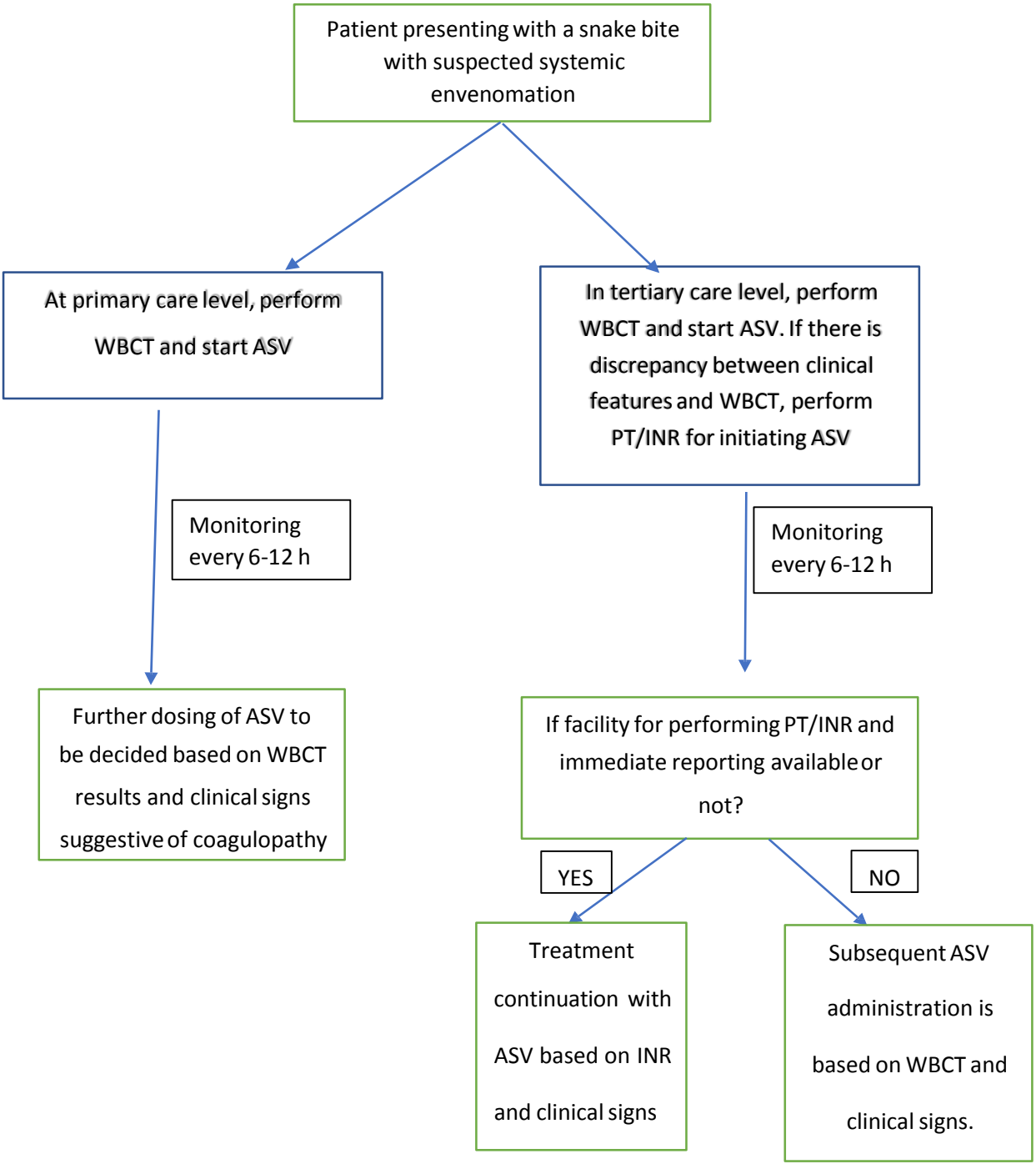


Figure 13

BIBLIOGRAPHY

1. Kasturiratne A, Wickremasinghe AR, De Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, et al. The global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths. Vol. 5, PLoS Medicine. 2008.

2. Fox JW, Serrano SMT. Structural considerations of the snake venom metalloproteinases, key members of the M12 reprolysin family of metalloproteinases. Toxicon. 2005;45(8).

3. Abubakar IS, Abubakar SB, Habib AG, Nasidi A, Durfa N, Yusuf PO, et al. Randomised controlled double-blind non-inferiority trial of two antivenoms for Saw-scaled or carpet viper (Echisocellatus) envenoming in Nigeria. PLoSNegl Trop Dis. 2010;4(7).

4. Maduwage K, Scorgie FE, Silva A, Shahmy S, Mohamed F, Abeysinghe C, et al. Hump-nosed pit viper (Hypnalehypnale) envenoming causes mild coagulopathy with incomplete clotting factor consumption. ClinToxicol. 2013;51(7).

5. Alfred S, Bates D, White J, Mahmood MA, Warrell DA, Thwin KT, et al. Acute Kidney Injury Following Eastern Russell's Viper (Daboiasiamensis) Snakebite in Myanmar. Kidney Int Rep. 2019;4(9).

6. Habib AG, Abubakar SB. Factors affecting snakebite mortality in north-eastern Nigeria. Int Health. 2011;3(1).

7. Chippaux JP, Massougbodji A, Diouf A, Baldé CM, Boyer L V. Snake bites and antivenom shortage in Africa. Vol. 386, The Lancet. 2015.

8. de Silva HA, Pathmeswaran A, Ranasinha CD, Jayamanne S, Samarakoon SB, Hittharage A, et al. Low-dose adrenaline, promethazine, and hydrocortisone in the prevention of acute adverse reactions to antivenom following snakebite: A randomised, double-blind, placebo-controlled trial. PLoS Med. 2011;8(5).

9. Ratnayake I, Shihana F, Dissanayake DM, Buckley NA, Maduwage K, Isbister GK. Performance of the 20-minute whole blood clotting test in detecting venom induced consumption coagulopathy from russell's viper (Daboiarusselii) bites. ThrombHaemost. 2017;117(3).

10. Pongpit J, Limpawittayakul P, Juntiang J, Akkawat B, Rojnuckarin P. The role of prothrombin time (PT) in evaluating green pit viper (Cryptelytropssp) bitten patients. Trans R Soc Trop Med Hyg. 2012;106(7).

11. Benjamin JM, Chippaux JP, Sambo BT, Massougbodji A. Delayed double reading of whole blood clotting test (WBCT) results at 20 and 30 minutes enhances diagnosis and treatment of viper envenomation. Journal of Venomous Animals and Toxins Including Tropical Diseases. 2018;24(1).

12. de Brito Sousa JD, Sachett JAG, de Oliveira SS, Mendonça-da-Silva I, Marques HO, de Lacerda MVG, et al. Accuracy of the lee–white clotting time performed in the hospital routine to detect coagulopathy in bothropsatrox envenomation. American Journal of Tropical Medicine and Hygiene. 2018;98(5).

13. Nduagubam OC, Chime OH, Ndu IK, Bisi-Onyemaechi A, Eke CB, Amadi OF, et al. Snakebite in children in Nigeria: A comparison of the first aid treatment measures with the world health organization's guidelines for management of snakebite in Africa. Ann Afr Med. 2020;19(3).

14. Snakebite Expert Committee of Sri Lanka Medical Association. SLMA Guidelines for the Management of Snakebite in Hospital - 2021. 2021.

15. Simpson ID, Norris RL. Snakes of medical importance in India: Is the concept of the "Big 4" still relevant and useful? Wilderness Environ Med. 2007;18(1).

16. Alirol E, Sharma SK, Bawaskar HS, Kuch U, Chappuis F. Snake bite in south asia: A review. Vol. 4, PLoS Neglected Tropical Diseases. 2010.

17. Suleman MM, Shahab S, Rab MA. Snake bite in the Thar Desert. J Pak Med Assoc. 1998;48(10).

18. Ariaratnam CA, Sheriff MHR, Theakston RDG, Warrell DA. Distinctive epidemiologic and clinical features of common krait (Bungaruscaeruleus) bites in Sri Lanka.American Journal of Tropical Medicine and Hygiene. 2008;79(3).

19. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, et al. Snakebite mortality in India: A nationally representative mortality survey. PLoSNegl Trop Dis. 2011;5(4).

20. White J, Mahmood MA, Alfred S, Thwin KT, Kyaw KM, Zaw A, et al. A comprehensive approach to managing a neglected, neglected tropical disease; The Myanmar Snakebite Project (MSP). Toxicon X. 2019;1.

21. Noutsos T, Currie BJ, Lek RA, Isbister GK. Snakebite associated thrombotic microangiopathy: a systematic review of clinical features, outcomes, and evidence for interventions including plasmapheresis. PLoSNegl Trop Dis. 2020;14(12).

22. Parajuli SB, Bhattarai S, Paudel I, Pokharel PK, Rayamajhi RB, KC H. Clinico-Epidemiological Profile, Health Care Utilization and Practices Regarding Snake Bite at Ilam District of Eastern Nepal. Birat Journal of Health Sciences. 2017;2(2).

23. Karaye KM, Mijinyawa MS, Yakasai AM, Kwaghe V, Joseph GA, Iliyasu G, et al. Cardiac and hemodynamic features following snakebite in Nigeria. Int J Cardiol. 2012;156(3).

24. Mehta SR, Sashindran VK. Clinical features and management of snake bite. Med J Armed Forces India. 2002;58(3).

25. Valenta J, Stach Z, Michálek P. Snakebite Envenoming by Sochurek's Saw-scaled Viper EchisCarinatusSochureki. Prague Med Rep. 2016;117(1).

26. Kularatne SAM, Silva A, Weerakoon K, Maduwage K, Walathara C, Paranagama R, et al. Revisiting Russell's Viper (Daboiarusselii) bite in Sri Lanka: Is abdominal pain an early feature of systemic envenoming? PLoS One. 2014;9(2).

27. Porath A, Gilon D, Schulchynska-Castel H, Shalev O, Keynan A, Benbassat J. Risk indicators after envenomation in humans by Echiscoloratus (mid-east saw scaled viper). Toxicon. 1992;30(1).

28. Berling I, Isbister GK. Hematologic effects and complications of snake envenoming. Vol. 29, Transfusion Medicine Reviews. 2015.

29. Bawaskar HS. Snake bite poisoning: A neglected life-threatening occupational hazard. Vol. 18, Indian Journal of Critical Care Medicine. 2014.

30. Maduwage K, Isbister GK. Current Treatment for Venom-Induced Consumption Coagulopathy Resulting from Snakebite.PLoSNegl Trop Dis. 2014;8(10).

31. Ghosh S, Mukhopadhyay P, Chatterjee A. Management of snake bite in India. Vol. 64, Journal of Association of Physicians of India. 2016.

32. Lamb T, Abouyannis M, de Oliveira SS, Rachana SK, Geevar T, Zachariah A, et al. The 20-minute whole blood clotting test (20wbct) for snakebite coagulopathy—a systematic review and meta-analysis of diagnostic test accuracy.PLoSNegl Trop Dis. 2021;15(8).

33. Sano-Martins IS, Fan HW, Castro SCB, Tomy SC, Franca FOS, Jorge MT, et al. Reliability of the simple 20 minute whole blood clotting test (WBCT20) as an indicator of low plasma fibrinogen concentration in patients envenomed by Bothrops snakes. Toxicon. 1994;32(9).

34. Dsilva AA, Basheer A, Thomas K. Snake envenomation: Is the 20 min whole blood clotting test (WBCT20) the optimum test for management? QJM: An International Journal of Medicine . 2019;112(8).

35. Saengnoi T, Chantrathammachart P, Puavilai T, Sangchaisirisak U, Wananukul W, Srisuma S. Clotting tests associated with hypofibrinogenemia and systemic bleeding in green pit viper or Russell's viper bite patients. Journal of the Medical Association of Thailand. 2019;102(11).

36. Anjana RM, Unnikrishnan R, Deepa M, Pradeepa R, Tandon N, Das AK, et al. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). Lancet Diabetes Endocrinol. 2023;11(7).

ANNEXURES

PROFORMA

Particulars of the patients

NAME:

AGE: ____ YEARS

SEX: MALE/FEMALE

OCCUPATION:

LOCATION:

HOSPITAL NUMBER:

DATE AND TIME OF ADMISSION : __/__/20__ AT __:__ AM/PM

DATE OF DISCHARGE:__/__/20__

ADMISSION DIAGNOSIS:

BRIEF HISTORY:

SYMPTOMS ON PRESENTATION:

- □ Icterus
- □ Nausea
- □ Vomiting
- □ Palmar erythema
- □ Hematemesis
- □ Headache
- □ Dizziness
- □ Weakness
- □ Abdominal Pain
- □ Reduced appetite
- □ dyspepsia
- □ Hematemesis
- □ gastritis
- □ amenorrhea
- □ Peripheral edema/swelling
- □ Restlessness

PRIOR TREATMENT:

□ **YES** □ **NO**

PROVIDER : SUPPORTIVE : TREATMENT :

PAST HISTORY:

- □ DIABETES MELLITUS
- □ HYPERTENSION
- □ LIVER DISORDER
- □ RENAL DISORDER
- □ TUBERCULOSIS
- □ BRONCHIAL ASTHMA
- □ CARDIOVASCULAR DISEASE

PERSONAL HISTORY:

- DIET:
- APPETITE:
- SLEEP:
- BOWEL AND BLADDER:
- HABITS:
- SOCIOECONOMIC STATUS

GENERAL PHYSICAL EXAMINATION: Height: ____Cms , Weight: ____ kgs ,

BMI: ____kg / m^2

Pallor/Cyanosis/Icterus/Clubbing/edema/Generalized

VITAL DATA

- Pulse: ___ bpm

a. Temperature:____^{o}F
b. BP: ____ mmHg
c. Respiration rate: ____ cpm
d. SpO2: ____% @ RA

Systemic examination :

- Per abdomen:
- Respiratory system:
- Cardio vascular system:
- Central nervous system:

INVESTIGATIONS:

- **Baseline WBCT20 and PT/INR at the time of diagnosis**:
- Dose of ASV at the time of Admission
- Duration of ASV administration
- Time of initiation of ASV
- Time of repeat test.
- Repeat WBCT20, Clotting time and PT/INR After initiation of ASV at specific time intervals

	R1	R2	R3	R4
WBCT				
PT/INR				
Clotting time				

- Clinical Outcome

INFORMED CONSENT FORM

I, Mr./Mrs./Miss . ……. have been explained in my own understandable language, that I will be included in the above mentioned report, being conducted in RL JALAPPA HOSPITAL.

- I have been explained that my clinical findings, investigations, treatment and prognosis will be assessed and documented for study purpose.
- I have been explained my participation in this report is entirely voluntary and I can withdraw from the study any time and this will not affect my relation with my doctor or treatment for my ailment.
- I have been explained about the risk/benefit of the report. I understand that the medical information produced by this report will become part of institutional records and will be kept confidential by my said institute.
- I agree not to restrict the use of any data or result that arise from this report provided such a use is only for scientific purpose.
- I have principal investigator mobile number for enquiries. I have been informed that standard of care will be maintained throughout the treatment period.

I in my sound mind give full consent to be added in the part of this study.

_____ _____

Name of Patient/Guardian

(Relation with patient)

_____

(Signature of Patient / Attendant)

ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ

ನಾನು, ಶ್ರೀ / ಶ್ರೀಮತಿ _____, ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ನಡೆಸಲಾಗುತ್ತಿರುವ ಮೇಲೆ ತಿಳಿಸಿದ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನನ್ನು ಸೇರಿಸಿಕೊಳ್ಳಲಾಗುವುದು ಎಂದು ನನ್ನದೇ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

- ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಸಂಶೋಧನೆಗಳು, ತನಿಖೆಗಳು, ಚಿಕಿತ್ಸೆ ಮತ್ತು ಮುನ್ನರಿವುಗಳನ್ನು ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುತ್ತದೆ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.
- ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಮತ್ತು ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು ಮತ್ತು ಇದು ನನ್ನ ವೈದ್ಯರೊಂದಿಗಿನ ನನ್ನ ಸಂಬಂಧ ಅಥವಾ ನನ್ನ ಕಾಯಿಲೆಯ ಚಿಕಿತ್ಸೆಯ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.
- ಅಧ್ಯಯನದ ಅಪಾಯ/ಪ್ರಯೋಜನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ. ಈ ಅಧ್ಯಯನದಿಂದ ಉತ್ಪತ್ತಿಯಾಗುವ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯು ಸಾಂಸ್ಥಿಕ ದಾಖಲೆಗಳ ಭಾಗವಾಗುತ್ತದೆ ಮತ್ತು ನಾನು ಹೇಳಿದ ಸಂಸ್ಥೆಯು ಗೌಪ್ಯವಾಗಿಡುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.
- ಈ ಅಧ್ಯಯನದಿಂದ ಉಂಟಾಗುವ ಯಾವುದೇ ಡೇಟಾ ಅಥವಾ ಫಲಿತಾಂಶದ ಬಳಕೆಯನ್ನು ನಿರ್ಬಂಧಿಸದಿರಲು ನಾನು ಸಮ್ಮತಿಸುತ್ತೇನೆ, ಅಂತಹ ಬಳಕೆಯನ್ನು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.
- ವಿಚಾರಣೆಗಾಗಿ ನಾನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯನ್ನು ಹೊಂದಿದ್ದೇನೆ. ಚಿಕಿತ್ಸೆಯ ಅವಧಿಯುದ್ದಕ್ಕೂ ಆರೈಕೆಯ ಗುಣಮಟ್ಟವನ್ನು ನಿರ್ವಹಿಸಲಾಗುವುದು ಎಂದು ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದ ಭಾಗದಲ್ಲಿ ಸೇರಿಸಲು ನನ್ನ ಉತ್ತಮ ಮನಸ್ಸಿನಲ್ಲಿ ನಾನು ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

_____

ರೋಗಿಯ ಹೆಸರು / ರಕ್ಷಕ

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

_____

(ರೋಗಿಯ / ಅಟೆಂಡೆಂಟ್‌ನ ಸಹಿ)

PATIENT INFORMATION SHEET:

STUDY TITLE: Validating the 20 Minute Whole Blood Clotting Time With Coagulation Profile After The Initiation Of Anti Snake Venom In Hemotoxic Snake Bite
GUIDE : DR.SRINIVASA SV
STUDY CONDUCTED BY: DR. MANI MOHAN REDDY K P
STUDY LOCATION: R L Jalappa Hospital and Research Centre attached to
Sri Devaraj Urs Medical College, Tamaka, Kolar.

All Patients diagnosed with Hemotoxic snake bite will be included in this study. Patients in this study will undergo routine investigations, coagulation profile, principal investigator will bear the expenses of special investigations required for the study.
Your participation is the study will help us to use the outcomes of this study for future subjects and will bring to limelight the importance and potentiate the clinical application of micro albuminuria as a diagnostic and prognostic tool for sepsis.
Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study, we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.
All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee.
There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.
The purpose of the study is explained in detail to us and all information collected is for study purpose only. The data collected is submitted to the department of General Medicine, SDUMC, Kolar and confidentiality ensured. The merits and demerits explained briefly to us.

Name of the Patient

Signature/Thumbprint

Name of the investigator

Signature of the Investigator

ರೋಗಿಯ ವಿವರ ಪತ್ರ:

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಹೆಮೋಟಾಕ್ಸಿಕ್ ಹಾವಿನ ಕಡಿತದಲ್ಲಿ ಹಾವಿನ ವಿಷವನ್ನು ಪ್ರಾರಂಭಿಸಿದ ನಂತರ ಹೆಪ್ಪುಗಟ್ಟುವಿಕೆಯ ಪ್ರೊಫೈಲ್‌ನೊಂದಿಗೆ 20 ನಿಮಿಷಗಳ ಸಂಪೂರ್ಣ ರಕ್ತ ಹೆಪ್ಪುಗಟ್ಟುವಿಕೆಯ ಸಮಯವನ್ನು ಮೌಲ್ಯೀಕರಿಸುವುದು

ಮಾರ್ಗದರ್ಶಿ : ಡಾ.ಶ್ರೀನಿವಾಸ ಎಸ್.ವಿ

ನಡೆಸಿದ ಅಧ್ಯಯನ: ಡಾ. ಮಣಿ ಮೋಹನ್ ರೆಡ್ಡಿ ಕೆ ಪಿ

ಅಧ್ಯಯನ ಸ್ಥಳ: ಆರ್ ಎಲ್ ಜಾಲಪ್ಪ, ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರವು ಶ್ರೀದೇವರಾಜ್ ಅರಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು, ಟಮಕ, ಕೋಲಾರ.

ಹೆಮೋಟಾಕ್ಸಿಕ್ ಹಾವಿನ ಕಡಿತದಿಂದ ಗುರುತಿಸಲ್ಪಟ್ಟ ಎಲ್ಲಾ ರೋಗಿಗಳನ್ನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ರೋಗಿಗಳು ವಾಡಿಕೆಯ ತನಿಖೆಗಳಿಗೆ ಒಳಗಾಗುತ್ತಾರೆ, ಹೆಪ್ಪುಗಟ್ಟುವಿಕೆ ಪ್ರೊಫೈಲ್, ಮುಖ್ಯ ತನಿಖಾಧಿಕಾರಿಗಳು ಅಧ್ಯಯನಕ್ಕೆ ಅಗತ್ಯವಾದ ವಿಶೇಷ ತನಿಖೆಗಳ ವೆಚ್ಚವನ್ನು ಭರಿಸುತ್ತಾರೆ.

ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಯು ಈ ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಭವಿಷ್ಯದ ವಿಷಯಗಳಿಗೆ ಬಳಸಲು ನಮಗೆ ಸಹಾಯ ಮಾಡುತ್ತದೆ ಮತ್ತು ಪ್ರಾಮುಖ್ಯತೆಯನ್ನು ಬೆಳಕಿಗೆ ತರುತ್ತದೆ ಮತ್ತು ಸೆಪ್ಸಿಸ್‌ಗೆ ರೋಗನಿರ್ಣಯ ಮತ್ತು ಮುನ್ನರಿವಿನ ಸಾಧನವಾಗಿ ಮೈಕ್ರೋ ಅಲ್ಬುಮಿನೂರಿಯಾದ ಕ್ಲಿನಿಕಲ್ ಅಪ್ಲಿಕೇಶನ್ ಅನ್ನು ಪ್ರಬಲಗೊಳಿಸುತ್ತದೆ.

ದಯವಿಟ್ಟು ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬದ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ.

ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಮ್ಮತಿಸಿದರೆ, ನಾವು ನಿಮ್ಮಿಂದ ಅಥವಾ ನಿಮ್ಮಿಂದ ಅಥವಾ ಇಬ್ಬರಿಗೂ ಜವಾಬ್ದಾರರಾಗಿರುವ ವ್ಯಕ್ತಿಯಿಂದ ಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು.

ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೀತಿ ಶಾಸ್ತ್ರ ಸಮಿತಿಯು ಪರಿಶೀಲಿಸಿದೆ ಮತ್ತು ನೀವು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ.

ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಒತ್ತಾಯವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿಯು ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂ ಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸಿದರೆ ಮಾತ್ರ ನೀವು ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತನ್ನು ಒದಗಿಸಬೇಕಾಗುತ್ತದೆ. ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ನಮಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯು ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ. ಸಂಗ್ರಹಿಸಿದ ಡೇಟಾವನ್ನು ಜನರಲ್ ಮೆಡಿಸಿನ್, SDUMC, ಕೋಲಾರ ಇಲಾಖೆಗೆ ಸಲ್ಲಿಸಲಾಗಿದೆ ಮತ್ತು ಗೌಪ್ಯತೆಯನ್ನು ಖಾತ್ರಿ ಪಡಿಸಲಾಗಿದೆ. ಅರ್ಹತೆ ಮತ್ತು ದೋಷಗಳನ್ನು ನಮಗೆ ಸಂಕ್ಷಿಪ್ತವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ.

ರೋಗಿಯ ಹೆಸರು **ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು**

ಸಹಿ / ಹೆಬ್ಬೆರಳು **ತನಿಖಾಧಿಕಾರಿಯ ಸಹಿ**

S.No	Age of the patient	Sex	Time of admission since bite	Baseline WBCT 20	Baseline PT	Baseline INR	ASV Vials given.	Repeat WBCT 20 at 12h	Repeat PT at 12h	Repeat INR at 12h	Repeat WBCT 20 at 18h	Repeat PT at 18h	Repeat INR at 18h
1	55	male	12h	<20min	15.2	1.15	10 vials	<20min	18.2	1.43	<20 min	18.3	1.44
2	23	male	4h	>20min	19.1	1.51	20 vials	>20min	23.1	1.9	<20min	25.7	2.17
3	28	male	7h	<20 min	17.4	1.35	10 vials	<20min	37.8	3.48	<20min	28	2.41
4	55	female	4h	>20min	20.6	1.65	10 vials	<20min	18.4	1.44	<20min	18.1	1.41
5	26	male	1h	>20min	16.1	1.24	5 vials	>20min	14.6	1.11			
6	48	female	2h	>20min	15	1.15	6 vials	<20min			<20min		
7	45	female	14h	>20min	>180	~30	10 vials	<20min	18.1	1.42	<20min	21.3	1.7
8	26	male	2h	>20min	13.2	0.96	10 vials	>20min					
9	25	male	6h	>20min	13.9	1.03	10 vials	>20min	13.6	1	<20min	13.7	1.01
10	36	male	2h	>20min	80.9	7.69	10 vials	>20min			<20min		
11	28	male	8h	>20min	17.2	1.34	10 vials	<20min	15.6	1.2	<20min	16	1.23
12	28	male	4h	<20min	44	4.19	10 vials	<20min	28	2.4	<20min		
13	60	male	5h	<20min	17.8	1.28	15 vials	>20min	18.2	1.31	<20min		
14	50	female	4h	>20min	19.2	1.4	10 vials	>20min			<20min	17	1.21
15	20	male	2h	<20min	22.3	1.67	6 vials	<20min	20	1.5			
16	50	female	2h	<20min	45.5	4.36	10 vials	<20min	16.8	1.29	<20min	13.7	1.01
17	32	male	3h	>20min	13.5	1.02	10 vials	<20min	15	1.15	<20min		
18	21	male	2h	>20min	16.1	1.24	10 vials	<20min	16.8	1.31	<20min		
19	63	male	6h	>20min	>180	~30	28 vials	>20min	>180	~30	>20min	122	4.5
20	20	male	4h	<20min	107	12.4	10 vials	<20min			<20min	14.1	1.05
21	25	male	5h	>20min	18.5	1.46	10 vials	<20min			<20min	15.6	1.18
22	48	male	10h	>20min	15.4	1.16	10 vials	<20min	14.7	1.1	<20min	12.7	0.92
23	36	male	3h	>20min	80.9	7.69	10 vials	<20min	17.2	1.4	<20min	12.2	1.07
24	45	female	4h	<20min	32.9	2.78	6 vials	<20min	17.3	1.35	<20min	17.8	1.39
25	48	female	3h	>20min	15	1.15	10 vials	<20min	13.7	1.03	<20min		1.34
26	35	male	2h	>20min	18.4	1.44	10 vials	<20min	17.8	1.38	<20min		1.34
27	22	female	2h	>20min	16.2	1.25	10 vials	<20min					
28	36	female	4h	>20min	11.8	0.88	10 vials	>20min	17.2	1.3	<20min	11.4	0.84
29	65	female	4h	<20min	14	1.05	6 vials	<20min	12.9	0.964	<20min	12.7	0.95
30	54	female	4h	>20min	22.9	1.73	10 vials	>20min	23	1.74	<20min	23.6	1.81

31	32	Male	8h	>20min	12.4	0.92	10 vials	<20min	12.9	0.96	<20min		
32	36	Male	2h	<20min	12.5	0.91	10 vials	<20min	13	0.97	<20min	13	0.97
33	46	Female	3H	<20MIN	20.3	0.98	10 vials	<20 min	24.3	1.2	<20min	12.3	1.23
34	32	Male	4H	>20MIN	21.2	1.45	20 vials	>20min	34..2	1.3	>20min	16.3	1.2
35	48	Female	4H	<20MIN	32	1.54	10VIALS	<20 min	22.3	1.43	<20 min	13.4	0.8
36	39	Male	6H	>20MIN	32	1.34	25 vials	>20 min	34.5	1.64	<20 min	15.6	0.9
37	44	Female	2H	<20MIN	22.03	1.3	10vials	<20 min	22.2	1.32	<20 min	18.8	1.2
38	30	Male	2H	>20MIN	24	1.35	20 vials	>20 min	36.6	1.23	<20 min	16.7	1.1
39	49	Female	2H	>20MIN	43.2	1.35	20 vials	>20 min	23.3	1.5	<20 min	14.6	0.7
40	32	Male	8H	>20MIN	33.5	1.34	20 vials	>20 min	43.3	1.2	<20 min	19.8	0.6
41	32	Male	1H	>20MIN	26.4	1.34	10 vials	<20 min	21.3	1.34	<20 min	16.7	1.4
42	49	Female	13H	>20MIN	38.3	1.45	10 vials	<20 min	23.4	1.23	<20 min	19.8	0.9
43	33	Male	2H	>20MIN	28.2	1.23	20 vials	>20 min	43.4	1.23	<20 min	15.5	1.2
44	36	Male	3H	>20MIN	27.4	1.3	20 vials	>20 min	46.6	1.23	<20 min	14.5	0.8
45	34	Male	2H	>20MIN	26.4	1.4	10 vials	<20 min	23.4	1.56	<20 min	18.6	0.5
46	34	Male	2H	>20MIN	25.4	1.2	10 vials	<20 min	21.3	1.4	<20 min	14.5	1.3