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RESEARCH ARTICLE

A STUDY OF EPIDEMIOLOGY AND OUTCOME OF SNAKE ENVENOMATION ADMITTED AT A TERTIARY CARE CENTRE, NORTH KERALA

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Snake Bite, Capillary Leak Syndrome, ASV, Pit Viper, Cobra, Krait, Russell's Viper

Abstract

Aims and Objectives: Snake envenomation is a medical emergency of significant public health concern faced by rural populations mainly in tropical and subtropical countries with heavy rainfall and humid climate. Although India is a single large contributor of snake bites, reporting is very poor. Very few studies describe epidemiology and outcome of snake bite from Kerala. Hence, this study was planned to collect information on various aspects of snake bite in a tertiary care hospital. This tertiary care centre caters to all six districts of Kerala including Kozhikode, Kannur, Malappuram, Kasargod, Palakkad and Wayanad.

Study Setting and Design: This is a descriptive, observational and cross-sectional study carried out at Govt Medical College, Kozhikode.

Materials and Methods:

Sampling Procedure: This was a descriptive cross-sectional study of all patients admitted with snake envenomation at Snake Bite unit, Govt Medical College, Kozhikode. Study period was from July 2017 – June 2018. Patients are included if they had a definite history of poisonous snake bite and developed features of envenomation and are evaluated based on a proforma with detailed history and clinical examination. Data are collected regarding age, sex, occupation, time of bite, symptoms, investigations, mode of treatment given and complications. Sample size is 110.

Study Analysis: Data are analysed using computer software, Statistical Package for Social Sciences (SPSS) version 18. Data are expressed in its frequency and percentage. To elucidate the associations and comparisons between different parameters, qualitative variables are analysed using Chi-square test and quantitative variables by t-test. The Institutional Ethics Committee of Govt. Medical College, Kozhikode approved the research project. Written informed consent is obtained from all patients who had participated in this study in their vernacular language.

Results: Detailed history with special reference to the type of snake, circumstances leading to the bite and clinical consequences are studied and final outcome is noted. Males (n=71) are bitten more often than females (n=31). 46 cases are in the age range of 40-60 years. 57 (55%) cases are during the monsoon. Most (n=67) are encountered in the lower limbs. Viper is the most common poisonous snake encountered (73%) (n=75). 49 (48%) cases are from rural area. Among the viper

bite Russell's viper constitutes 26(25.4%) and Pit viper of 50(49%).Coagulation time is prolonged in 36 cases(35.3%). Hemotoxic symptoms present in 40(39.2%) victims ,neurotoxic features present in 32(31.3%) victims ,both hemotoxic and neurotoxic features are present in 12(11.7%) victims.Polyvalent anti snake venom (ASV) is given to 66 cases. Hypersensitivity to ASV is noted in 13 cases out of 66 cases.Bite to needle time is >6hrs in all the victims who expired.The mortality rate among snake bite victims is 6.8%.The morbidity and mortality can be reduced substantially by early medical care and providing health education.

Conclusion: On the basis of study findings ,Pit viper bites were predominant in our area which was less fatal.Eventhough the antisnake venom doesnot cover Pitviper,it was given empirically if coagulation failure occurs. Death was more in neurotoxic bites .Duration of hospital stay was more in Viper bites .Victims with bite to needle time <4 hrs were recovered earlier without complications. Morbidity and mortality due to this can be reduced by early administration of antisnake venom and management of complications.So prompt referral of victims with poisonous snake bite to centres where facilities in managing snake bite is crucial in preventing mortality.

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Introduction:-

Snake bite poisoning is an occupational health hazard often faced by farmers, plantain workers, herders and laborers of tropical and subtropical countries. WHO has included snake bite in the list of neglected tropical conditions. The true global burden of snake bite is not known due to lack of standardized reporting and under reporting. It is documented that there are 54,00,000 snake bites with 2,50,000 envenomations and around 1,25,000 fatalities annually in the world¹However, there is no accurate statistics of morbidity and mortality which could certainly be higher because most of the victims initially approach traditional healers for treatment and are not registered in the hospital. Ignorance of primary care (first aid) and approaching traditional healers further delays proper treatment and contributes to high mortality and morbidity².

Results and Observations:-

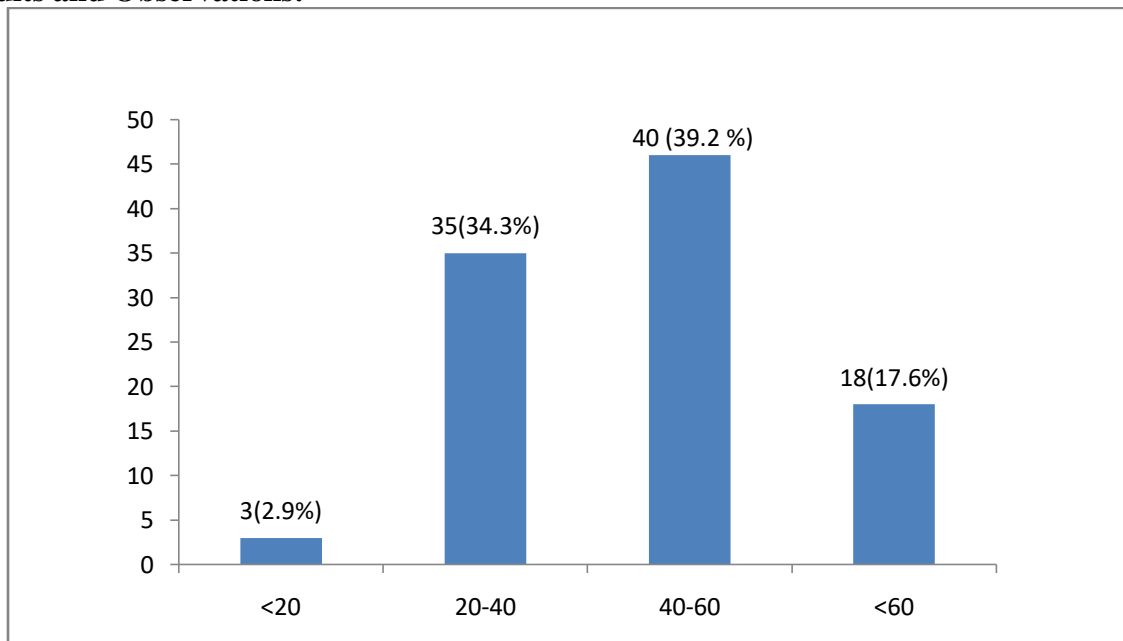


Fig.1:- Distribution of Patients in relation to Age.

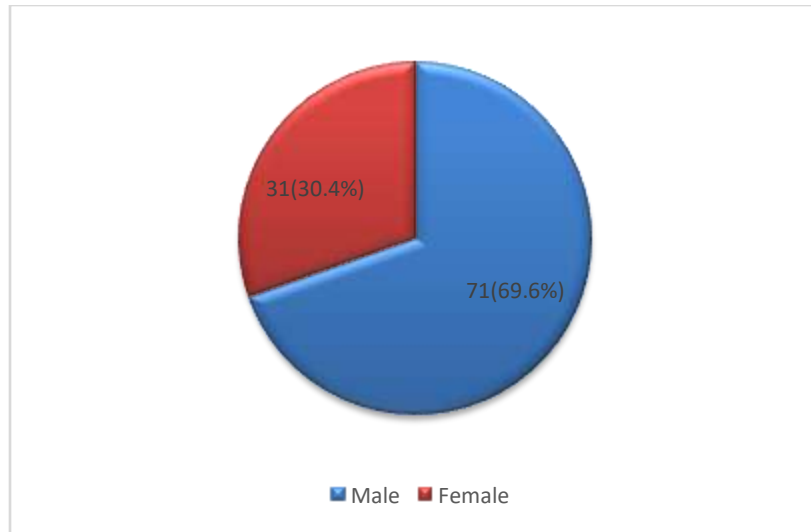


Fig. 2:- Distribution of Patients according to sex.

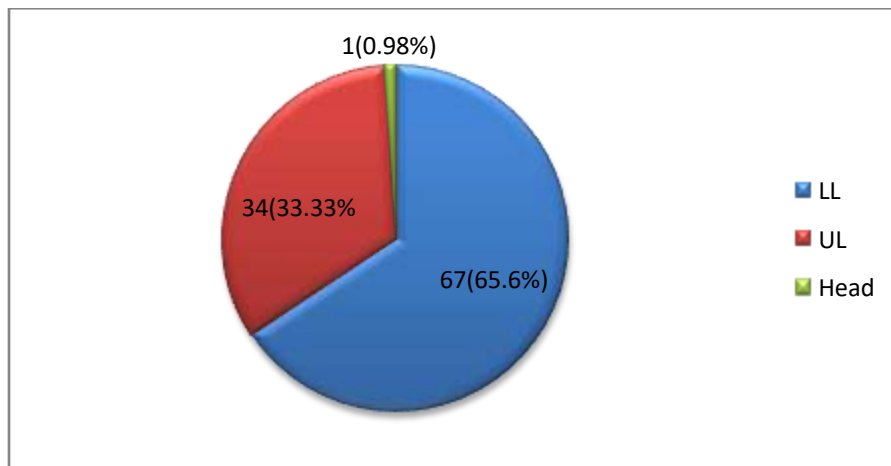


Fig. 3:-Site of Bite.

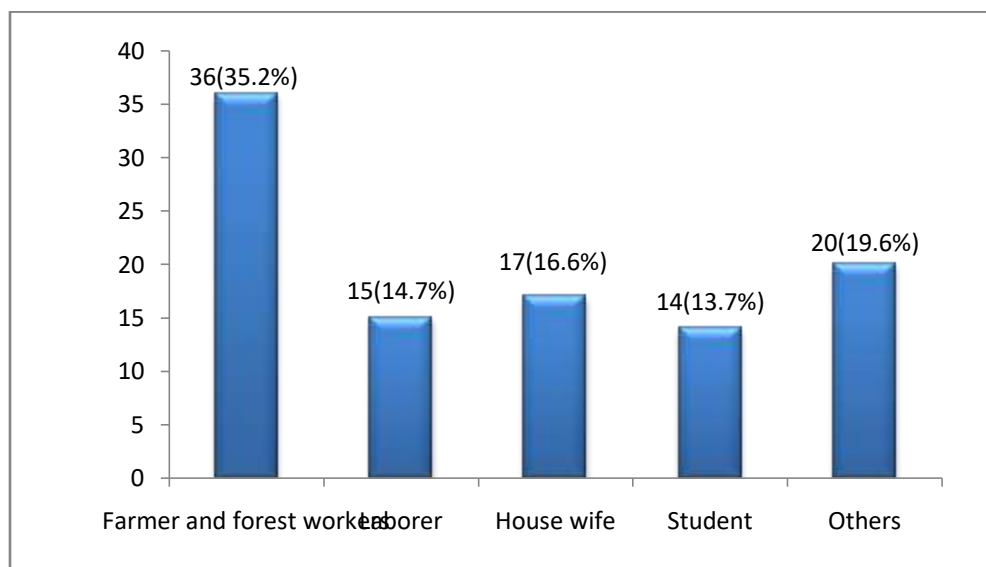


Fig. 4:- Distribution of Patients according to Occupation.

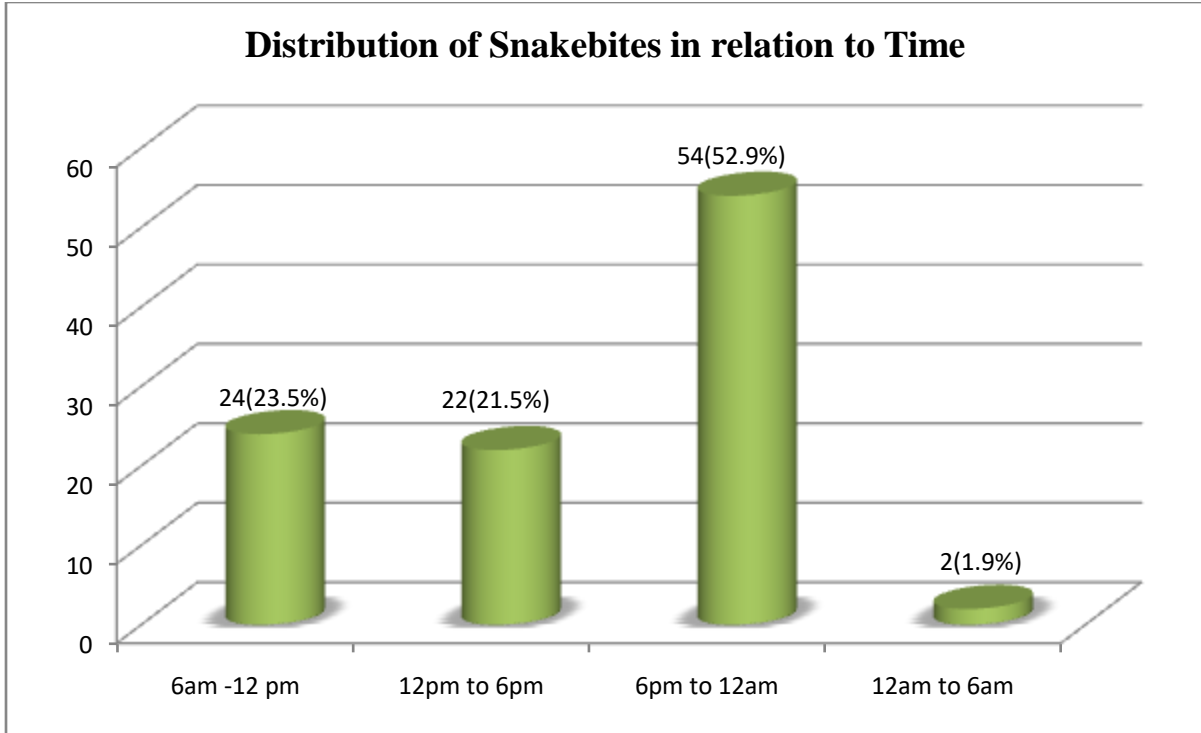


Fig. 5:- Distribution of patients according to Time of bite.

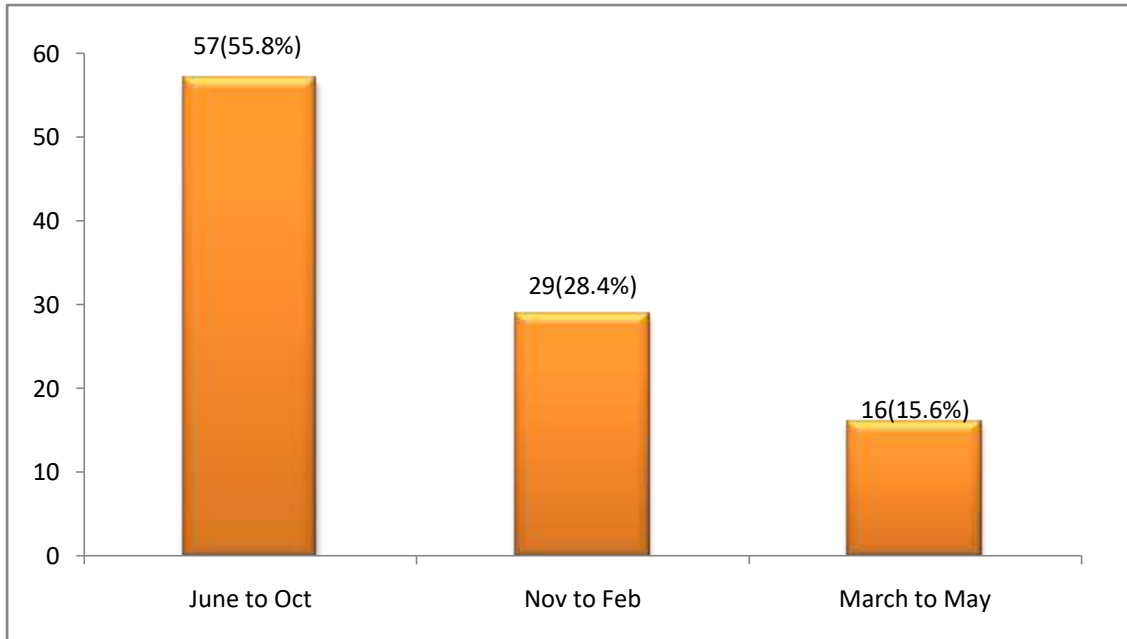


Fig. 6:- Distribution of Snakes bites in relation to season.

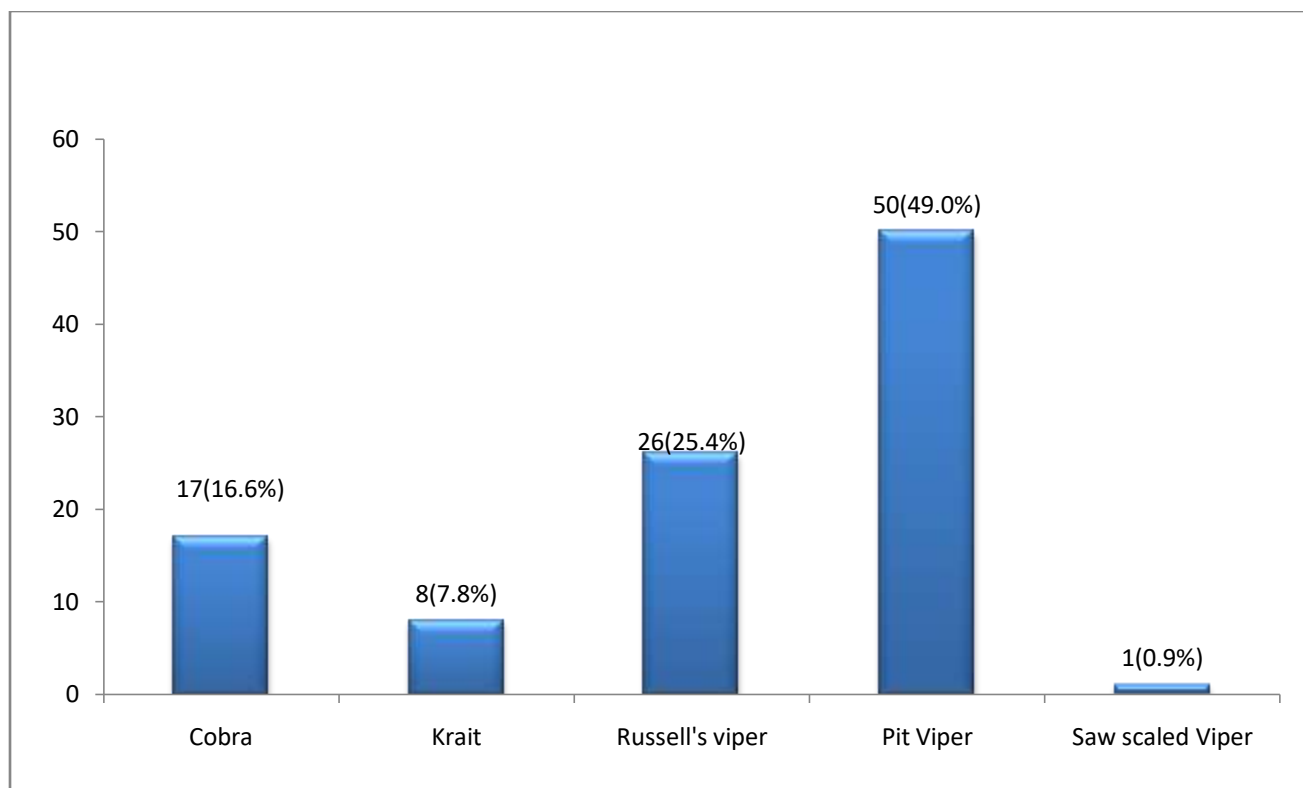


Fig. 7:-Distribution of Types of Snakes.

Table 1:-Distance between two fang marks in snake bites.

| Type of Snakes | Mean | Minimum | Maximum | Standard Deviation |
|------------------|---------|---------|---------|--------------------|
| Common Cobra | 0.594cm | 0.1cm | 2.5cm | 0.808 |
| Common Krait | 0.885cm | 0.1cm | 2.4cm | 1.186 |
| Russell;s Viper | 1.26cm | 0.1cm | 4cm | 1.225 |
| Pit viper | 1.11cm | 0.1cm | 3.5cm | 1.086 |
| Saw scaled viper | 0.800cm | 0.80cm | 0.80cm | 0.80 |

Clinical features:

Table 2:- Frequency of Constitutional symptoms in various snake bites.

| Types of Snakes | Vomiting | Abdominal Pain | Giddiness | Anxiety |
|------------------|-----------|----------------|-----------|-----------|
| Common Cobra | 3(17.6%) | 5(29.4%) | 6(35.3%) | 5(29.4%) |
| Common Krait | 3(37.5%) | 4(50%) | 4(50%) | 4(50%) |
| Russell's Viper | 14(53.8%) | 16(61.5%) | 17(65.4%) | 14(53.8%) |
| Pit Viper | 5(10%) | 8(16%) | 12(24%) | 14(28%) |
| Saw scaled viper | 0 | 0 | 0 | 0 |

Table 3:-Frequency of Local reactions in various Snake bites:

| Snake | Pain | Swelling | Cellulitis | Lymph node enlargement | Bleed from needle site | Blister |
|-----------------|------------|-----------|------------|------------------------|------------------------|-----------|
| Common Cobra | 14(82.35%) | 12(70.6%) | 10(58.8%) | 4(23.5%) | 4(23.5%) | 4(23.5%) |
| Common Krait | 8(100%) | 7(87.5%) | 6(75%) | 1(12.5%) | 3(37.5%) | 3(37.5%) |
| Russell's Viper | 24(92.3%) | 22(84.6%) | 20(76.9%) | 15(57.7%) | 17(65.4%) | 16(61.5%) |
| Pit Viper | 44(88%) | 36(72%) | 36(72%) | 7(14%) | 14(28%) | 21(42%) |

| | | | | | | | |
|--------------|--------|---------|---------|---------|---|---|---|
| Saw viper | scaled | 1(100%) | 1(100%) | 1(100%) | 0 | 0 | 0 |
|--------------|--------|---------|---------|---------|---|---|---|

The minimum duration of hospital stay for Cobra bites is 2days and maximum of 28days with a mean of 6.53days and SD of 6.578. The minimum duration of hospital stay for Krait is 3days and maximum of 7days with a mean of 4.14days and SD of 1.676. The minimum duration of hospital stay in Russell’s viper is 1day with a maximum of 25days and mean of 7.96days and andSD of 6.648. The minimum duration of Hospital stay for Pit viper is 1day with a maximum of 9days and mean of 1.81days and SD of 1.593.

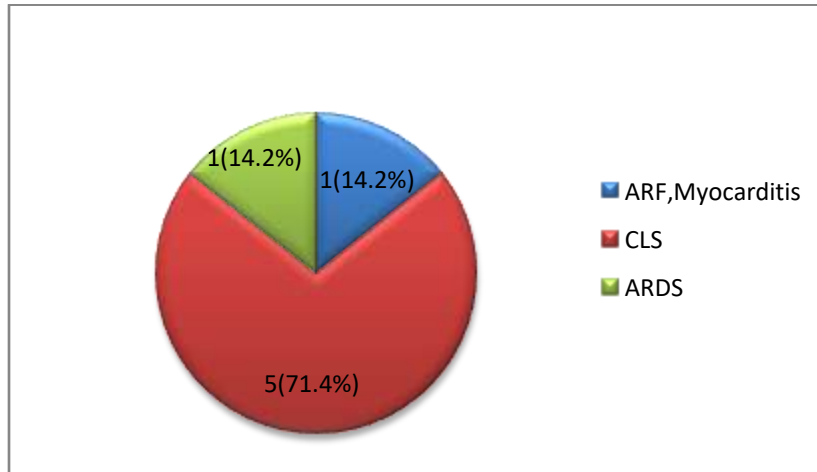


Fig. 8:- Cause of death:

In present study, the most common cause of death is the Capillary leak syndrome in 5(71.4%) victims followed by acute respiratory distress syndrome in 1(14.2%) and acute renal failure in 1 (14.2%).

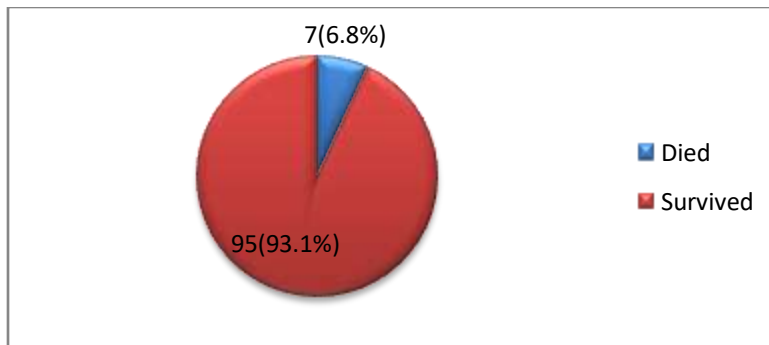


Fig.9:- Outcome:

Discussion:-

Epidemiological aspects:

In our present study total number of male victims was 71(69.6%) as compared to females which was 31(30.4%). Our finding concurred with earlier studies conducted by Hati AK³ et al , Yogesh C etal⁴ in Bangalore, Suchitra N etal⁶ in Kerala .Males were more bitten by snakes due to more involvement in out door activities and sleeping in the farmyards during harvesting. Commonest affected age group was 40-60 yrs (39.2%) probably due to their ambulant nature. Minimum age was 13 and maximum 72 with mean age of 44.99yrs. Similar findings were observed in the study conducted by Yogesh C etal⁶¹ and Bhardwaj A etal.⁵

Occupation:

Out of 102 cases ,36 (35.2%) were farmers or Forest workers ,17(16.6%) were housewives ,15 (14.7%) were laborers ,14(13.7%) were students and 20 (19.6%) belongs to carpenters, drivers, teachers and shopkeepers. This is similar to the studies conducted by Hati k etal³ and Suchitra N etal⁶.

Time of bite

Majority of bite occurred between 6pm to 12am (52.9%). Similar diurnal variation has also observed by Bawaskar HS et al⁷, Monteiro NP et al⁸. Least incidence occurred in between 12 am to 6am (1.9%).

Seasonal variation

Maximum bites falls during the months from June to October (55.8%). Victims were lowest during the summer (15.6%). This finding is similar to study conducted by Hansdak S Getal¹⁰, Lahori UC et al¹¹, Yogesh C et al⁹. During rainy season rain water floods their burrows and snakes then try to take shelter near human dwellings which increases chances of snakes feeling threatened or provoked by human beings and biting them in defence.

Site of bite

Lower limb was most observed bitten part of the body (65.6%) and commonest site was foot. Upper limbs are involved in people who are cutting the grass or women who blindly try to remove the dryashes from their mud furnaces (33.3%). This was similar to findings of Yogesh C et al⁹, Kulkarani ML et al¹².

Types of snakes:

Among the snake bites, Pit viper bite predominates 50(49%) followed by Russell's viper 26(25.4%), Cobra 17 (16.6%), Krait 8(7.8%) and Saw scaled viper 1(0.9%). This is unison with the studies of Hati K et al¹⁹ and Mukhopadhyay PP et al¹³.

Fang mark features:

Fang marks were present in 98 (96.1%) and absent in 4 victims (3.9%). 46.9% had one fang mark and 53.1% had two fang marks. In Cobra bites minimum distance was 0.1 cm and maximum of 2.4cm with a mean of 0.594 cm. In Krait bites minimum distance was 0.1 cm and maximum of 2.5cm. In Russell's viper bites minimum distance was 0.1cm and maximum of 4cm. In Pit viper bites the minimum distance was 0.1cm maximum upto 3.5cm. In Saw scaled viper as there is only one case in our study the distance between bite mark was 0.8cm. Fang marks were present in 69% of patients in a study conducted by Anil kumar H et al¹⁵.

Bite to needle time

80 of the victims reached the hospital within 6 hrs and 15 reached the hospital after 6 hrs. It was noted that patients who developed acute kidney injury and capillary leak syndrome had a significantly longer bite-to-hospital time. Athappan et al¹⁶ in his study also found that bite to needle time more than 2 hours was an independent risk factor for the development of kidney injury. On the contrary, Danis et al¹⁷ observed that there was no such association. The bite to hospital time varies depending on the availability of medical facilities and the settings in which the study has been done. Various studies which shows a direct relation between increased rates of complications or mortality with late arrival to hospital. In our study, death occurred in victims who reached the hospital after 6 hrs. The delay in reaching our hospital can be attributed to distance from the villages, traffic problems, poor transportation facilities, lack of knowledge about the complications of snake bite time may be wasted for application of tourniquet and herbal medicines. Similar results were observed by Sharma D et al¹⁸.

Influence of first aid and traditional healers.

In the present study first aid in the form of pressure bandage and tight tourniquet was applied by 67.6% proximal to site of bite. No death occurred in victims who had got first aid. 21.5% went to traditional healers and took oral herbal medicines and locally applied herbs and roots. 9.09% death occurred in victims those who went to traditional healers in southern India confirmed that delayed antivenom administration was associated with an increased risk of complications.

Constitutional symptoms:

Abdominal pain was present predominantly present in 16 of Russell's viper bites, followed by 4 of Krait bites, 5 of Cobra bites and 8 of Pit viper bites and absent in one Saw scaled viper bite. Gastro intestinal symptoms observed in 32.2% cases in a study conducted by Monterio et al⁸. While Saini et al¹⁹ reported it in 16% cases. Persistent vomiting and abdominal pain in Russell's viper bites due to intraperitoneal bleed and pancreatitis is an indication for antivenom administration.

Management:

In our study specific treatment composed of Polyvalent Antisnake Venom was given. Abnormal local site or coagulation disturbances or neurological manifestation are considered as indication for ASV therapy. If there are allergic reactions in the form of fever, itching or urticaria, polyvalent ASV administration is continued with corticosteroids and antihistamines.

In the present study In Cobra and Krait bites minimum of 10 vials and maximum of 20 vials of ASV was given. While in Russell's viper bite maximum of 30 vials..and in Pit viper bites a maximum of 36 vials was given. Sharma et al⁷⁵ found that average dose of antivenom was 51.2 vials for elapid bites and 31 vials for viper bites.

ASV anaphylaxis noted in total 12 cases.4 out of 6 in Cobra bites,3 out of 22 in Russell's viper bite ,5 out of 25 in Pit viper bites. Mild reactions like itching,urticaria,fever,tachycardia,palpitations were noted in 6 patients. 2 cases showed features of bronchospasm,hypotension and angioneurotic edema and they were given adrenaline, steroids and antihistamines.No death occurred in patients developed anaphylaxis to ASV. Bawaskar HS et al⁷ noted that three patients were sensitive to ASV.In a study conducted by Halesha et al²⁰ 12% , develop a reaction either early (within a few hours) or late (five days or more) after being given the antivenom

Atropine and neostigmine was given in 2(25 %) of Krait bites , 3(17.6 %) of Cobra bites ,2(7.6%) of Russell's viper bites and 1(2%)of pit viper bites who developed neurotoxic features.Ventilator was required in 1(12.5%) of Krait bites 2(11.5 %)of Cobra bites,3(11.5 %) of Russells viper bites and 1(2%)of Pit viper bites .

The **coagulopathy** observed in Russell's viper envenomationwas significantly associated with low platelet count and clinical bleeding, suggesting venom-induced consumption coagulopathy as the mechanism. DIC developed in 6(23.1 %) of Russels viper bites,2(4 %) of Pit viper bites and absent in victims bitten by Cobra,Krait and Saw scaled viper. Fresh Frozen plasma of average 6 pints was required in all victims having coagulation failure. Packed Red Blood Cells was given to 6(23.07 %)of Russell's viper bites ,1(12 .5 %) of Krait bites and 1(2%) of Pitviper bites . Plasmapheresis required in 1(5.8%) of Cobra bites,1(12.5%) of Krait bites 10(38.4%) of Russell's viper bites.

Compartment syndrome developed in3 (11.5%) of Russell's viper bites ,4(8%) of Pitviper ,1(5.9%) of Cobra bites and was absent in Krait and Saw scaled viper and Fasciotomy done in all cases .In the present study compartment syndrome is more in viper bites due to their cytolytic property

Acute respiratory distress syndrome developed in 5(19.2%)of Russell's viper bites and 10(2%) of Pit viper bites presented with non cardiogenic pulmonary edema and bilateral lung infiltrates in the chest Xray .They required PEP ventilator support and treated with antibiotics and bronchodilators . Among them one of the victim bitten by Russell's viper died and others recovered.As described by Warrel et al⁴⁷ there will be pulmonary vascular endothelial damage caused by direct effect of venom on vascular endothelium,causing spontaneous bleeding due to the presence of activators of factors V, X, IX, and XIII, platelets, protein C, and hemorrhagins in the viper venom.

Cardiotoxicity was developed in 38.8% of Russell's viper bites..In the present study one of the victim bitten by Russell's viper, who survived developed venom induced myocarditis and sinus bradycardia,ECG shows T inversion in Lead 2,3 AVF and V₄ to V₆..

In our study, all the deaths due to Russell's viper bites were due to **capillary leak syndrome** which is characterized by hypotension with hemoconcentration, hypoalbuminemia ,albuminuria,and generalized edema. This syndrome is frequently recognized from the southern parts of India, especially from the state of Kerala. Acute kidney injury often requiring dialysis is invariably present in all patients because of reduced renal perfusion and ischemic acute tubular necrosis as a result of hypotension. Hypoproteinemia occurred in 6 cases with capillary leak syndrome which was treated with 20% intravenous Human albumin.

Nephrotoxicity in the form of Acute renal failure developed in 13(50%) of Russell's viper bites,3(6%) of Pitviper ,1(5.9 %) in Cobra bites. Among them all required dialysis. 6(85.7%) of dead victims required dialysis. Renal failure reported in 1.69% cases in study conducted by Pradeep et al²¹.

Complications:

Major complications noted were compartment syndrome, Disseminated intravascular coagulation, Acute renal failure and Respiratory failure. These were also the major complications seen in the study conducted by Anilkumar H¹⁵. Coagulopathy is a marker of the vasculotoxicity and hemotoxicity of the poison, which means that these patients will have nephrotoxicity due to damage to renal microvasculature. In study conducted by Halesha et al²⁰, the most common complication was respiratory paralysis, followed by acute renal failure, gangrene at the bite area and intravascular coagulation, whereas Saini et al⁷⁹ had reported that only 4% of the cases developed renal failure.

Duration of Hospital stay:

The minimum duration of hospital stay in Cobra bite was 2 days and maximum of 28 days. The minimum duration of hospital stay for Russell's viper was 1 day and maximum upto 25. The minimum duration of hospital stay for pit-viper was 1 day and maximum of 9. The minimum hospital duration for Krait bite was 3 days and maximum was 7 days.

Cause of death

The cause of death in five were due to capillary leak syndrome, one was due to renal failure and myocarditis and one due to respiratory failure (ARDS). In another study by Redeward,²² cause of death was intracranial bleed due to coagulopathy and acute renal and respiratory failure. In the present study the major cause of death is the Capillary leak syndrome.

Mortality Rate

In the present study the mortality rate is 6.8% (7 died out of 102 cases). The major predictors of mortality rate were bite to needle time. In a study conducted by Sharma et al²³ mortality rate was 3.5%, In a study conducted by Hati AK et al¹⁹ mortality rate was 10%. High mortality rate in some might be due to non availability of medical facilities in remote rural areas, poor transport facility to hospital and also due to valuable time lost in giving traditional medicines.

Conclusion:-

1. In the present study, Pit viper accounts for 50(49%) is found to be the most common cause of snake envenomation in Malabar region followed by Russell's Viper. The most common affected age group is found to be 40 -60 yrs due to their ambulant nature. Lower limb is the most affected site in 67 of victims, suggestive of accidental stamping on to the snakes. Upper limb is the most affected part in 4 out of 7 death cases. The proximity of the site of bite to heart had an influence on the rapidity of developing cardiotoxicity in viperine envenomation. Nocturnal snake bite is predominant in the present study, about 54 of the victims were bitten during the time 6pm to 12 am. Monsoon season from June to October accounts for maximum bites 57(55.8%) cases, is found to be crucial time for snake bite in this region. In the present study, there is significant association between the first aid and mortality with P value <0.001.
2. Out of 102 cases, 69 victims got the first aid and all survived. Bite to needle time has got significant association with mortality with a P value <0.001. It is found that all the victims who died, has a delay of >6hrs to reach the hospital and to administer the antivenom. Abdominal pain and vomiting is predominant in Russell's viper bites as compared to others due to the occurrence of intraperitoneal bleed or pancreatitis.
3. Out of total 17 Cobra bites 3 showed clinical features of neurotoxicity. Out of 8 Krait bites, 3 showed clinical features of hemotoxicity. Out of 26 Russell's viper bites, 10 showed the features of neurotoxicity. Out of 50 Pit viper bites, 6 showed features of neurotoxicity.
4. Occurrence of Disseminated intravascular coagulation due to consumption coagulopathy in snake envenomation has got significant association with mortality with P value <0.001. Acute respiratory distress syndrome manifested in 5(19.2%) of Russell's viper bites and absent in others, among them only one died. All the patients presented with ARDS also has the features of Capillary leak syndrome and all of them required artificial ventilation. Acute renal failure is present in 50% of Russell's viper bites, 6% of pit viper bites and 5% of Cobra bites.
5. Out of 7 died victims, 6 has developed acute renal failure. Occurrence of Acute renal failure following snake envenomation has got significant association with mortality with a P value <0.001. Capillary leak syndrome is present in 9(34.6%) of Russell's viper bites and 2(11.8%) of Cobra bites, among them 5 victims died. Presence of Capillary Leak Syndrome following Russell's envenomation has got significant association with mortality with P value of <0.001.

Recommendations:-

High incidence of Pit viper bites in Malabar region is the major point highlighted in the present study and there is one case of death due to acute renal failure and myocarditis. Hence further studies are needed in developing Anti snake venom, which is effective against Pit viper also.

Russell's viper bites is associated with high incidence of mortality in Malabar region due to the unique capillary leak syndrome, as the conventional anti snake venom fails to neutralize a Hemorrhagin, Zinc metalloproteinase which is invariably seen in venom of certain species of Russell's viper due to geographical variations in northern Kerala. It is a challenging medical problem and needs further investigations.

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