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RESEARCH ARTICLE

TO STUDY THE ROLE OF LIPID PROFILE WITH SEVERITY AND OUTCOME IN SNAKE BITE PATIENTS

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ABSTRACT

Background: Snakebite is a major public health problem throughout the world and more so in tropical and subtropical countries, where people are more engaged in agriculture work have highest incidences of snake bites. Lipid profile at the time of admission can be helpful to predict severity, course as well as outcome of these snake bite patients. ***Methodology:*** This was a descriptive case control study which was carried out over all the patients of snake bite being admitted to various medical wards of Maharana Bhupal Government Hospital, attached to R.N.T. Medical College, Udaipur (Rajasthan) from January 2020 to November 2020. ***Result:*** Maximum incidence of snake bite was found in males (58%), from rural area (88%) and farmer (54%) by occupation. It was observed that bite was common in monsoon and post monsoon season (90%), bite was common in lower extremities (72%) and at day time(54%). Among all bites, 12% were contributed by non-poisonous and rest 88% were poisonous bites, out of which 54% were haemorrhagic and 34% were neuroparalytic. The mean serum total cholesterol levels were significantly lower (P<0.034) in severe cases (133.65 mg/dl) as compared to moderate (147.30mg/dl) and mild (149.50 mg/dl) cases. The mean serum triglyceride levels were lower in severe cases (116.15mg/dl), as compared to moderate (120.07 mg/dl) and mild (133.92 mg/dl) cases. The mean serum HDL levels were lower in severe cases (31.95mg/dl), as compared to moderate (33.69 mg/dl) and mild (37.42 mg/dl) cases. The mean serum LDL levels were lower in severe cases (61.50mg/dl), as compared to moderate (69.07 mg/dl) and mild (69.83 mg/dl) cases. ***Conclusion:*** Lipid profile (TC, TG, LDL, HDL) were significantly decreased in snake bite patients both with hemorrhagic and neuro-paralytic. In our study, we found that a negative correlation exits between serum TC,TG, HDL, LDL and severity of envenomation. Hence,we can use lipid profile as a surrogate marker of severity of snake bite envenomation and predicting the complication and recovery.

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INTRODUCTION

Snakebite is a major public health problem throughout the world and more so in tropical and subtropical countries. Worldwide snake bite occurs most frequently in the summer and rainy season when snakes are active, remains outside more and humans being also have more outdoor activities. Tropical and sub-tropical regions where people are more engaged in agriculture work have highest incidences of snake bites than anywhere else. With rapid urbanization and deforestation, the incidence of snake bites are increasing and contributes a significant number of hospital admissions. There are no accurate data available which can determine the exact epidemiological and mortality profile in snakebite cases as the true incidence of snakebite is difficult to assess and often is underreported. Despite of such under reporting, current available data suggest that 4.5 to 5.4 million people are beaten by snakes in a year, out of which 1.8 to 2.7 million people develop clinical illness and death ranging from 80000 to 138000 people per year worldwide[1]. The mortality is lowest in Europe, Australia and North America whereas highest in Sub- Saharan Africa, South Asia and South East Asia. In India, there are around 2.0 million snake bites reported annually, out of which 35000 to 50000 people of snake bite die every year[2]. Worldwide, around 3600 species of snake are identified, out which 216 species of snake were seen in India predominantly[3]. Maximum of snake bite are non-poisonous in nature. The poisonous snake bite can be classified according to their clinical presentation such as hemorrhagic manifestations (hemotoxic),which include bite from viperidae family (Russel Viper, Gaboon Viper, Saw Scaled Viper) , neurological manifestations (neurotoxic) which include bites from Elapidae family snakes(Cobras, Kraits, Mambas, Tiger snake) and renal manifestations(nephrotoxic) which includes bite from hydrophidae family snakes. Worldwide among the poisonous bite, most common is viper bite whereas most dangerous bite is by common krait[4] .

The overall mortality rates for victims of venomous snakebites are low in regions where medical facility including anti-venom are available and rapidly accessed. Snake bite is one of the most life-threatening bio-weapon system in the nature which may cause local to systemic complications in the form of neurotoxicity, haemotoxicity or both. Recently, studies showed very low total serum cholesterol levels in several patients bitten by *V. palaestinae,* well before development of local or systemic manifestations[5]. These observations led us to conduct a chart review of all our cases of V. *palaestinae* bite to examine the possible correlation between low serum cholesterol levels and severity of envenomation. Crude viper venom contains several toxic components such as proteolytic enzymes, hyaluronidase, phospholipase A2, and phosphor-esterases which cause capillary endothelial damage[10]. This results in extravasation of plasma and plasma proteins. The possibility of the decrease in cholesterol level due to lipoprotein leakage should therefore be considered. Indeed, in the patients with highest severity of envenomation, hypocholesterolemia was accompanied by a decrease in total serum proteins and albumin, possibly caused by extravasation. However, in patients with moderate envenomation, the marked decrease in cholesterol concentration was not associated with a fall in serum proteins. Hypocholesterolemia preceded local signs of edema.

Notwithstanding, at low venom doses, a significant decrease in cholesterol level occurred far in excess of the concomitant change in serum albumin level. The incubation of HDL with phospholipase A2 results in the accumulation of cholesterol ester in cultured hepatocytes and in consequent enhanced bile acid formation. The products of phospholipase A2 hydrolysis of VLDL and HDL (e.g., sodium oleate) stimulate the cholesteryl-ester transfer protein-mediated transfer of cholesteryl ester from HDL to VLDL[6]. It thus appears that phospholipase A2 hydrolysis of plasma VLDL and HDL may be capable of enhancing reverse cholesterol transport in plasma. Accordingly, we suggest that the phospholipase A2 found in snake venom may contribute to the rapid decrease in total plasma cholesterol level observed after *V. palaestinae* bite. The effect of hydrolysis of lipoproteins is probably expressed by enhanced scavenging of low density lipoprotein. Concomitantly, more cholesterol is cleared to the liver, either by HDL or by VLDL remnants through stimulated reverse cholesterol transport. With recovery from envenomation, the enlarged cholesterol pools can be released into the blood stream by the liver in the form of newly synthesized VLDL.

Complications of Snake Bite: Cobra bite causes significant local envenoming; pain, swelling, blistering, and severe local necrosis as well as acute systemic envenoming; ptosis, diplopia, external ophthalmoplegia, and descending paralysis[7]. Common krait bites cause a distinct clinical syndrome consisting of minimal or no local envenoming, abdominal pain, vomiting, ptosis, diplopia, external ophthalmoplegia, and descending paralysis that most often lead to respiratory paralysis[8]. Russell's viper bite is venomous enough to develop local envenoming, spontaneous bleeding, incoagulable blood, neurological manifestations, ptosis, ophthalmoplegia, descending paralysis, rhabdomyolysis, and acute kidney injury (AKI)[9] Saw-scaled viper bite is responsible for coagulopathy and spontaneous systemic hemorrhage and local envenoming. Hump-nosed viper bite mostly accounts for severe local swelling, hemorrhagic blisters, local tissue necrosis, incoagulable blood, spontaneous bleeding mainly haematuria, and AKI.

AIMS AND OBJECTIVES

- Estimation of Lipid Profile in snake bite.
- To correlate lipid profile with severity and complications in a patient of snake bite.

MATERIAL AND METHODS

Source of study: The study was conducted over 50 consecutive patients admitted with snake bite in various Medical wards of MBGH Attached with RNT Medical College, Udaipur during the study period of eleven months from January 2020 – November 2020.

Method of collection of data: 50 healthy individuals of age and gender matched were enrolled in this study as control group, who attend hospital OPD for routine check-up and lipid testing was done. First 50 snake bite patients were considered as study subjects (cases) fulfilling inclusion and exclusion criteria.

Inclusion criteria

Any patient with history of snake bite was included in the study.

The snake bite can be:

- Non-poisonous
- Hemorrhagic
- Neuro-paralytic

Exclusion criteria

- Patients with chronic disorders, anaemia or other hematological disease and acute bacterial infection.
- Any patients who presented with any other form of unknown bite

RESULTS

Table 1. Clinical profile of snake bite

	Characteristics			Percentage
1	Age	Less than 30 years		50%
		More than 30 years		50%
2	Gender	Male		58%
		Female		42%
3	Residence	Rural		88%
		Urban		12%
4	Occupation	Farmer		54%
		Labour		2%
		Housewife		12%
		Student		8%
5	Site of bite	Hand		18%
		Foot		58%
		Back		6%
		Other		18%
6	Time of bite	Day		40%
		Night		60%
7	Type of snake	Nonpoisonous		12%
		Poisonous	Neuroparalytic	34%
			Hemorrhagic	54%
8.	Month of bite	January to june	5 (10%)	
		July to November	45(90%)	

In the present study, 50 patients of snake bite were studied. Maximum incidence of snake bite was found in age groups 21 to 30 years of age(30%), males (62%) were bitten more than females (38%).Snake bite was observed more common in rural population (78%), farmer by occupation(38%) followed by labours(16%). Predominant bite was seen in lower limb(56%) and in night time(60%).The bite was predominantly poisonous(60%),out of poisonous snake bite hemorrhagic and neuroparalytic bite contributed equally. The bite was mainly seen in monsoon and post monsoon season and it was 88% from month of July to November and maximum bite was seen in month of September (26%).

Table 2. Snake bite and Lipid profile

Lipid profile (Mean+SD)	Case (n=50)	Control (n=50)	P-Value
Total Cholesterol (TC)	146.10±22.43	181.72±25.99	0.000
Triglyceride (TG)	126.42±36.11	163.56±23.97	0.000
HDL	34.64±7.00	40.34±3.96	0.000
LDL	67.38±17.42	88.80±18.02	0.000

The mean serum total cholesterol levels were significantly lower (P=0.000) in cases (146.10 mg/dl) as compared to controls (181.72 mg/dl).The effect of snake bite on the total cholesterol levels was significant. The mean serum triglyceride levels were significantly lower (P=0.000) in cases (126.42 mg/dl) as compared to controls (163.56 mg/dl).The effect of snake bite on the total cholesterol levels was significant. The mean serum HDL levels were significantly lower (P=0.000) in cases (34.64 mg/dl) as compared to controls (40.34 mg/dl). The effect of snake bite on the HDL levels was significant. The mean serum LDL levels were significantly lower (P=0.000) in cases (67.38 mg/dl) as compared to controls (88.80 mg/dl). The effect of snake bite on the LDL levels was significant.

Table 3. Severity of snake bite and Lipid profile

Lipid profile (Mean±SD)	Mild (n=12)	Moderate (n=13)	Severe (n=20)	P-Value
Total Cholesterol (TC)	149.50±19.59	147.30±23.02	133.65±11.12	0.034
Triglyceride (TG)	133.92±33.25	120.07±44.00	116.15±27.55	0.393
HDL	37.42±8.50	33.69±6.44	31.95±5.32	0.104
LDL	69.83±14.89	69.07±23.67	61.50±12.64	0.334

The mean serum total cholesterol levels were significantly lower (P<0.034) in severe cases (133.65 mg/dl), as compared to moderate (147.30mg/dl) and mild (149.50 mg/dl) cases. The mean serum triglyceride levels were lower in severe cases (116.15mg/dl), as compared to moderate (120.07 mg/dl) and mild (133.92 mg/dl) cases. This difference were not significant (P=0.398). The mean serum HDL levels were lower in severe cases (31.95mg/dl), as compared to moderate (33.69 mg/dl) and mild (37.42 mg/dl) cases. This difference were not significant (P=0.104). The mean serum LDL levels were lower in severe cases (61.50mg/dl), as compared to moderate (69.07 mg/dl) and mild (69.83 mg/dl) cases. This difference was not significant (P=0.334).

Table 4. Co-relation of Lipid profile with outcome in hemorrhagic snake bite patients

	Outcome	TC	TG	HDL	LDL
Hemorrhagic Snake Bite (n=26)	Discharged (n=25)	145.12±20.94	123.76±39.44	34.76±7.07	69.84±19.84
	Death (n=1)	139.00	125.00	31.00	54.00
	P value	0.777	0.976	0.607	0.441

In the hemorrhagic snake bite, the mean serum total cholesterol levels in discharged patients were (145.12mg/dl) and in died patients were (139.00mg/dl).This difference was not significant (P=0.777). In the hemorrhagic snake bite, the mean serum triglyceride levels in discharged patients were (123.76mg/dl) and in died patients were (125.00mg/dl).This difference was not significant (P=0.967). In the hemorrhagic snake bite, the mean serum HDL levels in discharged patients were (34.76mg/dl) and in died patients were (31.00mg/dl).This difference was not significant (P=0.607). In the hemorrhagic snake bite the mean serum LDL levels in discharged patients were (69.84mg/dl) and in died patients were (54.00mg/dl).This difference was not significant (P=0.441).

Table 5. Co-relation of Lipid profile with outcome in Neuro-Paralytic snake bite patients

	Outcome	TC	TG	HDL	LDL
Neuro-paralytic Snake Bite (n=19)	Discharged (n=16)	140.44±15.48	120.94±29.69	33.69±6.78	62.87±12.79
	Death (n=3)	119.00±8.29	101.00±24.26	25.33±1.25	48.33±5.79
	P value	0.045	0.339	0.057	0.094

In the neuro-paralytic snake bite, the mean serum total cholesterol levels in discharged patients were (140.44mg/dl) and in died patients were (119.00mg/dl).This difference was significant (P=0.045). In the neuro-paralytic snake bite, the mean serum triglyceride levels in discharged patients were (120.94mg/dl) and in died patients were (101.00mg/dl).This difference was not significant (P=0.339).

In the neuro-paralytic snake bite, the mean serum LDL levels in discharged patients were (33.69mg/dl) and in died patients were (25.33mg/dl).This difference was not significant (P=0.057). In the neuro-paralytic snake bite the mean serum LDL levels in discharged patients were (62.87mg/dl) and in died patients were (48.33mg/dl).This difference was not significant (P=0.094).

DISCUSSION

The present study was carried out in 50 cases of snake bite admitted in various medical wards of Maharana Bhupal Government Hospital and R.N.T. Medical College, Udaipur from 1st January 2020 to 30th November 2020. In the present study, we found that 27 patient (54%) snake bite patient were between the age group of 21-40 year followed by 9 patients (18%) were between age group 41-50 year and 4 patients (8%) of patient were between 51-60year age group. Hatiet al[10]performed a similar type of study and he observed that the maximum patient was in the age group 21-30 years and was 69%. Reid et al[11] studied and found that 50% cases were between 20 and 50 years of age. All these studies results match with present study. In the present study, 29 patients (58%) patients were male, whereas females were 21 (42%) in number. The reason for this may be that males are more involved in outdoor activities compared to females. Male predominance was also notice by other studies done by Reid et al[11], who reported 72% males and 28% females victims. In present study, rural prevalence of snake bite was 44 out of 50 cases, (88%). The prevalence in urban area was only 6 cases out of 50 (12%). The higher incidences of snake bite in rural areas may be due to the fact that large number of people working in fields in rural areas, habit of walking barefoot, and their houses are built of mud which provides access and shelter to snakes.[12,13] Sleeping on the floor and outside the house or in farms may also be responsible for increased number of cases in rural areas. However, there was no relation of mortality with patients from any particular area (rural/urban). Kulkarni et al (1994)[14]also found same type of result in his study and he observed that 90%patient of snake bite were from rural areas. Naik et al (1997)[15] reported that 83.6% were from rural areas.

On the basis of occupation, the present study was showing that 54% victims were farmers, 24% were housewives, 16% were students and 4% were labourer. This may be because farmers are still not using good protective shoes for their safety. This observation is closely related with the study conducted by Warrell et al[16]. Studies undertaken by Bhat et al[17] Saini et al[18] and Sarangi et al[19] showed the incidence in farmers to be 75%, 78% and 72%, respectively. Maximum numbers of patients were admitted during rainy and post rainy season. 90% bites occurred between July to November. Probably because of the heavy rains, the holes and burrows are filled up with water and snakes come out of it and number of encounters of men with snakes increases which can lead to increasing incidence of snake bites. The breeding habits of preys like frogs also follow the monsoon[20]. Naik et al (1997) reported that 60.6% cases occurred between June to November[15]. Hansdak et al[21] (1998) reported that 51% cases occurred during monsoon (August-October). Incidence of bites sites in this study were as follows: 72% bites were on the lower extremities, 18% on the upper extremities, 6% on the back and 4% were on the neck. It clearly suggests that the site of bite was predominantly determined by accidental contact with reptiles during activities. Reid et al[11] mentions that most of the bites in tropical countries are on lower extremities because the victims are bitten by treading on or near the snake which resemble to our study where maximum bite occurred in lower limb while in non-tropical countries most bites are on fingers and hands because the victim deliberately handles the snake. Similar incidence was seen in study conducted by Saini et al[18]. Barefoot walking in the fields predisposes farmers for frequent bites. Apart from farm bites, other incidents took place in the house, reflecting that people still have the habit of sleeping out of their houses and fields due to poor housing conditions and to safeguard their farms. In this study 46% snake bite incidents took place in night time. Bites are common during dusk and in poor lighting conditions where people inadvertently step on the snakes.

There was no relation of timing of bite (during day/night) with mortality. Sharma et al (2005)[22] found that 60.6% bite occurred during night and similar observation was made by Virmani and Dutt[23], they reported 88% bites in the night time which also matches with present study. In the present study, 12% patients were bitten by non-poisonous snake, 54% by hemorrhagic and 17% by neuro-paralytic snakes. Usually after an episode of snake bite, a person is gripped by fear and may not be able to see the snake properly. The snake also doesn't remain at that site after bite. So, it is difficult to identify the type of snake. The snake can be identified correctly only if the culprit snake is brought to the hospital for examination but even examining the snake may be dangerous if it is not confirmed that snake is dead. Therefore, WHO has advised the syndromic approach for treatment of snakebite patients[24]. In a study of 633 cases conducted by Kulkarni et al (1994)[14] the biting species was identified in only 388 cases (61.2%). The commonest was viper (242 cases-38.2%). These findings were somewhat comparable to our study. Punde et al (2005)[25] found that out of the 427 patients envenomed by poisonous snake, 274 (64.2%) were bitten by saw-scaled viper. Our study demonstrated a highly significant decrease in serum mean TC, TG, HDL and LDL in snake bite cases when compared with controls (146.10,126.42,34.64 and 67.38 mg/dl v/s 181.72,163.56,40.34 and 88.80mg/dl respectively) (P value= 0.00).

The mean serum total cholesterol levels were significantly lower (P<0.034) in severe cases (133.65 mg/dl), as compared to moderate (147.30mg/dl) and mild (149.50 mg/dl) cases. For comparison, not much study available on lipid profile in snake bite. E Winkler at el[26] found that decreased serum cholesterol level after snake bite as a marker of severity of envenomation. He found that serum cholesterol levels were negatively correlated with severity of envenomation (mean±SD 175±49, 137±36 and 96±40 mg/dl respectively in cases with mild, moderate and severe clinical manifestation (P< 0.0001). The mean serum triglyceride levels were lower in severe cases (116.15mg/dl), as compared to moderate (120.07 mg/dl) and mild (133.92 mg/dl) cases. This difference were not significant (P=0.398).The mean serum HDL levels were lower in severe cases (31.95mg/dl), as compared to moderate (33.69 mg/dl) and mild (37.42 mg/dl)cases. This difference were not significant (P=0.104).The mean serum LDL levels were lower in severe cases (61.50mg/dl), as compared to moderate (69.07 mg/dl) and mild (69.83 mg/dl)cases. This difference were not significant (P=0.334). The mean serum total cholesterol levels were significantly lower (P=0.00) in poisonous snake bite cases (Hemorrhagic-144.88 & Neuro-paralytic-137.05mg/dl),as compared to non-poisonous snake bite cases (178.17mg/dl). The mean serum triglyceride levels were significantly lower (P=0.016) in poisonous snake bite cases (Hemorrhagic-123.81 & Neuro-paralytic- 117.79 mg/dl),as compared to non-poisonous snake bite cases (165.00mg/dl). The mean serum HDL levels were significantly lower (P=0.037) in poisonous snake bite cases (Hemorrhagic-34.61 & Neuro-paralytic- 32.37 mg/dl),as compared to non-poisonous snake bite cases (41.00mg/dl). The mean serum total LDL levels were significantly lower (P=0.046) in poisonous snake bite cases (Hemorrhagic-69.23 & Neuro-paralytic- 60.57 mg/dl),as compared to non-poisonous snake bite cases (60.57mg/dl). Out of 50 patients, 46 (92%) were discharged and 4 (8%) were died due snake bite. In the present study, the mean TC, TG, HDL and LDL in hemorrhagic snake bite patients who were discharge was 145.12±20.94, 123.76±39.44, 34.76±7.07 and 69.84±19.84 respectively whereas in patients who died, it was 139.00, 125.00, 31.00 and 54.00 respectively. When compared, discharged and death group in these hemorrhagic snake bite patient group, it was found statistically not significant (p= 0.777, 0.976,0.607 and 0.441 respectively). In the present study, the mean TC, TG, HDL and LDL in neuro-paralytic snake bite patient who were discharge was 140.44±15.48, 120.94±29.69, 33.69±6.78 and 62.87±12.79 respectively whereas patients died it was 119.00±8.29, 101.00±24.26, 25.33±1.25 and 48.33±5.79 respectively. When compared discharged and death group in these neuro-paralytic and LDL, it was statistically not significant (P= 0.339, 0.057 and 0.094 respectively).

CONCLUSION

In the present study, we conclude as follows

- Snake bite is more common in male sex with younger age group (21-40 years) who belongs to rural areas principally affecting agricultural worker in rainy season.
- The common site of bite was lower limb with the local site bleeding as the most common clinical manifestation. Most bites occur during night time.
- Maximum bites were poisonous but some non-poisonous bites also contribute in total snake bite patients.
- In poisonous bites, hemorrhagic and neuro-paralytic contribute almost equally.
- TC, TG, HDL and LDL were significantly decreased in snake bite patients both hemorrhagic and neuro-paralytic.
- TC have strong association with severity and significant, while TG, HDL and LDL was decreased but not significant.
- LDL has strong association with lag period and significant, while TC, TG and HDL were decreased but not significant.
- TC and HDL have strong association with hospital stay and significant, while TG and LDL was decreased but not significant.

Thus, it can be reasonably concluded that all the patient of snake bite should be evaluated for TC, TG, HDL and LDL at the time of admission which can be helpful to predict severity, course as well outcome of these snake bite patients. In our study ,we found that a negative correlation exits between serum TC,TG,HDL, LDL and severity of envenomation. Hence, we can use lipid profile as a surrogate marker of severity of snake bite envenomation and predicting the complication and recovery.

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