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# SERUM LIPID PROFILE AS A PROGNOSTIC INDICATOR FOR SEVERITY IN SEPSIS

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## ABSTRACT

### Background

In intensive care units (ICUs), sepsis is the primary cause of death for patients who are critically unwell. Sepsis may cause changes in lipid metabolism. The aim of present study was to evaluate the serum lipid profile as a prognostic indicator for severity in sepsis.

### Methods

The cross sectional study was conducted in the tertiary care hospital in Channapatna(SRI CHAMUNDESHWARI MEDICAL COLLEGE HOSPITAL AND RESEARCH INSTITUTE), India from the Department of General Medicine over a period of 5 months from November 2023 to March 2024 among 75 patients admitted to the ICU and medical ICU with sepsis and who survived for more than 48 hours. All the basic and lipid profile investigations were done and results were analyzed using SPSS version 25.0.

### Results

Out of 75 patients with severe sepsis 8% of patients died during the hospital stay and 92% patients survived and were discharged from the hospital. The mean age of patients in survived and non survived groups was between 60 and 70 years. The mean APACHE II score among survived patients was 27.12± 3.8 and in non survived was 24.31±2.8. The length of hospital stay was 5.8 days among survived and 5.5 days among non survived. The level of TG was significantly higher in non-survivors than in survivors. Cholesterol, HDL, and LDL levels did not show statistically significant differences between the two groups

**Conclusion**
Our study found that In patients with severe sepsis, lipoprotein concentrations fluctuate quickly. The HDL fractions show the pattern of an early, sharp drop in cholesterol and a delayed recovery in the LDL fractions. Hence some lipoproteins may be used as a clinical indicator to assess the outcome of patients with sepsis.

**Keywords-** sepsis, lipid, prognosis.

## INTRODUCTION

Sepsis is a systemic inflammatory response syndrome that has a proven or suspected microbial aetiology [1].Severe sepsis is a potentially fatal disease that has become more common over the last 40 years [2]. Sepsis continues to have a higher death rate despite a great deal of study and better care standards. Numerous cytokines are released during an infection and subsequent inflammation. Various alterations in plasma lipids and lipoprotein concentration result from this [3,4].
An essential part of the outer membrane of Gram-negative bacteria is lipopolysaccharide (LPS, endotoxin), which is responsible for starting the inflammatory response in Gram-negative sepsis. Large-scale randomised clinical trials, however, did not demonstrate the survival benefit of anti-endotoxin therapies introduced in the early 1990s [5]. Lipoproteins have been shown recently to be important for the inherent defence against LPS [6,7]. Lipoproteins can lower the cytokine response and mortality rates in animal models of sepsis both in vitro and in vivo [8-10]. Lipoproteins virtually completely prevent the release of proinflammatory cytokines in a human endotoxemia model [11]. Sepsis patients, people with infections, and severely sick patients all have low lipid concentrations [12]. Reduced levels of lipoproteins may weaken the body's natural defences against endotoxins. Moreover, inflammation also alters the apoprotein composition of high-density lipoprotein (HDL). One of the three main acute phase proteins, serum amyloid A, replaces apolipoprotein (apo) A-1 and is linked to HDL [13,14]. The structural alterations in HDL could affect its protective properties and have an impact on metabolism [15]. These lipid alterations in sepsis may play a therapeutic role in addition to aiding in prognostic prediction.
However, little is understood about how lipoprotein metabolism occurs in cases of severe sepsis. Furthermore, most of these studies on lipid profile alterations in sepsis were conducted in western population. Further studies with Indian patients are necessary because of ethnic differences, namely, lower body mass indices (BMIs) low-fat and high carbohydrate diet. Hence the present study was conducted to evaluate the serum lipid profile as a prognostic indicator for severity in sepsis.

## MATERIAL AND METHODS

The cross sectional study was conducted in the tertiary care hospital in Channapatna (SRI CHAMUNDESHWARI MEDICAL COLLEGE HOSPITAL AND RESEARCH INSTITUTE), India, over a period of 5 months from November 2023 to March 2024 in the Department of General Medicine among patients admitted to the ICU and medical ICU with sepsis and who survived for more than 48 hours. Ethical clearance was taken from the institutional ethical committee before commencement of study. Patients were asked to sign an informed consent form after explaining them about the complete procedure.
Convenience sampling was done and total 75 patients of severe sepsis admitted to hospital were selected on the basis of inclusion and exclusion criteria.

### Inclusion criteria

1. Patients between the ages of 18 to 75 years.
2. Patients with Established Sepsis as defined by Surviving sepsis campaign international guidelines criteria for diagnosis of sepsis

### Exclusion criteria

1. Patients with liver cirrhosis

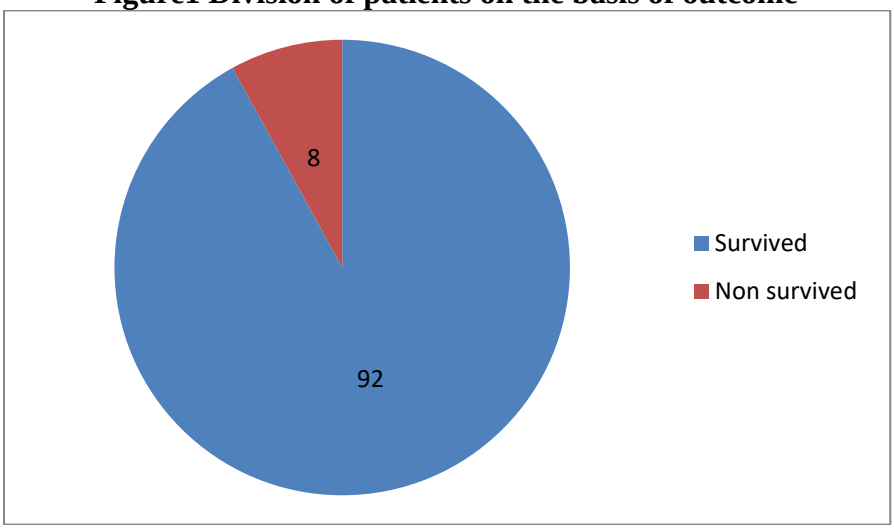
2. Immuno-compromised patients (acquired immune deficiency syndrome , neutropenia of <1000 cells/ml or transplant surgery)

All patients had undergone a detailed clinical examination. Routine investigations such as complete haemogram, kidney function tests, liver function tests, coagulation profile, and chest X-ray was done for all patients on admission. For each patient, data on age, gender, BMI, co morbidity, infection strain, administration of vasoactive drugs, length of stay, and in hospital mortality was assessed. In addition, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, and laboratory data , including cholesterol ,TG, HDL and LDL will be collected on days 0 (ICU admission) and day two. Primary end point is when the CRP and Total WBC counts return to normal.
The Statistical Package for the Social Sciences (SPSS version 25.0, Chicago, IL) was utilised for statistical analysis. Where appropriate, paired Student's t-tests and repeated-measures analysis of variance were utilised to examine differences in continuous variables. To account for missing values for patients who passed away after day 2, the analysis of variance was limited to the data from days 0–2. Spearman's rank-correlation test and, when suitable, multiple-level regression analysis was used to estimate correlation coefficients. P values below 0.05 were regarded as significant. The findings are shown as mean ±SD.

## RESULTS

Out of 75 patients with severe sepsis 8% of patients died during the hospital stay and 92% patients survived and were discharged from the hospital as shown in figure 1.

**Figure1 Division of patients on the basis of outcome**




The mean age of patients in survived and non survived groups was between 60 and 70 years. The number of male and female showed the presence of more number of males (24%,40%) as compared to females (16%, 20%). The prevalence of hypertension and diabetes mellitus was there among sepsis patients. The mean APACHE II score among survived patients was 27.12± 3.8 and in non survived was 24.31±2.8. The length of hospital stay was 5.8 days among survived and 5.5 days among non survived. The CRP level was 15.1±2.1 mg/dL in survived and18.7±3.2 in non survived. Value of WBCs in survived group was $11.1 \times 10^9$ and among non survived group was $11.4\times 10^9$ as shown in table 2.

**Table 2 Characteristics of Patients with sepsis**

| Variable | | Survived | Non survived |
|---|---|---|---|
| Mean age (years) | | 68.32±33.4 | 70.67±21.2 |
| Gender | Male | 18 (24) | 30 (40) |
| | Female | 12 (16) | 15 (20) |

| | | | |
|---|---|---|---|
| Co morbidity | Hypertension | 20 (26.6) | 25 (33.3) |
| | Diabetes mellitus | 10 (13.3) | 20 (26.6) |
| Mean APACHE II score | | 27.12± 3.8 | 24.31±2.8 |
| Length of hospital stay | | 5.8±0.3 | 5.5±0.2 |
| CRP (mg/dL) | | 15.1±2.1 | 18.7±3.2 |
| WBCs (L) | | $11.1 \times 10^9$ | $11.4\times 10^9$ |

Lipid profile of patients who survived and those who does not survived was checked and it was found that the level of TG was significantly higher in non-survivors than in survivors. Cholesterol, HDL, and LDL levels did not show statistically significant differences between the two groups as shown in table 3.

**Table 3 Lipid profile of Patients with sepsis**

| Indicator | Survived | Non survived | P value |
|---|---|---|---|
| TG, mg/dL | 110.27±20.12 | 101.4±22.18 | 0.001 |
| Cholesterol, mg/dL | 143.80±27.8 | 140.2±21.2 | 0.113 |
| LDL, mg/dL | 77.89±20.8 | 80.19±19.1 | 0.876 |
| HDL, mg/dL | 36.98±11.2 | 36.47±7.29 | 0.212 |

## DISCUSSION

Examining the biomarkers with diagnostic and prognostic significance in sepsis is essential [16]. In this study, 75 adult sepsis patients in a medical ICU at a tertiary hospital had their lipid profiles assessed. The patients under study had a mortality rate of 8% and a mean age of 68 years. In a study done by Paoli CJ et al found that the overall death rate was 12.5%. The rates vary depending on the severity of the condition—5.6%, 14.9%, and 34.2% for sepsis without organ dysfunction, severe sepsis, and septic shock, respectively [17].

The lipid profiles of 101 critically ill adult patients who were subsequently hospitalized to a medical ICU at a university medical facility in Basel, Switzerland, were examined by Luthold et al [18]. The death rate was 23% and the median age was 59 years. In 91 adult sepsis patients receiving therapy in the intensive care unit (ICU) of a university hospital in Osaka, Japan for longer than two weeks, Yamano et al [19] examined 15 biochemical indices. The patients' average age (± standard deviation) was 64 ± 18 years, and their mortality rate was 41.8%. In a different investigation, Lee et al [20] assessed the lipid profiles of 117 adult patients hospitalized to the intensive care unit (ICU) of a sizable tertiary university medical center in Seoul, South Korea, with sepsis and septic shock. The patients' average age was 62.7 ± 16.2 years, and 44.4% of them died within the hospital.

About the alterations in the lipid profile, we discovered that the non-survival group had lower mean values for TG, total cholesterol, and HDL than the survival group did, although only the difference in mean TG levels was statistically significant. Similarly, non-survival patients with sepsis on the day of arrival had considerably lower levels of TG and free fatty acids, according to Lee et al [20]. Additionally, non-survival sepsis patients had greater beginning cholesterol levels than survival patients, according to Barati et al [21], but there was no discernible difference in TG levels.

Luthold et al [18] discovered in earlier investigations that infectious critically sick patients had lower total and HDL cholesterol levels than non-infectious critically ill patients. They also came to the conclusion that procalcitonin had a higher diagnostic accuracy than HDL, while C-reactive protein (CRP) did not have a greater diagnostic accuracy than HDL. Additionally, septic patients had significantly lower cholesterol levels on the first day following admission than non-septic patients, according to Abdollahi et al [22]. Additionally, they discovered a statistically significant inverse connection between septic patient mortality and HDL level. Yamano et al [19] found that the prognosis of patients with severe sepsis was exclusively correlated with low total cholesterol and high total bilirubin.

Regarding mechanism, under normal circumstances, HDL particles are important in the reverse transport of cholesterol from peripheral tissues—including foam cells in the arterial wall—to the liver,

while LDL particles transfer cholesterol, phospholipids, and lipidsoluble vitamins from the liver to extra-hepatic tissues. However, acute diseases can have an impact on plasma lipids [23].

There has never been a complete understanding of the precise pathophysiological mechanisms behind the alterations in plasma lipid levels in sepsis and severe diseases [24]. Endotoxins can be bound by lipoprotein [25]. When endotoxin lipopolysaccharide levels are high, as they are in severe sepsis, lipoprotein lipase activity is suppressed and triglyceride clearance is hampered, which leads to noticeably elevated plasma triglycerides. According to a study, men's triglyceride production increases rather than decreases in acute circumstances like sepsis or septic shock [26]. A few researchers proposed that phospholipid emulsion and statins would be useful in treating or avoiding sepsis. Nevertheless, statins' capacity to decrease cholesterol may not be a determining factor in their anti-inflammatory benefits [27,28].

There were several limitations firstly the pattern of lipid profile alterations was unclear, and serum lipid levels were only assessed once. The lack of a nonseptic control group was another drawback of the current investigation. It would be preferable if it will be evaluated for patient status at the time of ICU admission using a scoring system.

## CONCLUSION

In patients with severe sepsis, lipoprotein concentrations fluctuate quickly, with low recovery levels. The HDL fractions show the pattern of an early, sharp drop in cholesterol and a delayed recovery in the LDL fractions. The amount of particles in HDL particles varies in terms of apoprotein and cholesterol content, while the amount in LDL particles likely decreases. Since lipoproteins have been shown to be important for both in vivo and in vitro innate immunity, more research is required to understand how hypolipoproteinemia occurs in severe sepsis.

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