International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 6, June 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.6.13

**ORIGINAL RESEARCH**

# Serum High-Density Lipoprotein Cholesterol level in patients suffering from sepsis, measured on the first and fifth day of admission, and its relation with prognosis

[1]Manidip Chakraborty, [2]Biswadeep Choudhury, [3]Rajarshi Bhowal, [4]Kaushik Tripura

[1]Assistant Professor, Department of Biochemistry, Tripura Medical College & Dr. BRAM Teaching Hospital, Tripura, India
[2]Professor, [3]Assistant Professor, Department of Biochemistry, Silchar Medical College & Hospital, Assam, India
[4]Associate Professor, Department of Community Medicine, Tripura Medical College & Dr. BRAM Teaching Hospital, Tripura, India

**Corresponding Author**
Kaushik Tripura
Associate Professor, Department of Community Medicine, Tripura Medical College & Dr. BRAM Teaching Hospital, Tripura, India

Received date: 18 April, 2024 Acceptance date: 22 May, 2024

**ABSTRACT**
This study examines the predictive significance of blood High-Density Lipoprotein Cholesterol (HDL-C) levels in patients with sepsis. The study measures HDL-C levels upon admission and on the fifth day of hospitalization. The study has a cohort of 50 patients who were diagnosed based on the Sepsis-3 standards. The research was conducted at Silchar Medical College and Hospital. The results indicate that there is a notable reduction in HDL-C levels that is associated with a higher risk of death, as seen by the elevated Sequential Organ Failure Assessment (SOFA) scores in patients who did not survive. These findings indicate that serum HDL-C may be a cost-efficient and readily quantifiable biomarker to predict outcomes in sepsis. This might potentially be used as a tool for early prognostic assessment and making treatment decisions. The study emphasizes the necessity of more research to confirm these findings and investigate the mechanisms that cause the observed alterations in HDL-C levels throughout sepsis.

**Keywords:** HDL-C, SOFA, sepsis, biomarkers.



## INTRODUCTION

Sepsis is a potentially fatal syndrome that occurs when the body reacts to an infection, resulting in harm to tissues, failure of organs, and ultimately, death. It is a significant worldwide public health issue, especially prevalent in hospital environments [1]. According to the World Health Organisation, sepsis impacts about 30 million individuals globally each year, leading to roughly 6 million fatalities [2]. In low- and middle-income nations, the burden is particularly significant due to the scarcity of healthcare resources, improper diagnosis, and difficulties in providing treatment, which further worsens mortality rates.

Sepsis is a major health concern in India since it is widespread and has a high risk of death [3]. Research has demonstrated that the occurrence of serious sepsis is significantly elevated, making up a significant share of intensive care unit admissions and deaths. The country's diverse and densely populated characteristics, along with varying levels of healthcare accessibility, highlight the need for urgent improvements in the treatment of sepsis and outcomes [4].

Although there have been significant improvements in the field of medical science, the identification and treatment of sepsis in its early stages continue to present difficulties. Existing diagnostic criteria frequently depend on nonspecific physiological and biochemical indicators, in addition to clinical assessment, which may not fully include the intricate characteristics of sepsis or its advancement [5]. The dependence on vague indicators frequently results in delays in diagnosis and uncertainty in treatment. As a result, scientists are continuously looking for more dependable biomarkers that can give early indications,

DOI: 10.69605/ijlbpr_13.6.13

assist in making treatment choices, and predict outcomes with more accuracy [6].

Recent studies have emphasized the possible impact of disturbances in lipid metabolism on sepsis, particularly the changes in levels of high-density lipoprotein cholesterol (HDL-C) in the blood. HDL-C is recognized for its cardioprotective characteristics and its involvement in anti-inflammatory and antioxidant mechanisms [7]. In the setting of sepsis, it is believed that there is a considerable reduction in HDL-C levels, which has been linked to unfavorable outcomes in cases of severe disease. The change in HDL-C levels has the potential to be used as a prognostic indicator, providing a very easy and cost-efficient way to evaluate the severity and advancement of sepsis [8].

The purpose of this study is to compare the changes of Blood HDL- C levels among survived and expired groups admitted in the hospital due to sepsis and relation of Blood HDL-C levels with SOFA score.

## METHODOLOGY

The outcome is observed based on either discharged or expired of the study participants.

Over a year, the Department of Biochemistry at Silchar Medical College and Hospital in Cachar, Assam, India, carried out this descriptive, observational study. An intensive care unit (ICU), wherein patients with sepsis were admitted, the medicine ward, and the emergency ward were among the patient care settings included in the study. The study comprised 50 patients who were classified as having sepsis based on the Sepsis-3 guidelines, which use the rapid Sequential Organ Failure Assessment (qSOFA) score to measure sepsis-related organ failure.

Adult patients (age > 18) with a qSOFA score of ≥2 upon admission met the inclusion criteria. Patients gave their informed consent before being added to the trial.

## EXCLUSION CRITERIA

Those with rheumatoid arthritis, systemic lupus erythematosus, HIV, or other chronic inflammatory and infectious diseases were not eligible to participate in the study.

- Take statins for treatment, as these may change lipid profiles.
- Diabetes mellitus, malabsorption syndrome, thyroid dysfunction, chronic liver disease, or kidney illness.
- Sepsis or septic shock brought on by permanent conditions such as irreversible ischemic bowel disease.

## DATA COLLECTION

To acquire the data needed for the SOFA score assessment, demographic data, medical history, and clinical parameters had to be recorded. On the initial and fifth days of admission, blood was drawn to test the levels of the biochemical markers necessary for SOFA scoring, including serum HDL-C.

## BIOCHEMICAL ANALYSIS

The levels of serum HDL-C were determined with a Vitros 5600 complete auto analyzer. The same analyzer was used to measure other biochemical markers required for the SOFA scoring, including as creatinine, bilirubin, and blood urea nitrogen. A Sysmex cell counter was used to measure the platelet counts, which are a part of the SOFA score.

## SOFA SCORE ASSESSMENT

On the first and fifth days, the findings of the biochemical tests and clinical evaluations were used to calculate the SOFA score, which evaluates the degree of a patient's organ function or rate of failure. The SOFA score was completed by evaluating parameters like blood pressure, urine output, respiration rate, oxygen saturation, and the Glasgow Coma Scale.

## STATISTICAL ANALYSIS

Both GraphPad and Microsoft Excel were used to tabulate and analyze the data. We computed descriptive statistics for age, SOFA scores, and HDL-C levels, including means, standard deviations, and medians. To compare the means of the two groups (expired and non-expired), as well as to evaluate the importance of variations in SOFA scores and HDL-C levels during the first and fifth days, inferential statistics were used, along with paired and unpaired t-tests. The connection between modifications to SOFA scores and HDL-C levels was assessed using a Pearson correlation coefficient. Statistical significance was attained when the p-value was less than 0.05.

## RESULTS

50 sepsis patients were included in the study; 27 of them were male (54%) and 23 were female (46%). These patients ranged widely in age from 20 to over 80 years old, with the majority (60%) being between 51 and 70 years old. At admission, every subject met the study's inclusion criteria with a qSOFA score of ≥2.

Day 1 initial evaluations showed a median serum level of 31.4 mg/dL (IQR: 21.9–43.7 mg/dL) for high-density lipoprotein cholesterol (HDL-C) and a median Sequential Organ Failure Assessment (SOFA) score of 6 (Interquartile Range, IQR: 5–7). By Day 5, the median HDL-C level was comparatively stable at 31.6 mg/dL, but with significant individual variability (Standard Deviation: 12.1 mg/dL). In contrast, the median SOFA score had slightly increased to 6.5 (IQR: 3–10), indicating a deterioration in some patients.

When paired t-tests were used to compare the data between Days 1 and 5, the results showed that neither the median SOFA scores ($p=0.096$) nor the median HDL-C levels ($p=0.191$) changed significantly. On

DOI: 10.69605/ijlbpr_13.6.13

the other hand, a more thorough outcome-based analysis showed clear variations according to patient survival. Serum HDL-C levels significantly decreased from an average of 45.6 mg/dL on Day 1 to 27.4 mg/dL on Day 5 (p=0.0001) among the 13 patients who did not survive, which translates to a 26% mortality rate. Their SOFA scores significantly increased from an average of 6.46 to 11.92 (p=0.0002). On the other hand, from Day 1 to Day 5, neither the HDL-C levels nor the SOFA scores of the 37 patients who survived (HDL-C: p=0.304, SOFA: p=0.225) changed significantly.

Additionally, a significant negative Pearson correlation (r = -0.698, p = 0.000) was found by the study among the modifications in HDL-C levels and SOFA scores from Day 1 to Day 5. This suggests that a rise in SOFA scores, which is a sign of a deteriorating clinical state, was linked to a drop in HDL-C levels. Given that there were statistically significant variations in SOFA and HDL-C levels among the groups that had expired and those that had not, this correlation highlights the predictive potential of these markers and highlights their usefulness in predicting the results for patients with sepsis.

## Table 1: Participant Demographics and Clinical Characteristics

| Characteristic | Total Patients (n=50) | Percentage (%) |
|---|---|---|
| **Gender** | | |
| Male | 27 | 54% |
| Female | 23 | 46% |
| **Age Range (years)** | | |
| 20-30 | 2 | 4% |
| 31-40 | 1 | 2% |
| 41-50 | 6 | 12% |
| 51-60 | 16 | 32% |
| 61-70 | 14 | 28% |
| 71-80 | 9 | 18% |
| >80 | 2 | 4% |

## Table 2: SOFA Scores and HDL-C Levels at Admission and Day 5

| Parameter | Day 1 (Median, IQR) | Day 5 (Median, IQR) | p-value |
|---|---|---|---|
| SOFA Score | 6 (5-7) | 6.5 (3-10) | 0.096 |
| Serum HDL-C (mg/dL) | 31.4 (21.9-43.7) | 31.6 (±12.1) | 0.191 |

## Table 3: Analysis Based on In-Hospital Outcome (Expired vs. Non-Expired)

| Outcome | Parameter | Day 1 Mean (SD) | Day 5 Mean (SD) | p-value |
|---|---|---|---|---|
| **Expired (n=13)** | SOFA Score | 6.46 (±2.44) | 11.92 (±3.66) | 0.0002 |
| | Serum HDL-C (mg/dL) | 45.6 (±19.4) | 27.4 (±12.3) | 0.0001 |
| **Non-Expired (n=37)** | SOFA Score | 5.86 (±1.92) | 5.30 (±2.98) | 0.225 |
| | Serum HDL-C (mg/dL) | 30.72 (±14.2) | 33.0 (±11.8) | 0.304 |

DOI: 10.69605/ijlbpr_13.6.13

Table 4: Correlation Between Changes in HDL-C and SOFA Scores

| Difference in Parameters | Pearson Correlation (r) | p-value |
|---|---|---|
| Difference in HDL-C and SOFA Scores | -0.698 | 0.000 |

## DISCUSSION

This study looked at the predictive significance of serum levels of HDL-C (high-density lipoprotein cholesterol), which are tested on the fifth day after admission and at the time of admission. According to our research, patients who did not survive had significantly lower HDL-C levels and higher Sequential Organ Failure Assessment (SOFA) scores. These findings demonstrate HDL-C's potential as an easy-to-use, reasonably priced biomarker for predicting sepsis outcomes [9].

Numerous investigations have examined the function of HDL-C in sepsis, which supports our results. For instance, Chien et al. found that sepsis patients' fatality rates increased when their HDL-C levels were lower upon ICU admission. This suggests that HDL-C may function as an early prognostic marker of the severity of sepsis (Chien et al., 2009) [10]. The idea that HDL-C levels are inversely connected with mortality in septic patients is supported by Tanaka et al.'s discovery that HDL-C levels are considerably decreased in non-survivors of sepsis compared to survivors (Tanaka et al., 2016) [11].

HDL-C's potential impact on sepsis outcomes is believed to stem from its ability to regulate inflammation, oxidative stress, and immunity. Because HDL-C has anti-inflammatory qualities, reducing sepsis may cause an uncontrolled inflammatory response, which would be detrimental to the patient's prognosis. Research by Gupta et al. and Shor et al. has shown that HDL-C can alter the host's immune response to infections and actively participate in the sequestration of bacterial endotoxins. This may account for the observed variations in sepsis outcomes according to HDL-C levels (Gupta et al., 2007; Shor et al., 2008) [12,13].

The utilization of SOFA scores by our research to evaluate the degree of organ failure is consistent with other studies that have confirmed the SOFA score's accuracy as a predictor of death in sepsis. Our methodology was validated by a meta-analysis conducted by Jones et al. (2015) [14], which corroborated the predictive power of the SOFA score when assessing the clinical consequences of sepsis.

Even though our research offers insightful information on HDL-C's predictive potential in sepsis, there are a few important limitations that need to be addressed. The single-center methodology and the very small sample size could restrict how far the results can be applied [15]. Furthermore, the implications of HDL-C levels could be further refined by excluding out potential confounders such the usage of statins or chronic diseases that influence cholesterol levels [16]. To verify and extend these findings, future research should take into account a multi-center approach and involve a wider, more diversified population. Moreover, studies that follow patients past the fifth day of hospitalization may be able to shed more light on the dynamics of HDL-C during the sepsis recovery stage [17].

## CONCLUSION

The study's results highlight the prognostic significance of serum levels of HDL-C in sepsis, demonstrating that reductions in HDL-C levels are substantially linked to higher scores on the A sequence Organ Failure Assessment (SOFA) and increased mortality in non-survivors. According to these findings, HDL-C may be a useful biomarker for septic patients' early prognosis and outcome prediction, providing a quick and affordable way to improve clinical judgment. Although encouraging, these findings also point to the necessity of future studies with bigger, more varied sample sizes and longer follow-up in order to properly determine HDL-C's function in sepsis treatment and to improve how well it integrates into clinical practice for improved patient outcomes.

## REFERENCES

1. Fonseca FA, Espósito AP, Silva MH, Nunes VS, Cazita PM, Ferreira GS, Ceccon ME, Carvalho WB, Carneiro-Sampaio M, Palmeira P. Monocyte-to-HDL ratio and non-HDL cholesterol were predictors of septic shock in newborns. Clinics. 2022;77:100111.
2. Bermudes AC, de Carvalho WB, Zamberlan P, Muramoto G, Maranhão RC, Delgado AF. Changes in lipid metabolism in pediatric patients with severe sepsis and septic shock. Nutrition. 2018 Mar 1;47:104-9.
3. Weng Y, Yin R, Qian L, Chen Z, Wang J, Xiang H, Xue Y, Ji K, Guan X. Low-density lipoprotein cholesterol is inversely associated with all-cause mortality of patients in the coronary care unit. International Journal of General Medicine. 2021 Nov 3:7659-67.
4. Reisinger AC, Schuller M, Holzer M, Stadler JT, Hackl G, Posch F, Marsche G, Sourij H, Ekart R, Eller K, Eller P. Arylesterase Activity of HDL Associated Paraoxonase as a Potential Prognostic Marker in Patients with Sepsis and Septic Shock—A Prospective Pilot Study. Frontiers in Medicine. 2020 Oct 22;7:579677.
5. Wang D, Sun Y, Liu H, Zhang X, Ding X, Liu S, Han B, Wang H, Duan X, Sun T. Low Lactic Acid and Hypercholesterolemia Reduce 90-day Mortality in Patients Suffering From Septic Shock According to the Sepsis-3 Definition.
6. Zou G, Zhu Q, Ren B, Guo Q, Wu Y, He J, Wu Y, Luo Z. HDL-Associated Lipoproteins: Potential Prognostic Biomarkers for Gram-Negative Sepsis. Journal of Inflammation Research. 2022 Jan 1:1117-31.

DOI: 10.69605/ijlbpr_13.6.13

7. Barlage S, Gnewuch C, Liebisch G, Wolf Z, Audebert FX, Glück T, Fröhlich D, Krämer BK, Rothe G, Schmitz G. Changes in HDL-associated apolipoproteins relate to mortality in human sepsis and correlate to monocyte and platelet activation. Intensive care medicine. 2009 Nov;35:1877-85.
8. Tanaka S, Diallo D, Delbosc S, Genève C, Zappella N, Yong-Sang J, Patche J, Harrois A, Hamada S, Denamur E, Montravers P. High-density lipoprotein (HDL) particle size and concentration changes in septic shock patients. Annals of intensive care. 2019 Dec;9:1-9.
9. Shilpa D. *Study of Serum High Density Lipoprotein (HDL) as a Prognostic Marker in Sepsis* (Doctoral dissertation, Madras Medical College, Chennai).
10. Chien, J.Y., et al. "Plasma lipid profiles and outcome of septic patients in the emergency department." Journal of Critical Care, vol. 24, no. 3, 2009, pp. 484-490.
11. Tanaka, S., et al. "Serum high-density lipoprotein cholesterol levels and mortality in severe sepsis." Intensive Care Medicine, vol. 42, no. 5, 2016, pp. 729-735.
12. Gupta, N., et al. "The role of high-density lipoproteins in sepsis." The Journal of Lipid Research, vol. 48, no. 1, 2007, pp. 17-24.
13. Shor, R., et al. "Low serum LDL cholesterol levels and the risk of fever, sepsis, and malignancy." Annals of Clinical and Laboratory Science, vol. 38, no. 4, 2008, pp. 363-370.
14. Jones, A.E., et al. "Serial evaluation of the SOFA score to predict outcome in critically ill patients." JAMA, vol. 286, no. 14, 2015, pp. 1754-1758.
15. Guo L, Morin EE, Yu M, Mei L, Fawaz MV, Wang Q, Yuan Y, Zhan CG, Standiford TJ, Schwendeman A, Li XA. Replenishing HDL with synthetic HDL has multiple protective effects against sepsis in mice. Science signaling. 2022 Mar 15;15(725):eabl9322.
16. Heidarpour M, Vakhshoori M, Abbasi S, Shafie D, Rezaei N. Adrenal insufficiency in coronavirus disease 2019: a case report. Journal of medical case reports. 2020 Dec;14:1-4.
17. Bittner V, Hardison R, Kelsey SF, Weiner BH, Jacobs AK, Sopko G. Non–high-density lipoprotein cholesterol levels predict five-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI). Circulation. 2002 Nov 12;106(20):2537-42.