ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 01 | January - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A PROSPECTIVE STUDY ON CORRELATION OF SERUM LIPID PROFILE AND SEPSIS SEVERITY IN ADULT PATIENTS DIAGNOSED WITH SEPSIS IN A TERTIARY CARE HOSPITAL.

Biochemistry

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ABSTRACT

Introduction: Sepsis causes, extensive physiological and biochemical abnormalities. Literature shows that infections cause reasonable alterations in lipid metabolism and in the composition of lipoproteins. In these situations, there is an increase in the levels of triglycerides and VLDL cholesterol and decrease in levels of HDL and LDL cholesterol. Patients with sepsis, having hypocholesterolaemia indicates disease severity when other causes of this condition are to be ruled out. Hence this study was done to understand the role of serum lipids in patients with sepsis. **Material and methods:** A prospective study was done in 60 adults patients admitted with sepsis (According to the Third International consensus Definitions for Sepsis and Septic Shock 2016 (Sepsis – 3), in medical wards and medical ICU of a tertiary care teaching hospital during December 2021 to April 2022 after obtaining institutional ethical committee clearance and consent from patients. All patients who gave informed consent were enrolled consecutively till the sample size was reached. Patients were subjected to detailed history taking, clinical examination and biochemical investigations were done and data was recorded in a semi-structured questionnaire. Data was entered in MS excel and analysis was done using SPSS -20, Data represented in frequency tables. Correlation between parameters assessed and APACHE II and SOFA score was done using pearsons correlation coefficient with $P<0.05$ considered as statistically significant. **Results:** Mean age of the study population was 40.22±11.831. Majority of the study patients were males (71.7%). Respiratory tract infection (33/55%) was the major source of infection. Diabetes mellitus was the most common type of comorbidity (27/ 45%). HDL cholesterol was negatively correlated with both sepsis prognostic severity scores (APACHE II and SOFA score) which were highly significant statistically. Pearsons correlation coefficient shows that total cholesterol, LDL cholesterol is poorly correlated with sepsis severity and triglycerides though negatively correlated the association is weak. **Conclusions:** Sepsis patients, shows alterations in lipid metabolism. Higher values of SOFA and APACHE II scores were associated with low HDL levels. Lipoproteins may function as potential biomarkers (especially high-density lipoprotein) in systemic inflammatory response syndrome and sepsis.

KEYWORDS

Sepsis, Lipid profile, correlation, APACHE II score, SOFA score.

INTRODUCTION

Sepsis is a medical emergency due to body's systemic immunological response to an infectious process that can lead to end-stage organ dysfunction and death. [1] The global burden of sepsis in 2017 globally as noted by World Health Organization (WHO) was 48.9 million cases and 11 million sepsis-related deaths with approximately 85.0% of sepsis cases and sepsis-related deaths worldwide occurred in low- and middle-income countries.[2]

Sepsis causes, extensive physiological and biochemical abnormalities. The Third International Consensus (Sepsis-3) defines sepsis as an "organ dysfunction caused by a dysregulated host response to infection", with important role of the innate and adaptive immune response in the development of the clinical syndrome.3 Despite significant advancements in the understanding of the pathophysiology of this clinical syndrome, advancements in hemodynamic monitoring tools, and resuscitation measures, sepsis remains one of the major causes of morbidity and mortality in critically ill patients.[4]

Literature shows that infections cause reasonable alterations in lipid metabolism and in the composition of lipoproteins. In these situations, there is an increase in the levels of triglycerides and VLDL cholesterol and decrease in levels of HDL and LDL cholesterol. Endotoxin release from infections alters the composition of HDL and size by the reduction of phospholipids and apolipoprotein (apo) A-I, serum amyloid A (SAA) and secretory phospholipase A2 (sPLA2) which are grossly increased. Even though there is no change in the total particle number, a marked decrease in the number of small and medium size particles is noted.[5]

Serum Lipid profile measured during infections will help to assess the severity of illness. Patients with sepsis, having hypocholesterolaemia indicates disease severity when other causes of this condition are to be ruled out. Such patients need intensive medical attention with the anticipation of MODS.

Thus understanding of the extremely complex mechanisms that regulate the inflammatory response, the ability of lipoproteins to bind and neutralize toxic bacterial substances has received more attention recently.[6] Hence this study was done to correlate serum lipids with sepsis severity scores like APACHE II score and SOFA score in adult patients with sepsis.

MATERIAL AND METHODS

A prospective descriptive analytical study was done in adults patients admitted with sepsis (According to the Third International consensus Definitions for Sepsis and Septic Shock 2016 (Sepsis – 3),[7] in medical wards and medical ICU of a tertiary care teaching hospital during December 2021 to April 2022 after obtaining institutional ethical committee clearance.

Inclusion Criteria: Patients > 18 years or either sex were included.
Exclusion Criteria: Patients on statins, with chronic liver disease, chronic kidney disease, thyroid dysfunction, diabetes mellitus, malignancy, chronic inflammatory conditions like Human immuno deficiency virus infection (HIV), Systemic lupus erythematosis (SLE), Rheumatoid arthritis(RA), malabsorption, pregnancy condition and patients who were not willing to participate were excluded.

Sample size was calculated using formula for finite population. Where, $Z\alpha$ is the standard normal deviate, 1.96 at 95% confidence interval.

As per previous past 6 month data obtained from medical record department in the present institute, prevalence of patients with sepsis admitted in hospital was 10.4%.

Hence P = Prevalence is 10.4%.
e = allowable error was 5%

N = study population (Adult patients diagnosed with sepsis admitted in hospital in the past 6 months in General Medicine department was) = 101

$$Sample\ size(n) = \frac{\frac{z^2 X\ p(100-p)}{e^2}}{1 + \frac{z^2 X\ p(100-p)}{e^2 N}}$$

$$Sample\ size(n) = \frac{\frac{(1.96)^2 X\ 10.4(100-10.4)}{(5)^2}}{1 + \frac{(1.96)^2 X\ 10.4(100-10.4)}{(5)^2\ 101}}$$

$$Sample\ size(n) required\ is = 59$$

Sample size was rounded up to 60.

Sampling Method

Purposive sampling method was used.

All patients who gave informed consent were enrolled consecutively till the sample size was reached. Patients were subjected to detailed history taking, clinical examination and biochemical investigations were done and data was recorded in a semi-structured questionnaire.

Procedure

Fasting venous blood samples were collected under aseptic precautions and sent for biochemical analysis. Variables that were recorded on admission included age, sex, primary diagnosis, source of infection, chronic Comorbidities. Clinical and laboratory data to calculate Acute Physiology and Chronic Health Evaluation II (APACHE II)[8] score and SOFA[9] score (using worst variable reading during the 1st 24 h of ICU admission) and worst Glasgow Coma Score (GCS) [10] before sedation or anesthesia. SOFA and APACHE II scores were calculated on the day of admission using a standard format. Serum Lipid profile for all the patients were done by enzymatic method using fully automated analyser Randox imola.

Statistical Analysis

Data was entered in MS excel and analysis was done using SPSS -20, Data represented in frequency tables. Correlation between parameters assessed and APACHE II and SOFA score was done using pearsons correlation coefficient with P<0.05 considered as statistically significant.

RESULTS

Majority of the patients belong to age group 51-61 years. Mean age of the study population was 40.22±11.831. Majority of the study patients were males (71.7%). (shown in table 1)

Table 1: Distribution of study participants by age and sex

Patients characteristics		Frequency (n=100)	Percent (%)
Age Group	20-30	15	25
	31-40	15	25
	41-50	14	23.3
	51-61	16	26.7
Sex	Male	43	71.7
	Female	17	28.3

Respiratory tract infection (33/55%) was the major source of infection. Diabetes mellitus was the most common type of comorbidity (27/45%). (shown in table 2)

Table 2: Distribution of study participants by source of infection and comorbidities

Study patients characterisitics		Frequency	Percent (%)
Sources of infection	Respiratory tract infections	33	55
	Gastro intestinal infections	9	15
	Uro-genital infections	11	18.3
	Blood infections	7	11.7
Comorbidities	Diabetes mellitus	27	45
	Hypertension	3	5
	Diabetes mellitus and hypertension	6	10
	Bronchial asthma	2	3.3
	Others	5	8.3
	Thyroid disorders	3	5

Hyperthermia and hypothermia was seen in 30 (50%) and 16(26.7%) patients respectively. Hypotension was seen in 35(58.3%) patients. Respiratory rate was abnormal in 33(55%) patients and 17(28.3%) patients needed ventilator support. (shown in table 3)

Table 3: Distribution of study participants by Vital signs

Vital signs		Frequency (n=100)	Percent (%)
Temperature	Hyperthermia	30	50
	Hypothermia	16	26.7
	Normal	14	23.3
Systolic Blood Pressure	<90 mmHg	35	58.3
	>90 mm Hg	25	41.7
Respiratory rate	Normal	33	55
	Abnormal	27	45
Ventilator support	No	43	71.7
	Yes	17	28.3

Minimum, maximum and mean ± SD of serum lipid profile, total count (TC), serum bilirubin, serum creatinine, platelet count, GCS, APACHE II score and SOFA score was assessed and represented in table 4.

Table 4: Distribution of study participants by various parameters assessed

Variables	Minimum	Maximum	Mean	Std. Deviation
HDL mg/dl	10	49	23.12	12.307
Total cholesterol mg/dl	97	432	195.92	66.275
LDL mg/dl	100	759	226.90	111.409
Triglyceride mg/dl	0	202	95.28	34.531
Total Count cells/ cubic mm	1600	26400	10633.33	8412.252
Bilirubin mg/dl	1	12	3.55	2.466
Creatinine mg/dl	1	7	3.00	1.904
Platelet count cells/ µl	8600	96000	25426.67	17963.040
GCS	5	15	11.60	2.912
APACHE II score	3	38	20.50	12.739
SOFA score	2	22	11.87	6.318

HDL cholesterol, platelet count and GCS are negatively correlated with both sepsis prognostic severity scores (APACHE II and SOFA score) where as serum creatinine was positively correlated which was highly significant statistically. Pearsons correlation coefficient shows that total cholesterol, LDL cholesterol is poorly correlated with sepsis severity and triglycerides though negatively correlated the association is weak.

Table 5: Correlation between parameters and sepsis severity

Parameters (n=60)	APACHE II score		SOFA score	
	Pearsons correlation	P value	Pearsons correlation	P value
HDL	-0.933	< 0.001	-0.931	< 0.001
Totalcholesterol	0.105	0.426	0.143	0.277
LDL	0.050	0.704	0.056	0.673
Triglyceride	-0.050	0.704	-0.062	0.636
Total Count	0.413	0.001	0.416	0.001
Bilirubin	0.836	0.000	0.852	0.000
Platelet count	-0.535	<0.000	-0.550	<0.001
Creatinine	0.889	0.000	0.892	0.000
GCS	-0.902	0.000	-0.902	0.000

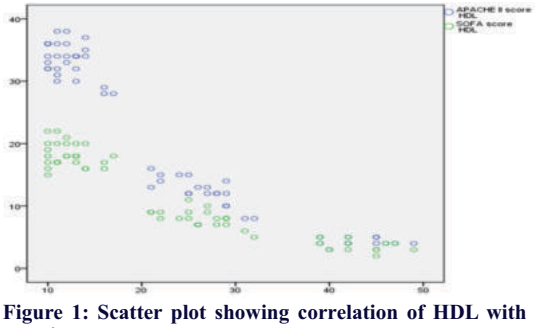

Figure 1: Scatter plot showing correlation of HDL with Sepsis severity

DISCUSSION

Previous studies were available on comparative study of serum lipids

between sepsis and severe sepsis groups or between survivor and nonsurvivor groups.[11,12] The current study correlated serum lipid profile with sepsis severity scores like APACHE II score and SOFA score.

In this study the mean±SD of age was 40.22±11.831 which was low compared to study by Nabavi A et al (65.1±18.6 years, which varied from 21 to 92 years (median 68 year)) and Tanaka S et al (62 [45–74]).[13,14]

In this study males were 71.7% with male: female ratio 43/17 which was similar to study by Tanaka S et al with males being 36 (72%),[14] In study by Nabavi a et al, The female to male ratio was 0.85; 54.1% of the participants (n=40) were male.[13] In study by Sunayana et al 42 were males and 28 were females.[15]

In this study respiratory tract infection (33/55%) was the major source of infection. Diabetes mellitus was the most common type of comorbidity (27/ 45%). Similar findings were seen in study by Sunayana et al, where the primary source of infection was lung in 28.6% of cases, followed by urinary tract in 24.3%, skin and blood stream infection in 5.7% each.[15]

In this study mean±SD of GCS score was 11.6± 2.912. In study by Tanaka S et al mean Glasgow score on day 1 was 15 [14–15]. [14] In this study mean±SD of total count was 10633.33±8412.252 with range 1600 – 26400. In study by Tanaka S et al mean Leukocytes/mm3 on day 1 with range was 13,920 [7350–22,350].[14]

In this study mean±SD of SOFA score was 11.87± 6.318 with range 2-22. In study by Tanaka S et al mean SOFA on day 1 with range was 7 [4–9].[14]

In this study correlation of HDL cholesterol versus APACHE II score (-0.933/<0.001) and SOFA score was (-0.931/ <0.001). Pearsons correlation coefficient shows that total cholesterol, LDL cholesterol is poorly correlated with sepsis severity, while triglycerides though negatively correlated the association is weak. Similar results were seen in study by Tanaka S et al, in septic patients, the severity of the disease (assessed by SOFA score or the need for mechanical ventilation) was negatively associated with HDL-C, whereas no significant association was found with LDL-C and triglyceride levels.[14] In the current study Total Cholesterol correlation coefficient was 0.143 with p 0.277, where as in study by Nabavi A et al the prevalence of hypocholesterolemia in sepsis patients was significantly higher than the general population. Also in study by Nabavi A et al total Cholesterol correlation coefficient was -0.428.[13] In study by Sunayana P et al they observed that HDL cholesterol and LDL cholesterol showed significantly lower values in patients with severe sepsis and septic shock compared to patients with sepsis. However, triglycerides showed a reverse pattern with higher triglyceride values observed in patients with septic shock. It has been proposed that these changes induce anti-inflammatory effects that contribute to host defense. [15] In the study of Maile et al., in 2020; high LDL and TG levels were found to be associated with lower mortality.[16]

In contrary study by Nabavi A et al, found that the lipid profile of the patients during their admission to the intensive care unit was not associated with mortality.[13] Also in study by Murat E et al in geriatric population stated that LDL, HDL and TG levels were not a predictor of adverse clinical outcomes.[17].

Also several other studies in the literature showed that low cholesterol levels are a risk factor for sepsis. Also they concluded that lipid levels change rapidly in early sepsis and can predict the results. [18,19,20,21]

CONCLUSIONS

Sepsis patients, shows alterations in lipid metabolism. Higher values of SOFA and APACHE II scores were associated with low HDL levels. Lipoproteins may function as potential biomarkers (high-density lipoprotein) in systemic inflammatory response syndrome and sepsis. This may be attributable to alterations in serum lipid metabolism during sepsis, thus modulating the host response to inflammation in patients with sepsis. Further studies are required to approve the role of lipid profile in the outcomes of sepsis patients.

Recommendations: A longitudinal study and molecular research on dynamics in serum lipids with sepsis severity.

Limitations: single centre study.

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