Original Article

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Internal Medicine Section

Fasting Lipid Profile and Disease Severity in Sepsis Patients

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ABSTRACT

Introduction: Sepsis is a systemic inflammatory response syndrome that has a proven or suspected microbial aetiology. Sepsis carries significant morbidity and mortality. During sepsis many changes occur in plasma lipids and lipoproteins. These changes help in fighting inflammation and contribute to host defence. Studies have shown that there is are relationship between low cholesterol and sepsis and the levels of total cholesterol and HDL decline during sepsis.

Aim: To assess lipid profile abnormalities in patients with sepsis and to study the relation between fasting lipid profile and disease severity and mortality in patients with sepsis.

Materials and Methods: This descriptive study was done at Government TD Medical College, Alappuzha, Kerala. The duration of study was one year. A total of 70 patients who were admitted to the medical intensive care unit who satisfied the American College of Chest Physicians/ Society of Critical Care Medicine (ACCP/SCCM) criteria for the diagnosis of sepsis were included in the study. Depending on the severity of sepsis, these patients were grouped into three groups-sepsis, severe sepsis and septic shock group.

Results: Significantly lower values of HDL cholesterol and LDL cholesterol were observed in patients with severe sepsis and septic shock compared to patients with sepsis. Total cholesterol also showed lower values in patients with septic shock but this observation was statistically not significant. Triglycerides showed an inverse pattern with higher values in septic shock group.

Conclusion: It is observed that low LDL cholesterol and high Triglycerides were associated with a significantly higher mortality in patients with sepsis.

Keywords: HDL cholesterol, LDL cholesterol, Triglycerides

INTRODUCTION

Sepsis is a systemic inflammatory response syndrome that has a proven or suspected microbial aetiology [1]. During an infection and inflammation many cytokines are released. This produces many changes in plasma lipids and lipoprotein concentration [2,3]. In patients with infection, decrease in serum levels of total cholesterol, LDL and HDL and increase of serum triglyceride have been reported in most studies [4]. These changes were independent of the underlying disease or infectious agents [5]. It has been proposed that these changes induce anti-inflammatory effects that contribute to host defense [6]. It is not clear whether these changes in plasma lipids will help in identifying inflammation due to the infection [7]. There are many studies showing the relationship between low cholesterol and sepsis [1,7]. In patients who develop severe sepsis, the total and HDL cholesterol level fell and reached 50% of recovery levels by the third day [8]. These changes in lipids in sepsis may help in predicting the prognosis and may have a therapeutic role also.

This study was conducted to assess lipid profile abnormalities in patients with sepsis: sepsis, severe sepsis and septic shock and to study the relationship between fasting lipid profile and disease severity and mortality in patients with sepsis and the usefulness of lipids as a prognostic indicator in patients with sepsis.

MATERIALS AND METHODS

This study was done at Government TD Medical College, Alappuzha and the study design was descriptive in nature. The study was conducted from the period of April 1, 2012 to March 31, 2013. A total of 70 patients who were admitted to medical intensive care unit were included in the study.

Inclusion criteria: Patients aged 18 to 75 years satisfying the ACCP/SCCM criteria [1] for the diagnosis of sepsis were included in the study.

Exclusion criteria: Patients with a documented history of systemic arterial hypertension/diabetes mellitus/dyslipidemia/liver diseases/thyroid abnormalities/ on treatment with statins, were excluded from the study.

After getting written informed consent from the patients or immediate relatives, the selected patients were examined in detail. Their vital signs like pulse, blood pressure, respiratory rate, temperature were checked. We looked for pallor, cyanosis, clubbing, icterus, oedema, generalised lymphadenopathy, skin infections and any other focus of infection. A detailed clinical examination of respiratory system, cardiovascular system, gastrointestinal system and nervous system was done in all patients. Laboratory investigations included complete haemogram, urine routine examination, blood sugar, renal function tests, liver function tests, culture of blood, urine, and sputum, chest X-ray, ECG, Echocardiography and serological tests like IgM leptospiral antibody, IgM dengue antibody, WIDAL test, Arterial blood gas analysis etc. Diagnosis of sepsis was made in patients who satisfied the ACCP/SCCM criteria. Patients were categorised into subgroups according to severity of sepsis as sepsis, severe sepsis and septic shock. Their fasting lipid profiles were measured on the next day morning. The development of complications like renal failure and the need for dialysis, pulmonary complications like Acute Lung Injury and Acute Respiratory Distress Syndrome (ALI/ARDS), need for ventilator support, hypotension and need for ionotropes and development of multiorgan failure and death were noted.

Serum total cholesterol was determined using CHOD-POD (cholesterol oxidase-peroxidase) method and triglyerides by enzymatic method using lipoprotein lipase, glycerol kinase, glycerol phosphate oxidase and peroxidase. HDL cholesterol measured using separation by precipitation with phosphotungstic acid and magnesium chloride. LDL cholesterol was calculated according to the formula, LDL-C= Total cholesterol- TGL/5-HDL.

The variables included in the study were age, sex, mortality, primary

source of infection, cultures of blood and other body fluids, serology, haematological parameters like haemoglobin, total count, differential count, platelet count, ESR, peripheral smear and biochemical parameters like renal function tests and liver function tests in addition to lipid profile. Chest X-ray, ECG, echocardiography, arterial blood gas analysis, central venous pressure, need for ventilator support and dialysis were also noted.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS data editor version 16.0 and Microsoft Office Excel 2007. Variables were compared using chi-square test and a p-value of <0.05 was considered significant.

RESULTS

A total of 70 patients were included in the study. Of these 42 were males and 28 were females. The most common cause of sepsis was leptospirosis, accounting for 34.3% of cases. 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. The primary site of infection could not be identified in four cases. A definite microbiological diagnosis could be obtained in 62.9% of cases. Of these, 34.3% cases were due to leptospirosis followed by *Klebsiella* (10%), *Staphylococcus aureus* (8.8%), *Pseudomonas* (5.7%) and *E. coli* (4.2%). Renal failure was the most common complication (47.1%) and 21.4% of patients with renal failure needed dialysis. Pulmonary complications in the form of ALI/ARDS occurred in 25.7% of patients.48.6% patients had hypotension. Out of the 70 patients, 19 (27.2%) died. We analysed the relationship of sepsis with lipid profile and mortality. There were three categories of patients: patients with sepsis, severe sepsis and septic shock. We observed that the percentage of patients with total cholesterol less than 200 mg/dL increased as sepsis (66.7%) progressed to severe sepsis (87.9%) and to septic shock (92.3%). However, this difference was not statistically significant. HDL cholesterol also showed similar pattern with HDL < 50 mg/dL in 50% of patients with sepsis, 87.8% in severe sepsis and 92.3% in septic shock. This observation was found to be statistically significant with p-value <0.001. LDL also showed a similar trend with 33.3% of patients with sepsis, 75.8% of patients with severe sepsis and 84.6% of patients with septic shock having LDL less than 100 mg/dL. This was statistically significant with p-value 0.001. The percentage of patients with triglyceride level > 150 mg/dL was 16.7% in sepsis group, 48.5% in severe sepsis and 30.8% in septic shock with p-value 0.04.

The mean total cholesterol in sepsis patients was 190.96±24.6 mg/dL, in severe sepsis 160.36±26.81 mg/dL and in septic shock 158.38±21.24 mg/dL. The mean HDL was 52.17 mg/dL, 41.81 mg/dL and 40.08 mg/dL respectively. The mean triglyceride was 123.38 mg/dL, 144.79 mg/dL and 146.9 mg/dL respectively which was not significant p-value 0.12. The mean LDL was 115.89 mg/dL in sepsis, 89.7 mg/dL in severe sepsis and 90 mg/dL in septic shock. The mean VLDL was 27.04 mg/dL in sepsis, 26.12 mg/dL in severe sepsis and 29.15 mg/dL in septic shock patients. 81.4% of patients had total cholesterol less than 200 mg/dL and 18.6% had total cholesterol more than 200 mg/dL. Among patients with total cholesterol more than 200 mg/dL, 15.4% patients died where as 29.8% of patients with total cholesterol less than 200 mg/dL died [Table/Fig-1]. But this difference was not statistically significant (p-value 0.2). Among patients with triglyceride more than 150 mg/dL, 46% patients died, where as mortality was 17.4% in patients with triglyceride less than 150 mg/dL and this difference in mortality was statistically significant (p-value 0.001) [Table/Fig-2]. In patients with HDL more than 50 mg/dL 11.8% mortality was observed and in patients with HDL less than 50 mg/dL, 32.1% mortality was observed but this was not statistically significant (p-value 0.1) [Table/Fig-3]. The mortality rate was 11.5% in patients with LDL more than 100 mg/dL compared to 36.4% mortality in those with LDL less than 100 mg/dL. This difference in mortality among patients with high and low LDL levels was significant (p-value 0.02) [Table/Fig-4]. We could not find any statistically significant relation between VLDL and mortality.

Mortality	Total cholesterol				Total	
	< 200 mg/dL		> 200 mg/dL			
	%	N	%	N	%	N
Died	29.8	17	15.4	2	27.1	19
Survived	70.2	40	84.6	11	72.9	51
Total	100	57	100	13	100	70

[Table/Fig-1]: Mortality and total cholesterol.
Chi-square-1.16 df-1 p-0.2

Mortality	TG > 150 mg/dL		TG < 150 mg/dL		Total	
	%	N	%	N	%	N
Died	45.8%	11	17.4%	8	27.1%	19
Survived	54.2%	13	82.6%	38	72.9	51
Total	100	24	100	46	100	70

[Table/Fig-2]: Mortality and triglycerides.
Chi-square value 6.452 df-1 p-0.001*

Mortality	HDL < 50 mg/dL		HDL > 50 mg/dL		Total	
	%	N	%	N	%	N
Died	32.1%	17	11.8%	2	27.1%	19
Survived	67.9%	36	88.2%	15	72.9%	51
Total	100%	53	100%	17	100%	70

[Table/Fig-3]: Mortality and HDL.
Chi-square-2.68 df-1 p-0.101

Mortality	LDL < 100 mg/dL		LDL > 100 mg/dL		Total	
	%	N	%	N	%	N
Died	36.4%	16	11.5%	3	27.1%	19
Survived	63.6%	28	88.5%	23	72.9%	51
Total	100%	44	100%	26	100%	70

[Table/Fig-4]: Mortality and LDL.
Chi-square-5.09 df-1 p-0.02

DISCUSSION

In our study the primary source of infection was lung in 28.6% of cases, followed by urinary tract in 24.3% of cases. 34.3% of cases were due to leptospirosis which is a common infection in our area. Skin infections accounted for 5.7% cases and primary site of infection could not be identified in 5.7% cases. In the BASES study [9], the lung and respiratory tract was the main source of infection. In the SOAP [10] study 46.2% patients had lung infection and Todi S et al., reported 46.2% cases with lung infection [11]. The aetiological agent was identified in 62.9% cases. In the case of leptospirosis, the diagnosis was made using serology, other cases were diagnosed based on culture of blood or body fluids. Cultures were positive in only 28.7% of cases. The organism most commonly isolated was *Klebsiella* (10%) followed by *Staphylococcus aureus* (8.8%). There were no cases due to anaerobes or fungi. In the SOAP study, 30% were gram positive organisms and 27% were gram negative organisms. Martin GS et al., reported 52.1% cases due to gram positive bacteria and 37.6% cases due to gram negative bacteria [12]. The mean total cholesterol, triglyceride, HDL and LDL cholesterol in our study were comparable to other similar studies [5,7]. The concentration of total cholesterol, HDL and LDL decreased during sepsis. This was more as the severity of sepsis increased. The reduction in HDL and LDL was statistically significant also. Studies [4,7] have shown reduction in total cholesterol, HDL and LDL during infection and inflammation. There is evidence that cholesterol

metabolism is related to inflammation and proinflammatory cytokines play a role in this [13,14]. Many studies have shown a reduction in LDL during infection and inflammation [8,15,16]. This is thought to be due to the host response which induces LDL oxidation resulting in lower LDL C levels [15,17,18]. The overall mortality rate among the study group was 27.2% and mortality was found to be higher in those patients with total cholesterol less than 200 mg/dL and HDL less than 50 mg/dL. However, this observation was not statistically significant. A study by Windler E et al., reported a higher mortality with lower cholesterol levels [19]. Many other studies [16,20] also reported that low cholesterol in septic patients was associated with poor outcome. Low serum HDL was found to be associated with increased mortality in many studies [20,21]. The mortality rate was higher in those with low LDL (less than 100 mg/dL) and this was statistically significant. We observed higher mortality rate of 45.8% in those with triglyceride > 150 mg/dL compared to mortality rate of 17.4% in those with triglyceride < 150 mg/dL and this was statistically significant. In the case of triglycerides in sepsis, different studies have reported conflicting findings, some saying there were low triglycerides in sepsis [8] and some saying presence of high triglycerides in sepsis [7].

LIMITATION

The sample size in each class of sepsis-sepsis, severe sepsis and septic shock group was not uniform. The lipid profile values of the patients prior to the present illness was not available. Serial measurement of lipids was not done in these patients during their ICU stay.

CONCLUSION

We tried to analyse the lipid profile of patients with sepsis. The patients were categorised into three groups depending on the severity of sepsis into sepsis, severe sepsis and septic shock. We 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. Significantly higher mortality rate was observed in sepsis patients with low LDL cholesterol and high triglyceride values.

Ethical approval: Study was approved by the Institutional ethical committee, Government T.D. Medical College, Vandanam, Alappuzha, Kerala, India.

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