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Original Research Article

Cholesterol levels: the prognostic significance in ICU patients

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ABSTRACT

Background: The aims of the study were to monitor the total cholesterol levels at different time intervals in ICU patients and to analogize the values with the outcome of disease, to study the prevalence of hypocholesterolemia among ICU patients and to assess the trend of hypocholesterolemia among various diseases.
Methods: Present study populace consists of 55 patients admitted in ICU. For these patients, lipid profile was done on the day of admission and day-3 of admission. The total cholesterol levels done on day 1 and 3 were compared with disease outcome.
Results: The mean cholesterol value among 33 survivors on day 1 was 120.76(±18.54) and day 3 was 145.30 (±55.65) with p value of 0.019, that is statistically significant. As the total cholesterol value increases during the period of ICU stay, it proves to be an early prognostic indicator of disease outcome. The patients showing increasing trend of total cholesterol levels has increased chances of survival. Similarly, HDL value among 33 survivors on day 1 was 31.70 (±3.98) and day 3 was 36.39 (±11.98), with p value of 0.033, that is statistically significant and also, the mean LDL value among 33 survivors on day 1 was 68.25 (±17.14) and day 3 was 78.78 (±24.74), with p value of 0.009, which was also found to be statistically significant. The mean cholesterol value among 22 non-survivors on day 1 was 131.64 (±15.24) and day 3 was 122.09 (±26.23), the mean HDL among 22 non-survivors on day 1 was 33.14 (±3.79) and day 3 was 31.32 (±4.23).
Conclusions: Present study's intend of monitoring the total cholesterol level was successfully demonstrated that it can be used as prognostic tool in ICU patients. The increasing trend in total cholesterol level indicates better prognosis of disease outcome. Similarly, the increasing trend in HDL and LDL levels also can be used as prognostic tool to determine the survival rate of patient.

Keywords: HDL, Hypocholesterolemia, Hypercholesterolemia, ICU patients, LDL, Total cholesterol

INTRODUCTION

Hypolipidemia is a decrease in plasma lipoprotein caused by primary (genetic) or secondary (acquired) factors. It is usually asymptomatic and diagnosed incidentally on routine lipid screening. The first report of hypocholesterolemia in the medical literature was in 1911 by Chauffard and coworkers, in patients with active tuberculosis.[1] Since then (about 95 years), only few dozens of studies were published in this regard. The terms Hypolipidemia, hypocholesterolemia and hypobetalipoproteinemia are used interchangeably in the literature, and refer to reduced plasma cholesterol. Most authors use the total serum Total cholesterol (TC) to define this condition. Yet, there is no consensus about the level below which a clinically significant hypocholesterolemia will ensue, and each author used a

different cut-off value. Most of the authors use a cut-off value between 120 mg/dl(3.1 mmol/l) and 150m/dl (3.88mmol/l).[2,3] However some authors use higher levels up to 190mg/dl (4.9mmol/l) while others use lower values such as 100mg/dl (2.59mmol/l).[4-8]

Epidemiologic studies have identified a relationship between hypocholesterolemia (<130mg/dL)and increased mortality from all causes and authors in present study have considered total cholesterol less than 160 mg/dL as hypocholesterolemia based on American Heart Association.[9,10] Hypocholesterolemia occurring with the development of infection was demonstrated during the 15-year period of the Kaiser Permanente study, conducted in 15000 healthy men and women.[11]

Other authors have associated hypocholesterolemia with inflammatory states.[12,13] A 30% or greater reduction in lipid and lipoprotein concentrations is known to occur in a variety of inflammatory states.[13] Interleukin-6 and tumor necrosis factor-α have been implicated as potent negative regulators of lipoprotein metabolism in vitro and in vivo.[14-16] Fraunberger and coworkers demonstrated a relationship between hypocholesterolemia and several disease states, as well as organ dysfunction.[15]

The present preliminary study is thus an attempt to document the cholesterol level at different time intervals in ICU patients and to compare it with the outcome of disease. In this study patients suffering from wide range of diseases are included.

The objectives of the study were to estimate the cholesterol levels at different time intervals in ICU patients, to assess the trend of cholesterol levels in different diseases and to compare the cholesterol levels with the disease outcome and the survival.

METHODS

A hospital based cross sectional study. The study group consisted of 55 patients admitted in the Department of General Medicine, in ICU, ICCU at Sri Manakula Vinayagar Medical College and Hospital, Puducherry during the period of 15 months from November 2014 until March 2016.

All patients with positive clinical findings were further the study was done in ICU patients suffering from sepsis, single or multiple organ failure during the given span of time. After getting the informed consent from the patient and patient's attenders, history taking regarding age, sex, marital status, chronic medical illness, family history of diabetes mellitus, hypertension, other cardiac disease are noted down.

Blood sample was collected on day of admission and on third day to do lipid profile. The increase or decrease in cholesterol value was compared with outcome of disease.

All the patients were examined and the following parameters were evaluated in all cases.

- Total cholesterol, high density lipoprotein, low density lipoprotein, and triglycerides are measured on day of admission (0 hours) and on day3 (72 hours).
- Complete blood count
- Liver function test
- Renal function test
- Arterial blood gas analysis
- Electrolytes
- Random blood sugar
- Chest X Ray
- ECHO
- CT Brain
- Cerebrospinal Fluid Analysis
- USG Abdomen or KUB

Sample size calculated as 55 using the prevalence value of 3.6% and allowable error as 5 by using the formula given below.[17,18]

$4*(\text{prevalence})\ (100 - \text{prevalence})/\ (\text{Allowable error})^2$

$4pq/L^2 = 4*(3.6)\ (100-3.6)/\ (5)^2 = 55$

The study participants were recruited randomly during the study period pertaining to the inclusion and exclusion criteria. The written informed consent was obtained from the close relatives regarding the research purpose and confidentiality was ensured. The sampling was done till we got the desired sample size.

Inclusion criteria

Patients suffering from following disease are included in the study

- Chronic liver disease
- Acute or chronic renal disease
- Malignancy
- Cardiac failure
- Multiple organ failure
- Sepsis
- Respiratory failure, pneumonia
- Encephalopathy, meningitis.

Exclusion criteria

Patients with following conditions

- Patients on statins treatment, with change in dosage in recent six months.
- Patients newly started with statin drugs within last six months.
- Poisoning.
- Stroke.
- Acute coronary syndrome.

- Electrolyte disturbance.

RESULTS

During the study period of 15 months from November 2014 to March 2016, total of 55 ICU patients were recruited in the study.

Out of the 55 patients taken up for study, 33 patients got recovered from disease and discharged, while 22 patients died of disease.

Age distribution among subgroups

The 55 patients included in the study belong to different age group. Majority were belonging to above 60 years and only 2 patients with the age less than 30yrs were in the study population, of which one survived and one died of disease. Among the 24 patients with the age above 60yrs in the study population, 16 patients survived and 8 patients died.

Gender distribution

The survival rate was more among males 67% (22) than females 33% (11) whereas in the non survivors group there was no much difference among genders. SMOKING: In the survivors subgroup 19 patients were non-smokers and 14 were smokers. Similarly, among the non-survivors subgroup non-smokers (13) were more than smokers (9).

Alcohol consumption

Among 55 ICU patients included in the study, 22 patients had the habit of alcohol consumption, of which 12 patients survived and 10 patients died of disease, whereas the patients who had no alcohol consumption habit, 21 survived and 12 died of disease.

Diabetes mellitus, hypertension and cad

Among the study population 22 were diabetic and 17 were hypertensive patients. The survival rate was similar in both diabetics and hypertensive patients which was 30%, but it was not statistically insignificant whereas the non survival rate was more 55% among diabetics than 32% hypertensive patients.

Among 55 ICU patients included in the study, 46 patients had no underlying Coronary Artery Disease, of which 29 patients survived and 17 patients died of disease. The non survival rate was 33% among patients with CAD which was not statistically significant.

Chronic kidney and renal disease

Among the study population 5 patients and one patient had chronic kidney and liver disease respectively. The survival and non survival were not influenced by either kidney or liver disease in this group (Table 1).

Lipid profile

In this study, lipid profiles among 55 patients were compared between day-1 and day-3 of the study period.

Table 1: Socio demographic and other variables in relation to disease outcome.

Variables	Survivors (33)	Non survivors (22)	P value
Age group			
<40 yrs	4	3	0.838
41 to 50 yrs	4	5	
51 to 60 yrs	9	6	
>60 yrs	16	8	
Gender			
Male	22	12	0.266
Female	11	10	
Smoking habit			
Yes	14	9	0.568
No	19	13	
Alcohol consumption			
Yes	12	10	0.346
No	21	12	
Diabetes mellitus			
Yes	10	12	0.654
No	23	10	
Hypertension			
Yes	10	7	0.568
No	23	15	
Coronary artery disease			
Yes	4	5	0.249
No	27	17	
Chronic kidney disease			
Yes	3	2	0.673
No	30	20	

In the comparison of total cholesterol among the survivors subgroup on day-1 and day-3, was found to be statistically significant.

Similarly, the comparison of HDL, LDL between day-1 and day-3, among the survivors subgroup was also found to be statistically significant.

Whereas the comparison of total cholesterol, HDL and LDL among the non-survivors sub group was not statistically significant.

The comparison of triglyceride and VLDL, between day-1 and day-3, among the survivors and non-survivors sub groups was not statistically significant. It is shown in the (Table 2).

Table 2: Analysis of lipid profile values among survivors and non survivors on first and third day.

		Survivors (n=33)* Mean±SD	p value	Non-survivors (n=22) Mean±SD	p value **
TC	Day 1	120.76±18.54	0.019	131.64±15.24	0.083
	Day 3	145.30±55.65		122.09±26.23	
HDL	Day 1	31.70±3.98	0.033	33.14±3.79	0.137
	Day 3	36.39±11.98		31.32±4.23	
LDL	Day 1	68.25±17.14	0.009	74.57±18.67	0.265
	Day 3	78.78±24.74		69.33±25.59	
TGL	Day 1	104.82±59.73	0.356	130.18±95.79	0.275
	Day 3	114.67±91.19		115.82±57.94	
VLDL	Day 1	19.97±10.89	0.871	23.52±13.95	0.443
	Day 3	19.81±8.64		21.86±9.7	

DISCUSSION

Cholesterol levels are adversely affected by infection or organ dysfunction, but the physiologic significance for these decreased concentrations is not known. The terms Hypolipidemia, hypocholesterolemia and hypobetalipoproteinemia are used interchangeably in the literature, and refer to reduced plasma cholesterol. Most authors use the total serum cholesterol (TC) to define this condition. Yet, there is no consensus about the level below which a clinically significant hypocholesterolemia will ensue, and each author used a different cut-off value. Most of the authors use a cut-off value between 120mg/dl (3.1 mmol/l) and 150m/dl (3.88mmol/l).[2,5] However, some authors use higher levels up to 190mg/dl (4.9mmol/l) while others use lower values such as 100mg/dl (2.59mmol/l).[4-8] Epidemiologic studies have identified a relationship between hypocholesterolemia (<130mg/dL)and increased mortality from all causes and we in present study have considered total cholesterol less than 160 mg/dL as hypocholesterolemia based on American Heart Association.[9,10] Among the patients admitted in ICU suffering from various diseases, 55 patients meeting inclusion criteria were taken up for this study. For these patients lipid profile were done on day 1 and day 3 of admission.

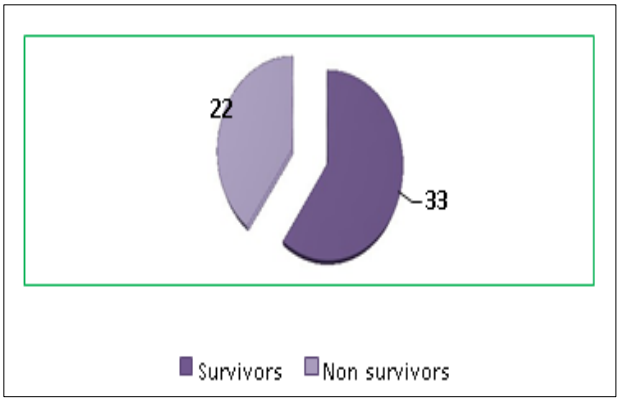

Figure 1: Distribution of cases according to disease outcome.

Total cholesterol and disease outcome

In this study the mean cholesterol value among 33 survivors on day 1 was 120.76(±18.54) and day 3 was 145.30(±55.65), it is statistically significant. Similarly, the previous study done by Das S et al among 55 patients in ICU, showed mean cholesterol value among 22 survivors on day 1 was 110(±11) and day 3 was 113(±12), which was statistically significant.[19] As the total cholesterol value increases during the period of stay in ICU, is proven to be early prognostic indicator of disease outcome. The patients showing increasing trend of total cholesterol levels has increased chances of survival. In the study done by Das S et al among 55 ICU patients, mean cholesterol value among 33 non-survivors on day 1 was 90(±9) and day 3 was 90(±8), which was statistically significant.[19] Whereas in my study, the mean cholesterol value among 22 non-survivors on day 1 was 131.64(±15.24) and day 3 was 122.09(±26.23), which was statistically not significant. As discussed by Das S et al patients showing decreasing trend of total cholesterol levels is a poor prognostic indicator of disease outcome, whereas my study does not confirm the above results.[19] This is because in Das S et al study ICU patients suffering from sepsis disease alone was taken for study, but in my study ICU patients suffering from various disease were included hence the disease outcome varies independent of total cholesterol value.[19]

HDL and disease outcome

In this study the mean HDL value among 33 survivors on day 1 was 31.70(±3.98) and day 3 was 36.39(±11.98), it is statistically significant. But in the previous study done by Das S et al among 55 patients in Icu, showed mean HDL value among 22 survivors on day 1 was 29(±3) and day 3 was 26(±3), which was statistically not significant. It has been found in this study that increasing trend in HDL level during the period of hospital stay can also be used as an early prognostic indicator of disease outcome. The patients showing increasing trend of HDL levels has increased chances of survival.[19] Further studies are required to confirm these results. In the study done by

Das S et al, mean HDL value among 33 non-survivors on day 1 was 23(±2) and day 3 was 22(±2), which was statistically not significant.[19] Similarly in my study, the mean HDL among 22 non-survivors on day 1 was 33.14(±3.79) and day 3 was 31.32(±4.23), which is also statistically not significant.

LDL and disease outcome

The mean LDL value among 33 survivors on day 1 was 68.25(±17.14) and day 3 was 78.78(±24.74) which is statistically significant found in this study also deferred from the previous study done by Das S et al showed mean LDL value among 22 survivors on day 1 was 36(±10) and day 3 was 42(±8), which was statistically not significant.[19] It has been additionally found in this study that increasing trend in LDL level during the period of hospital stay can also be used as an early prognostic indicator of disease outcome. The patients showing increasing trend of HDL levels has increased chances of survival. Further studies are required to confirm these results.

Lipid profile and various diseases

Among 55 patients included in the study, 5 patients were found to be suffering from end stage renal disease and were undergoing periodic hemodialysis. Among those 5 patients, 3 patients survived and 2 died of disease during the period of study. The patients who showed increasing trend of total cholesterol survived, and those showed decreasing trend died. Thus hypocholesterolemia was an independent predictor of death in patients on hemodialysis, which is similar to previous cohort study done by Iseki et al, on hemodialysis patients.[20] Totally 9 ICU patients suffering from coronary artery disease were in the study, out of which 4 survived and 5 died of disease. Among the survived patients there was increasing trend in total cholesterol was observed during the ICU stay, all though their values were less than 160mg/dl, whereas decreasing trend in total cholesterol value is seen among the non-survivors. Further studies are needed to assess the ideal total cholesterol value to be maintained in coronary artery disease patients. Although, similar pattern of increasing trend in total cholesterol levels were seen among 10 survivors of hypertensive patients and decreasing trend in total cholesterol levels among 7 non-survivors, the p value was not statistically significant. Among 22 diabetic patients included in the study, the pattern of increasing trend in total cholesterol levels were seen among 10 survivors of diabetic patients and decreasing trend in total cholesterol levels among 12 non-survivors, the p value was not statistically significant.

CONCLUSION

It is clear from present study that monitoring the total cholesterol level can be used as prognostic tool in ICU patients. The increasing trend in total cholesterol level indicates better prognosis of disease outcome. Similarly the increasing trend in HDL and LDL levels also can be used as prognostic tool to determine the survival rate of patient.

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