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Original Article

Variations in Lipid Profile During Critical Illness

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ABSTRACT

Objective: To determine to mean change in levels of Triglycerides (TG), Total cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), and low-density lipoprotein (LDL-C) in critically ill patients at admission,18 hours and 42 hours after admission.

Study Design: Cross-sectional study

Place and Duration of Study: Department of Chemical Pathology & Endocrinology, Armed Forces Institute of Pathology Rawalpindi (AFIP), in collaboration with Military Hospital Rawalpindi (MH), Combined Military Hospital Rawalpindi (CMH) and Armed Forces Institute of Cardiology Rawalpindi (AFIC) Pakistan, from Mar to Sep 2016.

Methodology: A total of Fifty patients admitted to intensive care units of MH, CMH and AFIC for coronary artery disease (CAD), sepsis, burns and cancer were included in the study. Patients on lipid-lowering drugs and post-surgery patients were excluded.TC, HDL-C, LDL-C and TG were analysed on ADVIA 1800 (SIEMENS, Germany).

Results: Fifty patients were included with mean age of 48.12±2.26 years. Parametric analyses revealed significant increase in serum TG levels during hospitalization in critically ill patients in various disease groups (Mean±SD at admission, 18 hours and 42 hours): TG (CNS disorders 1.35±0.18, 1.78±0.24 and 1.22±0.17; CVS 1.92±0.21, 2.15±0.28 ,2.32 ±0.20; sepsis 1.55±0.18, 1.38+0.24,1.54+0.17; malignancies 1.24±0.31, 1.28+0.42,1.35+0.30; renal disorders 1.39+0.35,1.82+0.47,1.08+0.33; (p<0.05). TC decreased in sepsis, CVS and cancer patients while increasing in CNS and renal disorders. HDL-C and LDL-C decreased in all diseases as an acute stress response.

Conclusions: During critical illness, TG and LDL-C may change significantly; therefore, they should be monitored and interpreted with extreme care if requested to be performed within the course of the disease.

Keywords: Critical illness, High-Density Lipoprotein Cholesterol (HDL-C), Lipemia of sepsis Total cholesterol (TC). Low-density lipoprotein (LDL-C) Triglyceride (TG).

How to Cite This Article: *Hassan M, Sharif TB, Ijaz A, Asif N, Fatima A, Bibi A. Variations in Lipid Profile During Critical Illness. Pak Armed Forces Med J 2022; 72(5): 1821-1825. DOI: https://doi.org/10.51253/pafmj.v72i5.9465*

INTRODUCTION

In clinical practice, lipid profile reportedly varies from the start of critical illness till the time of recovery.[1] These lipid parameters include TG, Total Cholesterol (TC), LDL-Cholesterol (LDL-C), HDL-Cholesterol (HDL-C), Non-HDL-Cholesterol (Non-HDL-C), and VLDL-Cholesterol.[2] The severity of these alterations has a direct impact on the results of these investigations. This is an adaptive metabolic response of our body towards stress to survive a critical illness, also called "lipaemia of sepsis".[2] An increase in TG results from the hydrolysis of TG and phospholipids to fatty acids. High levels of TG can intensify organ dysfunction, mainly pancreas, pulmonary or hepatic dysfunction, during critical illness.[3]

Critically ill patients suffer from dyslipidemia and hyperglycemia mainly because of increased hepatic lipogenesis and gluconeogenesis. The changes in lipids have been attributed to hormones affecting fat utilization during critical illness, including insulin, adrenaline, non-adrenaline, corticotropin, glucocorticoid, growth hormone, and thyroid hormones, but controversies exist about whether this change is due to acute critical illness or due to organ damage leading to acute illness.[4,5]

The magnitude of dyslipidemia is directly proportional to inflammation. Still, a consensus has not been achieved regarding the change in TG. Some studies showed that it remains unchanged with change only in HDL-C and TC levels. Controversy also prevails on VLDL levels. According to some studies, its level also increases due to increased hepatic synthesis and as compensation for decreased HDL phospholipids.[6]

Lipid profile is often advised in critically ill patients to diagnose or monitor diseases related to atherosclerosis. However, lipid tests can be misleading in such patients due to the abovementioned factors. There is no study on the subject in our country, and

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Received: 26 Jun 2019; revision received: 08 Nov 2021; accepted: 07 Dec 2021

there is a need for the data collection on this aspect of lipid abnormalities. Proper guidelines must be formulated to carry out lipid tests in such patients for better patient care and management. This study will help clear some of the controversies regarding lipid profile results during acute illness.

METHODOLOGY

This cross sectional study was conducted at the Department of Chemical Pathology & Endocrinology, Armed Forces Institute of Pathology Rawalpindi (AFIP), in collaboration with Military Hospital Rawalpindi (MH), Combined Military Hospital Rawalpindi (CMH) and Armed Forces Institute of Cardiology Rawalpindi (AFIC) Pakistan, from March to September 2016 The Institutional Review Board approved this study. Confidentiality was ensured by obtaining informed consent from the patients.

Prior informed consent was taken from patients after explaining the objectives of the study and its implications. The calculated sample size was 50, taking a 10% non-response rate.[7] Non-probability consecutive sampling technique was employed.

Inclusion criteria: Patients admitted in intensive care units of for coronary Disease(CAD), sepsis, burns, and cancer with age ranging from 18-75 years, were included in the study.

Exclusion criteria: Patients on lipid-lowering drugs and post-surgery patients were excluded from study.

Fasting blood specimens were collected in Gel tubes at admission,18 hours and 42 hours after admission from patients in ICU, HDU and CCU as per the inclusion criteria mentioned above. These specimens were centrifuged within 45 min in the hospital lab and verified by the pathologist.TC, TG, HDL-C and LDL- C were analyzed on Random Access, Fully Automated Clinical; Chemistry Analyzer ADVIA 1800 Siemens (Germany)using endpoint methods of analyses. LDL-C was done by the kit method.

The data was entered on Statistical Package for the social sciences (SPSS) version 23:00. Qualitative variables like gender, age and diseases were categorized in Renal, CNS, CVS, Sepsis and Oncology disorders and were measured as frequency and percentages. In contrast, for the quantitative variables, mean and SD were estimated. One way ANOVA test was used for the comparison. For inter-group comparison post hoc test was applied. The *p*-value of ≤0.05 was considered.

RESULTS

A total of 50 patients were included in the study. Patients were categorized based on diagnoses into different disease groups, including cerebrovascular diseases 15(30%) Sepsis/inflammatory diseases 15 (30%) cardiovascular diseases 11(22%) Cancer patients 5(10%) and renal diseases 4(8%). In addition, subjects were categorized based on five different age groups, including 23–33 years 4(8%) 34–43 years (4,8%), 44–53 years 5(10%), 54–63 years, 16(32%) and 64–73 years 21 (42%). There were 20(40.0%) female and 30(60.0%) male patients in the study.

There was significant variation in TG levels at the time of admission, 18 hours and 42 hours ($p<0.05$) and the values for the TC, LDL-Cholesterol and HDL-Cholesterol was not significant ($p>0.05$) as shown in Table-I. The inter Group comparison was shown in Table-II.

DISCUSSION

Patients hospitalized with the complaint of acute critical illness due to any cause usually may or may not be aware of their pre-admission lipid profile. The variations of the lipid profile during the initial days of hospitalization will determine the time frame to perform the first measurement of the lipid profile.[8,9] The clinical usefulness of measuring the lipid profile within the first 24 hours after hospitalization admitted with an acute critical illness is controversial.[10,11] It is because lipoproteins and apolipoproteins vary during the initial hours of critical illness.[12] The results of our study showed significant changes in lipid profile at admission, 18 hours, and 42 hours of blood sampling, depending on the diagnosis at the time of admission.

In our study, patients admitted with CAD showed a significant increase in TG attributable to the ongoing inflammatory process, hepatic synthesis and lipolysis at the time of illness. In a study conducted by Kamariya *et al*,[13] showed high levels of TG (>150 mg/dl) in 63(33%). However, Siniawski *et al*,[12] in reported altogether different results showing non-significant changes in TG levels.

Our study showed a decrease in LDL-C levels in the first 18 h followed by a rise at 42h, which is consistent with the studies conducted in the LATIN Trial showing early variations in LDL-C in cardiac patients.[14] In the LUNAR Trial, the greatest variation in LDL-C is between 18 and 42 hours. The results of the LUNAR trial are consistent with ours with regards to LDL-C.[15] These results are due to changes in cholesterol metabolism and liver regulation induced

Table-I: Variation in Lipid Profile with Time and Causative Disease (n=50)

Diseases	Lipid Profile	Admission	18 Hours	42 Hours	*p*-value
		Mean±SD	Mean±SD	Mean±SD	
CNS (n=15)	TG	1.3±0.6	1.6±0.8	1.5±0.69	0.64
	TC	3.6±1.0	3.4±1.2	3.2±1.0	0.61
	HDL-C	1.1±0.7	0.8±0.4	0.7±0.3	0.14
	LDL-C	2.5±0.9	1.8±0.8	1.7±0.6	0.03*
Sepsis/ inflammatory diseases (n=15)	TG	1.5±0.6	1.2±0.4	1.3±0.4	0.36
	TC	3.3±1.0	3.2±0.9	3.1±0.8	0.90
	HDL-C	0.9±0.3	0.8±0.4	0.7±0.2	0.30
	LDL-C	1.6±0.6	1.7±0.7	1.6±0.7	0.90
Renal disorders (n=11)	TG	1.3±0.9	3.2±1.6	1.3±0.8	0.08
	TC	2.7±1.8	3.4±0.6	2.3±0.8	0.24
	HDL-C	0.8±0.5	0.8±0.3	1.4±0.9	0.27
	LDL-C	1.3±0.4	1.0±0.5	1.4±0.8	0.64
CVS (n=5)	TG	1.9±0.9	1.3±0.3	1.3±0.4	0.06
	TC	3.5±0.9	2.8±0.6	2.9±0.7	0.06
	HDL-C	1.0±0.3	0.7±0.3	0.7±0.4	0.22
	LDL-C	2.1±0.7	1.3±0.2	1.6±0.4	0.003*
Cancer (n=4)	TG	1.2±0.1	2.6±1.2	2.9±1.3	0.05*
	TC	3.0±1.1	3.5±1.1	3.1±0.9	0.74
	HDL-C	0.8±0.4	0.9±0.1	0.8±0.2	0.85
	LDL-C	1.9±0.6	2.5±1.0	2.1±0.9	0.58

by the acute phase response.[16] The results of the lipid levels from a large cohort of patients hospitalized with a coronary event obtained in the first 24 hours showed mean LDL-C levels markedly low. TC in our study in CVS patients decreased consistently from 18 hours to 42 hours. Similarly, the LATIN trial showed a decrease in TC in patients with acute myocardial infarction (AMI) and unstable angina.[17]

Table-II: Pair Wise Mean Comparison of Different Levels (n=50)

Diseases	Dependent Variable	(I) Group	(J) Group	*p*-Value
CNS	LDL	admission	18hrs	0.037
			42hrs	0.014
CVS	TG	admission	18hrs	0.039
			42hrs	0.043
	Cholesterol	admission	18hrs	0.032
	LDL	admission	18hrs	0.001
			42hrs	0.021
Cancer Patients	TG	admission	18hrs	0.045
			42hrs	0.027

In the LUNAR Trial, the greatest reduction in TC levels occurred between admission and,[18] hours. In this setting, the results of the LUNAR Trial are consistent with ours with regards to TC,[18] while in an Argentinian FRICAS Trial, 50% of patients hospitalized with AMI had TC levels > 218 mg/dl.[19] HDL-C levels in our study decreased at 18 h and 42h. There is agreement in the literature that about 50% of men and women with ACS had HDL-C levels <40 and <50 mg/dl, respectively.[20] In a Space Rocket study,[21] on patients admitted with ACS strengthens our results with respect to decreasing TC, LDL-C and HDL-C but differs in TG which shows decreased levels.

In the sepsis disease group of our study, TG decreased at 18 hours followed by an increase at 42 hours, TC kept on decreasing at 18 hours and 42 hours, LDL-C decreased at 18 h followed by an increase in 42 hours and HDL-C at 18 hours and 42 hours decreased. This decrease in various fractions of cholesterol seems to be a negative acute phase response,[22] and an indicator of acute bacterial infection.[23] All these findings in TC, HDL-C and LDL-C are consistent with the results of a prospective longitudinal study,1except for TG levels which were found to be decreasing, while in our study it increased.

In our study, the lipid profile in Renal disorder patients indicated an increased TG at 18 hours, then decreased TC kept increasing from baseline till 42 h. LDL-C and HDL-C had the same pattern of decrease followed by an increase at 42 hours, probably due to the consumption and neutralization of lipopolysaccharides. Our results were consistent with another study in terms of TC and LDL-C.[24]

In cancer patients, the pattern is such that TG increased till 42 h from baseline while TC and HDL-C

followed a decreasing pattern till 42h, which is probably due to the tumour necrosis factor (TNF).[25] LDL-C decreased at 18 hours and rose at 42h showing the recovery phase. High cytokine levels lead to decrease lipoprotein production.[2.]

In patients with CNS disorders, we found an increase at 18 hours, then recovery at 42 hours in TG and TC, while LDL-C and HDL-C decreased till 42 hours.

LIMITATIONS OF STUDY

The individual meal choices before sample collection could not be assessed in random sampling. The small sample size did not allow statistical tools to pick minute changes in the lipid profile. In addition, inflammatory markers like CRP and ESR were not taken with each sample which, if we had done, could have provided a better correlation with the status of acute illness in the patient.

RECOMMENDATIONS

Apolipoprotein A-1 should be included, which might be the new therapeutic goal in the near future. Non-HDL-C should be calculated in a random lipid profile.

CONCLUSION

The moment of admission of patients with acute illness, especially cardiovascular diseases, is the most crucial for evaluating the lipid profile and, hence, for choosing the adequate treatment and, most importantly, when to start the treatment. The change in triglyceride levels is significant, and acute critical stress affects the level, and they fluctuate from admission between 18 hours and 42 hours. Because of this variation during critical illness, triglyceride should not be done. Instead, other parameters like HDL-C, LDL-C and Total Cholesterol can safely be advised.

Conflict of Intrest: None.

Author 's Contribution:

Following authors have made substantial contributions to the manuscript as under:

MH: Conception, Study design, drafting the manuscript, approval of the final version to be published, TBS & AI: Data analysis, critical review, approval of the final version to be published, NA: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AF & AB: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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