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Comparative Evaluation of Lipid Profile and Inflammation for prediction of Cardiac Medical Complications and Handling

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ABSTRACT

Background: Cardiovascular complications are predominant cause of global morbidity and mortality, dyslipidemia and inflammation representing critical risk factors contributing to their prevalence.

Objective: The purpose of this research was to determine the Lipid Profile levels and inflammatory biomarkers as risk predictors for the cardiac complications and also to compare the clinical results of patients with normal and abnormal lipid profile.

Methodology: The present study was A case-control study conducted over 12 months involving 400 patients who were selected and divided into two groups. Group- A with normal lipid profile and Group B with dyslipidaemia. The biomarkers for Serum lipid profiles were included blood serum levels of LDL, HDL, triglycerides, Cholesterol and for inflammations, CRP and IL-6 were tested. Data analysis was done using SPSS version 27.0 using paired and independent t-tests, MANOVA, and Pearson correlation statistical tests. $p \leq 0.05$ was considered statistically significant.

Results: Group B showed a high percentage of cardiac complications 28 % as compared to group A with only 10% of complications ($p<0.01$). It was found that LDL-C, HDL-C, and CRP are the good predictors of cardiac events. There was a decrease in LDL-C in Group B ($p < 0.001$) after statin treatment; however, the inflammatory markers were still high in Group B, which implies that they still posed cardiovascular risk. The Pearson correlation analysis revealed positive correlation between increased CRP and cardiac complications and increased LDL-C and cardiac complications; $r= 0.62$; $r = 0.57$ respectively.

Conclusion: High LDL-C, low HDL-C and high CRP values serve as accurate indicators of cardiac diseases. Although, implementation of lipid-lowering therapy successfully lowered the LDL-C level, persistent inflammation was a factor that maintained cardiovascular risk.

Keywords: Lipid profile, cardiovascular diseases, dyslipidaemia, cardiac complications, statins, prediction, therapeutic interventions.

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INTRODUCTION

Cardiovascular complications are the major cause of mortality globally with estimates showing that about 18 million people die of the diseases each year[1]. Another major modifiable risk factor of CVD is dyslipidaemia, which is the presence of atherogenic lipids in the bloodstream which include high LDL-C level, high triglyceride level, and low HDL-C level[2]. These lipid changes are associated with atherosclerosis and result in coronary artery disease, myocardial infarction, stroke and heart failure[3]. Evaluation of the lipid profile levels is part of a routine evaluation of cardiovascular risk. LDL-C is known as the 'bad cholesterol' as it contributes to the plaque formation in the arteries while a higher HDL-C is thought to be beneficial for atherosclerosis[4]. Triglycerides, although not associated in the same way, are usually increased in persons with metabolic syndrome and also raise the risk of cardiovascular disease[5]. It is commonly recognized that treating hyperlipidemia promptly after an acute myocardial infarction (AMI) lowers the risk of coronary heart disease (CHD)-related morbidity and death. But during acute diseases, lipid and lipoprotein levels fluctuate, delaying the decision of therapy. There are several processes that explain these alterations, including as the acute phase response linked to an increase in LDL-receptor (R) activity and a decrease in multiple crucial HDL regulatory proteins. Acute-phase response is linked to changes in blood concentrations of inflammatory markers in addition to lipoprotein modifications. Higher levels of interleukin (IL)-6 and C-reactive protein (CRP) are indicative of an intra-cardiac inflammatory response in individuals with severe adverse cardiac events (AMI), which appears to be the outcome of the development of myocardial necrosis. Still a significant risk factor for CHD is dyslipidemia. High levels of total cholesterol (TC), low levels of low-density lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C) have all been decisively associated to CHD incidence and death in epidemiological studies. Thus, while there is the evidence of association between lipid profiles and cardiac risk there is still controversy what lipid levels mean for clinical practice and how they should be used to address patients with different cardiovascular risks[6, 7]. The aims and objectives of this study was therefore to assess the role of lipid profile levels in determining cardiac medical complication and discuss how these levels inform clinical management and treatment. A comparison of the two groups, the normal lipid and the abnormal lipid group, will give the researcher an understanding of the lipid profile's ability in the prediction of cardiac events as well as the benefits of early intervention in the reduction of the same[8].

MATERIALS AND METHODS

It was a case-control study which was carried out for twelve months from June 2023 till June 2024 at Ghurki trust & teaching hospital Lahore, Pakistan. Total n=400 patients were enrolled in the study, all of them being between 40-70 years of age; A purposive sampling method was used to ensure the selection of patients based on their lipid profiles and absence of any past cardiac complications. the patients were divided into two groups based on their lipid profiles. Group- A included n=200 patients with normal lipid profile, while group-B include n=200 patients with dyslipidaemia. Patients with a history of previous cardiac events like myocardial infarction, stroke or heart failure were excluded from the study to eliminate the effects of the previous event on lipid profile and observed outcomes. Patients between the ages of 40-70 years, with no prior history of major cardiac events such as stroke, myocardial infarction or heart failure, in order

to eliminate confounding factors were included in the study. Informed consent was obtained from all the patients. Participants' permission to be in the study was sought and the study was approved by the institutional review board of Lahore University of Biological & Applied Sciences (UBAS) a project of Lahore Medical & Dental college(LM&DC), Lahore, Pakistan, ref no.: 2023/48D. Participants were asked to provide their informed consent to take part in the study, thereby they understood why the study was being conducted, what was going to be done and that they were free to withdraw from the study at any one time without any reason being asked from them all ethical considerations were followed for the study. At baseline, the patients completed a battery of tests, which included lipid panel analysis consisting of LDL-C, HDL-C, triglycerides, total cholesterol and apolipoprotein A1 and B. Further, the markers of inflammation were also quantified since they are associated with cardiovascular risk; C-reactive protein (CRP) and interleukin-6 (IL-6). Systolic and diastolic blood pressures, BMI, and fasting glucose levels were also measured to evaluate metabolic profile of the participants. Both groups of patients were monitored for a year with primary outcomes being new cardiac complications in form of myocardial infarction, stroke, and heart failure. Secondary end-points were variations in lipid biomarkers and inflammatory markers after interventions like statin therapy and life style changes in the dyslipidemia group. The patients were then evaluated at 6 and 12 months after the intervention to assess lipid profile and inflammatory markers as well as clinical status. The statistical analysis of the data was done with the help of SPSS version 27.0. The repeated measure t-tests were used to compare the differences in lipid and inflammatory markers within the intervention and control groups while the independent t-tests were used to compare the differences in these variables between the intervention and control groups. In order to determine the combined impact of lipid, and inflammatory biomarkers on the development of cardiac complications, Multivariate Analysis of variance (MANOVA) was used. Therefore, Pearson correlation coefficients test was carried out to analyse the correlation between lipid biomarkers, inflammatory markers and cardiovascular events. ($p<0.05$) was considered as statistically significant.

RESULTS

Total 400 patients who were enrolled, 200 in Group- A and 200 in Group B. Age, gender, BMI, and blood pressure were variables that comparable across the two groups ($p>0.05$). At baseline, however, compared to Group A, Group B had substantially higher levels of triglycerides, LDL-C, and inflammatory biomarkers (IL-6, CRP) ($p<0.01$). During the course of a year, Group B experienced a considerably greater incidence of cardiac problems (28%) than Group A (10%) ($p<0.01$). The greatest significant predictors of these problems were elevated LDL-C and low HDL-C. After 12 months ($p<0.001$) of statin medication, the mean LDL-C level in Group B dropped from 168.2 ± 25.4 mg/dL at baseline to 130.1 ± 22.7 mg/dL. Group B had a decrease in LDL-C, but inflammatory markers like CRP and IL-6 stayed high, indicating a continued cardiovascular risk. In contrast, Group A's inflammatory and lipid indicators did not change throughout the course of the 12-month follow-up.

Table 1: Comparison of Lipid and Inflammatory Markers Between Groups at Baseline and 12 Months

Biomarker	Group A Baseline (n=190)	Group B Baseline (n=190)	Group A 12 Months	Group B 12 Months	p-value
LDL-C (mg/dL)	112.5 ± 18.6	168.2 ± 25.4	115.3 ± 20.2	130.1 ± 22.7	<0.001[1]
HDL-C (mg/dL)	52.1 ± 6.1	38.4 ± 5.2	50.2 ± 6.5	43.0 ± 5.6	<0.05[1]
Triglycerides (mg/dL)	148.9 ± 22.7	224.3 ± 30.1	146.8 ± 24.0	195.2 ± 29.4	<0.05[1]
CRP (mg/L)	2.8 ± 1.2	5.6 ± 1.8	2.6 ± 1.3	4.8 ± 1.6	<0.01[2]
IL-6 (pg/mL)	1.9 ± 0.6	3.2 ± 1.1	1.8 ± 0.7	2.9 ± 1.0	<0.01[2]

[1]Paired t-test comparing baseline and 12-month LDL-C levels within groups.

[2]Independent t-test comparing HDL-C and triglyceride levels between Group A and Group B.

[3] Paired t-test for CRP and IL-6 at baseline and 12 months within groups.

To evaluate the combined impact of lipid biomarkers (triglycerides, HDL-C, and LDL-C) and inflammatory biomarkers (IL-6, CRP), on the incidence of cardiac problems, a multivariate analysis of variance (MANOVA) was performed. The results indicated that Triglycerides were not substantially linked with the incidence of problems ($p=0.06$), whereas elevated levels of LDL-C, low HDL-C, and high CRP were significant predictors of cardiac events ($p<0.01$), according to the research. Elevated CRP levels were strongly positively connected with cardiac issues ($r=0.62$, $p<0.01$), according to Pearson correlation analysis. There was also a substantial positive association between LDL-C levels and cardiovascular events ($r=0.57$, $p<0.01$). On the other hand, there was a negative connection ($r=-0.49$, $p\leq0.05$) between HDL-C levels and cardiac problems. These findings imply that although lipid-lowering medication was successful in decreasing LDL-C, Group B patients' ongoing elevation of inflammatory biomarkers, especially in those with increased CRP levels, suggests a prolonged cardiovascular risk.

Table 2: MANOVA Results for Lipid and Inflammatory Biomarkers as Predictors of Cardiac Complications

Biomarker	Wilks' Lambda	F-value	p-value
LDL-C	0.712	8.92	<0.01[1]
HDL-C	0.853	6.34	<0.05[2]
Triglycerides	0.932	3.51	0.06[2]
CRP	0.689	10.21	<0.01[1]
IL-6	0.724	9.33	<0.01[1]

[1] MANOVA test to evaluate the combined impact of lipid and inflammatory biomarkers (LDL-C, CRP, IL-6) on cardiac complications.

[2] MANOVA test to assess the association of HDL-C and triglycerides with cardiac events.

Table 2: Pearson Correlation Coefficients Between Biomarkers and Cardiac Complications

Biomarker	Pearson Correlation Coefficient (r)	p-value
LDL-C	0.57	<0.01
HDL-C	-0.49	<0.05
Triglycerides	0.32	0.07
CRP	0.62	<0.01
IL-6	0.55	<0.01

[1] Pearson correlation test to evaluate relationships between LDL-C, CRP, IL-6, and cardiac complications.

[2] Pearson correlation test to assess the association between HDL-C, triglycerides, and cardiac complications.

The fig-1 compares the baseline and 12-month values of inflammatory and lipid biomarkers for Group B (dyslipidaemia) and Group A (normal lipid profile). At baseline, Group B showed considerably greater levels of triglycerides, LDL-C, CRP, and IL-6 than Group A. After a year, statin medication successfully decreased LDL-C in Group B; nevertheless, inflammatory markers (IL-6 and CRP) persisted, suggesting continued cardiovascular risk. Throughout the trial, Group- B HDL-C levels showed a little improvement but stayed lower than those of Group A.

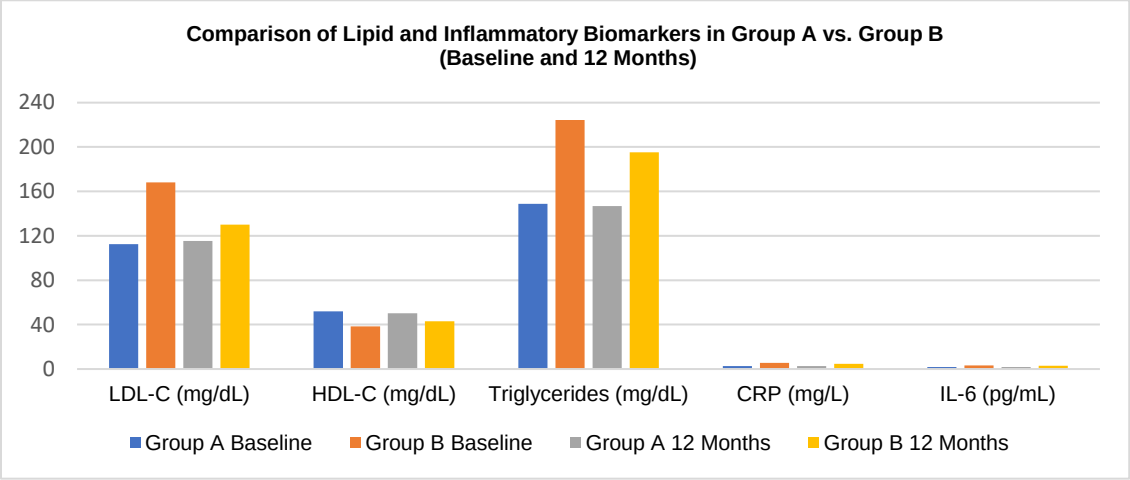

Fig-1: Comparative analysis of biomarker levels between Group A (normal lipid profile) and Group B (dyslipidemia) at baseline and after 12 months.

The MANOVA findings indicated that the levels of LDL-C and CRP were the most significant predictors of cardiac problems, with a respective Wilks' Lambda of 0.689 ($F=10.21$, $p<0.01$) for CRP and 0.712 ($F=8.92$, $p<0.01$) for LDL-C. Triglycerides did not significantly correlate with cardiac problems ($p=0.06$), whereas HDL-C did have a significant role in predicting complications (Wilks' Lambda = 0.853, $F=6.34$, $p<0.05$). The results of the Pearson correlation analysis showed that there was a negative association ($r=-0.49$, $p<0.05$) between HDL-C and cardiac events, but a high positive correlation ($r=0.62$, $p<0.01$) between increased CRP levels and cardiac problems and LDL-C levels and cardiovascular events.

DISCUSSION

The results of present study suggests that lipid profile and inflammatory markers are significant factors in determining the cardiac risk. In patients with dyslipidaemia, raised LDL-C levels, reduced HDL-C with high CRP levels were the main risk factors for adverse cardiovascular events[9]. However, the fact that CRP and IL-6 remained elevated in Group B after statin therapy points towards the fact that simple reduction of LDL-C may not be enough to reduce the cardiovascular risk in high-risk patients[10]. The significant direct relationship between CRP levels and cardiac events of the studied subjects = 0. 62, $p < 0.01$ indicates the role of inflammation in the development of cardiovascular disease[11, 12]. Patients with high CRP and IL-6 levels, even if they managed to achieve a very low level of LDL-C, were still at a higher risk of myocardial infarction, stroke and heart failure. This draws attention to the fact that focusing on lipid levels as a means of managing cardiovascular risk could be a problem[13, 14].

The continued protective role of the HDL-C was also confirmed with this study, the HDL-C levels were found to have an inverse relationship with Cardiac complications (r=-0. 49 p<0. 05)[15]. This has a implication on the fact that, in patients with dyslipidemia, it is not only important to reduce the levels of LDL-C but also to enhance the levels of HDL-C to better the cardiovascular prognosis. The small improvement in the HDL-C levels in Group B, despite statin therapy, may indicate that, in some cases, other treatment approaches including life-style modification and drugs that raise the level of HDL-C may be required[16, 17]. The weak correlation between triglycerides and other cardiac events (p= 0. 06) may point to the fact that though triglycerides are raised in dyslipidemic patients, they are not as potent a risk factor as LDL-C or HDL-C[18]. Nonetheless, it is naive to ignore the role of triglycerides in cardiovascular risk, especially in patients with metabolic syndrome or diabetes, in whom increased triglycerides are quite common[19, 20]. In present study despite a modest reduction in LDL-C following statin medication (mean reduction of 38.1 mg/dL, p<0.001), patients in Group B reported considerably higher cardiac problems. Even in individuals whose lipid profiles have improved, inflammation may still be a contributing factor to cardiovascular risk, as seen by the continuous rise of inflammatory markers like CRP and IL-6. By comparison, Group A experienced a much lower incidence of cardiac events (10%) than Group B (28%), while having normal lipid profiles and lower levels of inflammatory markers.This study supports the concept that in the management of cardiovascular risk, the reduction of lipid levels should be supplemented with the use of anti-inflammatory drugs. This is because despite the fact that statins have been known to reduce LDL-C, other therapies that are anti-inflammatory or life change programs may be needed for further reduction of the cardiovascular risk in patients with high inflammatory markers[21, 22].

CONCLUSION

The findings of current study proved that lipid profile and inflammatory biomarkers were significant predictors of the prognosis of cardiac complications. High LDL-C and decreased HDL-C levels and increased fibrinogen and CRP were found to be the most important risk factors of adverse cardiovascular outcomes. Indeed, despite the successful cholesterol-lowering impact of statin therapy, inflammation remained a considerable threat to dyslipidaemia patients, evidenced by the elevated levels of CRP and IL-6.

Conflict of interest:

The authors declared no conflict of interest for the publication of current study.

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Nill recived.

Authors' Contributions

H.C. and A.W. contributed to the study's design, analysis and data collection, M.A.H. and S.K.S.G. assisted with statistical analysis and manuscript drafting. M.M. and M.Z.R. studied the project, revised the submitted manuscript, and provided the final approval. All the authors agreed on publishing the submitted article.

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Data Availability:

The datasets generated and analyzed during the current study are available from the corresponding author, upon reasonable request

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