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Relationship between Lipid and Apolipoprotein Levels and Coronary Artery Disease Severity: Insights from a Tertiary Care Setting

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ABSTRACT

Background: Dyslipidemia is a major risk factor for coronary artery disease (CAD). Apolipoprotein B over apolipoprotein A1 (apoB/apoA1) ratio is a significant marker for CAD risk than traditional lipid values. Likewise, total cholesterol over high-density lipoprotein (TC/HDL) ratio and other metabolic syndrome components have a strong association with CAD.
Objectives: To compare lipid and apolipoprotein abnormalities in patients with single-, double- and triple-vessel CAD
Methods: The comparative cross-sectional study conducted at a tertiary care hospital in Lahore Pakistan included 300 CAD patients and categorized into three groups based on the number of affected vessels. Another 100 normal healthy volunteers were included in control group. Demographic and clinical data were collected using a structured questionnaire. Blood specimens collected from all patients and controls analyzed for serum lipid and apolipoprotein levels. Analysis of variance was used to compare the means of lipid parameters between groups.
Results: Mean age was 48.52±7.68 years. Total cholesterol, triglycerides and TC/HDL ratio were highest in double-vessel group, while apoB, LDL/HDL ratio was highest in triple-vessel group. Systolic and diastolic blood pressure and body mass index were also significantly different in patients with single-, double- and triple-vessel CAD ($p < 0.001$). Compared to the control group, significantly higher mean levels of apoB and lower levels of apoA1 were found in CAD patients ($p < 0.001$).
Conclusion: Serum lipid levels varied significantly between the four groups. Triglycerides and HDL2/HDL3 ratio were different between single- and double-vessel CAD, as well as single- and triple-vessel CAD groups.

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Introduction

Cardiovascular diseases (CVDs) are becoming more prevalent, posing a significant public health challenge and causing more fatalities than any other condition worldwide [1]. The incidence of coronary artery disease (CAD) is notably higher in South Asians, with some studies indicating that rates in the Indian subcontinent are comparable to those in industrialized nations [2]. Pakistan, located in South Asia, has a population of 240 million [3][4], and surveys show a very high prevalence of CVD risk factors, affecting over 30% of individuals over the age of 45 [5]. The Pakistani population faces a high risk of diabetes and coronary heart disease, with common risk factors for both conditions appearing at

younger ages [6][7]. Atherosclerosis is the primary cause of these diseases, and various risk factors have been identified that contribute to the early development of atherosclerosis [8][9].

Dyslipidemia and abnormalities in lipoprotein levels are major risk factors for CAD. In addition to traditional lipid markers, apolipoprotein B (apo-B) and apolipoprotein A1 (apo-A1), the main surface proteins of LDL and HDL, are recognized as independent risk factors for CAD. Several studies have emphasized that the apoB/apoA1 ratio provides more valuable information for CAD risk assessment than traditional lipid measures like LDL-C/HDL-C or total cholesterol. The TC/HDL ratio and HDL levels have also shown a strong correlation with CAD, which is part of the metabolic syndrome, with other components of the syndrome also strongly associated with CAD in this study [2][3][4].

The objective of this study was to assess and compare the abnormalities in traditional lipid profiles, as well as serum apolipoprotein A1, apolipoprotein B, and various lipid ratio parameters, in patients with single, double, and triple-vessel CAD.

Methods

The comparative cross-sectional study conducted at a tertiary care hospital in Lahore Pakistan. In this study, 300 male patients aged 35-65 years with angiographically confirmed CAD were included. The coronary angiography procedure was performed using the right femoral artery approach with a Judkins catheter. This allowed for the assessment of the severity of the disease in the coronary vessels. The control group consisted of 100 age-matched healthy subjects, free from medical conditions like hypertension and diabetes mellitus. These individuals had no evidence of CVD, making them suitable for comparison against the CAD patients.

Data collection included detailed information on various anthropometric, demographic, clinical, and biochemical parameters, which were gathered using a structured questionnaire. Blood samples were obtained from both the cases and controls for laboratory analysis. Total cholesterol, triglycerides, apoA1 and apoB were measured using commercially available kits. HDL cholesterol levels were determined in supernatants after precipitation with magnesium chloride-phosphotungstate reagent, and LDL-C concentrations were calculated using the Friedewald equation.

Data analysis was conducted using the Statistical Package for Social Sciences version 25. Descriptive statistics, including mean ± standard deviation (SD) and percentages, were used to summarize the demographic and cardiovascular risk factors for both cases and controls. The mean values of various lipid parameters among the four groups (control, single-vessel, double-vessel, and triple-vessel disease) were compared using Analysis of variance (ANOVA). Pairwise comparisons of the lipid parameters between the groups were conducted using Tukey's Post Hoc test. A p-value of ≤ 0.05 was considered statistically significant for all comparisons.

Table 1: Demographic and cardiovascular risk factor of cases and control

Parameters	Single-vessel CAD (n= 100)	Double-vessel CAD (n= 100)	Triple-vessel CAD (n= 100)	Control (n= 100)
Age (years)	46.8±7.33	50.38 ± 6.75	52.10 ± 6.97	44.8 +9.67
BMI (Kg/m2)	24.08± 2.93	24.08± 2.85	24.08± 2.85	20.94±2.50
Systolic BP (mm/Hg)	126.95±9.66	125.65±9.81	153.25±28.15	125.85±6.20
Diastolic BP (mm/Hg)	85.45 ± 6.08	83.85± 6.23	64.65± 6.37	82.62 ± 3.51
Urban residence	76%	82%	89%	100%
Family history of CVD	87%	78%	65%	14%
Exercise (yes)	42%	46%	32%	20%
Fatty diet (yes)	90%	20%	55%	13%

*Various demographic and cardiovascular risk factors for single, double, triple-vessel CAD with control group are significant with p-value <0.001.

Table 2: Comparison of mean values for lipid profiles among four groups

Parameter	Single-vessel CAD (n= 100)	Double-vessel CAD (n= 100)	Triple-vessel CAD (n= 100)	Control (n= 100)	p-value
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Total cholesterol	241.05 (16.99)	251.22 (16.05)	232.07 (12.43)	214.25 (22.25)	< 0.001
Triglycerides	157.52 (11.03)	167.19 (7.20)	154.87 (7.34)	135.14 (27.19)	< 0.001
LDL-C	163.73 (10.89)	173.58 (11.73)	179.96 (5.27)	126.50 (22.35)	< 0.001
HDL-C	36.80 (3.74)	32.44 (2.20)	30.81 (2.43)	51.10 (3.00)	< 0.001
HDL-C2	9.77 (2.71)	8.90 (1.18)	7.00 (1.65)	19.93 (2.39)	< 0.001
HDL-C3	37.11 (2.96)	35.25 (6.00)	33.90 (2.40)	31.07 (3.23)	< 0.001
TC/ HDL ratio	6.64 (1.00)	7.78 (0.77)	7.58 (0.73)	4.21 (0.56)	< 0.001
HDLC2/ HDLC3 ratio	0.27 (0.08)	0.26 (0.07)	0.21 (0.05)	0.65 (0.11)	< 0.001
LDL/ HDL ratio	4.50 (0.56)	5.37 (0.51)	5.88 (0.49)	2.49 (0.50)	< 0.001
APOA1	96.00 (6.35)	90.73 (6.74)	87.29 (5.97)	132.32 (13.75)	< 0.001
APOB	157.55 (10.07)	162.99 (10.74)	172.25 (14.21)	92.01 (16.81)	< 0.001

Table 3: Pairwise comparison among four groups for various parameters representing lipid profiles of the patients

Group (I) vs Group (J)		APOA	APOB	TC	TG	HDL-C	HDL-C2	HDL-C3	LDLC	TC/HDL ratio	HDL2 /HDL3 ratio	LDL/HDL ratio	APOB/ APOA1 ratio
A	B	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	C	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	D	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
B	C	< 0.001	0.020	< 0.001	< 0.001	< 0.001	0.016	0.005	< 0.001	< 0.001	0.996	< 0.001	< 0.001
	D	< 0.001	< 0.001	0.002	0.624	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
C	D	0.031	< 0.001	< 0.001	< 0.001	0.001	< 0.001	0.070	0.007	0.256	< 0.001	< 0.001	< 0.001

A: Control group **B:** Single-vessel disease group **C:** Double-vessel disease group **D:** Triple-vessel disease group

Results

A total of 400 male subjects, with a mean age of 48.52±7.68 years were selected to compare lipid and apolipoprotein abnormalities in patients with single, double, and triple-vessel CAD at a tertiary care hospital in Lahore. The average age in the triple-vessel group was 52.10±6.97, which was higher than that in the other groups. Systolic blood pressure was highest in the triple-vessel CAD group at 153.25±28.15, followed by the single-vessel group at 126.95±9.66. Most subjects in the single-vessel group (87%) had a family history of CVD, and 90% of them followed a fatty diet, compared to 55% in triple-vessel group (Table 1).

ANOVA was used to compare the mean lipid parameter values among the four groups (single-vessel, double-vessel, triple-vessel, and control). The results showed significant differences in the lipid parameters between the groups, with a p-value of <0.001 (Table 2).

The control group had significantly higher serum levels of ApoA1, HDL-C, HDL2, and the HDL2/HDL3 ratio compared to the disease groups, while HDL3 levels were higher in the single-vessel group. The table also shows that cholesterol, triglycerides, and TC/HDL ratios were

highest in the double-vessel group, while Apo-B, LDL-C, and the HDL-C ratio were highest in the triple-vessel group. Tukey's post hoc test was used for pairwise comparisons of the mean lipid levels among the four groups.

The results indicated significant differences in serum lipid levels between the groups, with triglycerides and HDL2/HDL3 ratios differing between the single vs triple and single vs double-vessel groups. However, no significant difference was found in the HDL3 and TC/HDL ratios between the double and triple-vessel groups (Table 3).

Discussion

Lipid abnormalities have long been considered a contributor to atherosclerosis; numerous studies have confirmed a strong association between total cholesterol, LDL-cholesterol (LDL-C), or low HDL-cholesterol (HDL-C) and the development of atherosclerosis-related diseases, such as ischemic heart disease, stroke, and peripheral vascular disease [10].

Several risk factors for CAD, including age, male sex, smoking, the presence of diabetes, hypertension, obesity, high LDL-C [11] and low HDL-C [12] are well-established. The findings of the present study support previously reported associations between these socio-demographic and biochemical risk factors with CAD. Numerous studies have reported changes in the serum lipid profiles of patients at risk for, or suffering from, CAD. Tarchalski et al. observed that the degree of coronary atherosclerosis is positively correlated with proatherogenic lipids, such as total cholesterol, LDL-C, and triglycerides (TG), while being negatively correlated with HDL-C [13]. März et al. suggested that LDL-TG may better reflect the atherogenic potential of LDL than LDL-C itself [14]. Subsequent research has focused on the impact of ratios of these lipid parameters compared to absolute values. Fernandez et al. demonstrated that TC/HDL ratio is a more sensitive and specific indicator than total cholesterol, TG, or HDL-C levels alone [15].

A study from Bangladesh examined the serum lipid profile in patients with acute coronary syndrome, finding that the HDL-C to total cholesterol ratio was significantly lower in patients with single, double, and triple-vessel disease compared to those without CAD. Additionally, the serum concentration of triglycerides was significantly higher in patients with single, double, and triple-vessel disease than in controls [16]. In contrast, our study found significantly higher serum levels of ApoA1, HDL-C, HDL2, and the HDL2/HDL3 ratio in the control group compared to the CAD groups, with HDL3 levels higher in the single-vessel group. Furthermore, cholesterol, triglycerides, and TC/HDL mean levels were higher in the double-vessel group, while serum Apo-B, LDL-C, and the HDL-C ratio were higher in the triple-vessel group.

In a large case-control study, abnormal plasma lipoproteins were shown to be a major risk factor for CAD. The apoB/apoA1 ratio was identified as the only variable that distinguished CAD patients from those without the disease and provided additional information beyond traditional lipid risk factors in low-risk populations [17]. Low levels of HDL-C have been reported to increase the risk of coronary heart disease (CHD), even when total cholesterol is not elevated [18]. Present study found that HDL-C levels were lower in CAD patients compared to controls. Additionally, high levels of total cholesterol and LDL-C were observed in patients, with an increased LDL/HDL ratio when compared to controls.

Authors' contributions

ICMJE criteria	Details	Author(s)
1. Substantial contributions	Conception, OR Design of the work, OR Data acquisition, analysis, or interpretation	1,2 1,2 3,4
2. Drafting or reviewing	Draft the work, OR Review critically for important intellectual content	2,3 1,4
3. Final approval	Approve the version to be published	1,2,3,4
4. Accountable	Agree to be accountable for all aspects of the work	1,2,3,4

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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