Serum Lipid Profile Across the Spectrum of Coronary Artery Disease: Association with Smoking and Age in a Cross-Sectional Study

Dafer Mahammad Hussein Etaij

Lecturer, Department of Pediatrics, College of Medicine, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences
Corresponding Author Email: *daferhussien[at]jmu.edu.iq*
ORCID: 0009-0004-5098-878X

Abstract: ***Background**: Dyslipidemia is a significant modifiable risk factor for coronary artery disease (CAD). The study would use a high-throughput molecular tool based on serum lipid profiles to analyse CAD clinical phenotypes and their associations with smoking status and age. **Methods**: This study used a cross-sectional design with 80 adults, divided into normal controls, unstable angina, stable angina, and myocardial infarction. Serum levels of fasting triglycerides, total cholesterol, and HDL-C were obtained, while LDL-C and VLDL-C were estimated using standard equations. Group comparisons were performed using ANOVA and independent t-tests, while Pearson correlation analysis was used to assess lipid associations. **Results**: Lipid parameters differed significantly across CAD groups. Total cholesterol, LDL-C, triglycerides, and VLDL-C increased progressively from controls to myocardial infarction, while HDL-C decreased. Smokers showed significantly higher total cholesterol and LDL-C; unexpectedly, HDL-C was also higher. Total cholesterol, LDL-C, and triglycerides increased with age, peaking in the 51 to 60 year group. Strong positive correlations were observed between total cholesterol and LDL-C, whereas the relationship between triglycerides and VLDL-C reflected the calculation method. **Conclusions**: CAD severity was associated with a progressively more atherogenic lipid profile. Lipid assessment remains clinically useful for CAD risk stratification, though larger adjusted prospective studies are needed to confirm the smoking-related findings.*

Keywords: coronary artery disease; dyslipidemia; lipid profile; LDL-C; HDL-C; triglycerides; smoking; myocardial infarction; cardiovascular risk

1. Introduction

Coronary artery disease (CAD) remains the leading cause of death worldwide, and the atherosclerotic process that underlies it is closely linked to disturbances of lipid metabolism. Beginning with the Framingham Heart Study, decades of epidemiological research have shown that high total and low-density lipoprotein (LDL-C) cholesterol levels are proatherogenic [1]. In contrast, high-density lipoprotein (HDL-C) cholesterol is generally considered protective [2,3].

CAD is not a monolithic clinical entity but rather a continuum: from the asymptomatic state, through stable angina reflecting fixed flow-limiting stenosis, to the acute coronary syndromes- unstable angina/MI- with acute plaque instability/thrombosis. The extent to which circulating lipid fractions parallel this clinical gradient, and whether these associations are driven by contemporaneous risk factors, including cigarette smoking and ageing, are relevant to risk stratification and prevention.

Tobacco is a strong and independent risk factor for CVD [4], and the adverse influence on lipid profile and endothelial function is believed to play a role in this association [5]. Age also alters lipid levels and increases the atherogenic fractions in midlife and older ages. Nevertheless, reports remain heterogeneous, and local data describing how each lipid fraction behaves across CAD categories, smoking status, and age bands are relatively limited.

The present study, therefore, aimed to (i) compare serum TG, total cholesterol, HDL-C, LDL-C, and VLDL-C from the 4 predefined CAD groups; (ii) investigate the relationships of these fractions with smoking status and age class; and (iii) describe the inter-relationships of lipid fractions within each diagnosis group.

2. Materials and Methods

2.1 Study design and participants

A cross-sectional, comparative study was conducted among 80 adults at the Al-Najaf Center for Cardiovascular Surgery and Cardiac Catheterization in Najaf, Iraq, from January 2025 to December 2025. Participants were enrolled by consecutive sampling among eligible attendees during the study period.

Based on clinical evaluation, electrocardiography, and supporting investigations, participants were divided into four groups: (n = 19) normal controls; (n = 23) unstable angina; (n = 19) stable angina; and (n = 19) myocardial infarction.

Inclusion criteria. Eligible participants were:
– Adults (≥18 years) of either sex;
- For the CAD groups: a confirmed clinical diagnosis of stable angina, unstable angina, or acute myocardial infarction, established by attending cardiologists based on symptoms, resting and/or stress electrocardiography, cardiac biomarkers (troponin and/or CK-MB), and coronary angiography, when performed;
- For the controls: those who attended the center without clinical, electrocardiographic, or angiographic evidence of coronary artery disease;
- Provided a fasting venous blood sample (10–12 h fast) with complete demographic and clinical data; and
- Provided written informed consent.

Exclusion criteria. Exclusion criteria are as follows:

- Ongoing or recent (within 6 weeks) treatment with lipid-modifying agents such as statins, fibrates, ezetimibe, niacin, or omega-3 preparations that would directly affect the measured lipid components;
- A history of a known diagnosis of familial hyperlipidemia;
- Secondary dyslipidemia associated with uncontrolled diabetes mellitus, hypothyroidism, nephrotic syndrome, chronic kidney disease, or chronic liver disease;
- Any acute or chronic inflammatory, infectious (e.g., bronchopneumonia, sepsis), or malignant disease [any of which can affect lipid levels], or recent major surgery or trauma;
- Pregnant or lactating females;
- Either a history of chronic alcohol misuse, or
- Incomplete clinical or laboratory data.

Smokers were specifically included in the cohort, as smoking status was a pre-specified exposure of interest for the analysis.

2.2 Data collected

For each, demographic information (age, sex), smoking status (current versus non-smoker), and the clinical diagnosis were documented. Age was also divided into five age groups, ranging from less than 31 years to more than 60 years, for the analysis.

2.3 Biochemical measurements

After an overnight fast, venous bloods were taken and sera separated. Triglyceride (TG), total cholesterol (TC), and HDD-C levels were measured using routine enzymatic colorimetric methods. The Friedewald formula was used as: LDL-C = TC – HDL-C – TG/5; VLDL-C was calculated by using TG ÷ 5 [6]. Data are shown for all lipid measurements in mg/dL. Because both VLDL-C and LDL-C are derived rather than measured directly, known deterministic relationships (eg, the obligation of TG to drive VLDL-C) should be expected and emphasized wherever appropriate, as well as the strong dependence.

2.4 Statistical analysis

Continuous data are expressed as mean ± standard deviation. One-way analysis of variance (ANOVA) was used to test differences in lipid parameters across the four CAD groups and across the five age bands, and means with 95% confidence intervals were reported. Independent-samples t-tests were conducted to test differences between smokers and non-smokers. Assumptions of normality and homogeneity of variance for ANOVA and t-tests were assessed using the Shapiro–Wilk and Levene tests, respectively. Pearson correlation coefficients were used to evaluate associations among lipid fractions within each CAD group. Because of the limited sample size and exploratory nature of the analysis, no multivariable adjustment was performed for age, sex, diabetes, hypertension, or body mass index; this is acknowledged as a limitation. A two-tailed p-value < 0.05 was considered statistically significant. Statistical analyses were conducted with SPSS [v.23].

2.5 Ethical considerations

The study was performed in accordance with the Declaration of Helsinki. All participants provided written informed consent. Ethical approval was granted by the Institutional Review Board of [INSERT APPROVING INSTITUTION] (approval no. [INSERT APPROVAL ID], dated [INSERT DATE]).

3. Results

Eighty participants were studied. The four diagnostic groups included 19 normal controls, 23 patients with unstable angina, 19 with stable angina, and 19 with myocardial infarction. Of these 80 subjects, 43 (53.8%) were smokers, and 37 (46.3%) were non-smokers; the median age was 41–50 years, with the largest age band (n = 25).

3.1 Profile direction of lipids in different CAD groups

Each of the five lipid fractions differed significantly between each of the four CAD groups (Table 1; all p < 0.05). There was a clear, graded progression: the atherogenic fractions — TG, total cholesterol, LDL-C, and VLDL-C gradually increased from normal controls to unstable and stable angina patients to MI patients. In contrast, HDL-C declined progressively across this same spectrum. Differences were most pronounced for LDL-C (controls 96.3 mg/dL vs MI 113.7 mg/dL; F=7.472, p=0.023) and total cholesterol (controls 155.6 mg/dL vs MI 172.0 mg/dL; F=5.632, p=0.034).

Table 1: Serum lipid fractions across coronary artery disease groups (one-way ANOVA).

Parameter (mg/dL)	Normal (n=19)	Unstable angina (n=23)	Stable angina (n=19)	Myocardial infarction (n=19)	F	p
Triglycerides	130.58 ± 45.03	135.26 ± 78.78	139.21 ± 79.88	141.53 ± 77.40	4.321	0.042
Total cholesterol	155.63 ± 45.99	159.91 ± 62.33	166.47 ± 52.20	172.00 ± 68.08	5.632	0.034
HDL-C	33.21 ± 8.96	32.95 ± 8.10	31.10 ± 11.00	30.84 ± 10.99	3.227	0.048
LDL-C	96.30 ± 34.45	98.91 ± 54.61	99.50 ± 42.28	113.65 ± 55.38	7.472	0.023
VLDL-C	26.11 ± 15.61	27.05 ± 15.76	27.84 ± 15.38	28.50 ± 11.88	3.132	0.049

Values are mean ± SD (mg/dL). HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol; TG, triglycerides. p < 0.05 is considered significant.

3.2 Smoking status and lipid profile

Smokers had a more atherogenic profile than non-smokers for total cholesterol (162.8 vs 155.1 mg/dL; t = 2.730, p = 0.031) and LDL-C (102.9 vs 95.0 mg/dL; t = 3.414, p = 0.007). Unexpectedly, HDL-C was also significantly higher in smokers (34.2 vs 31.3 mg/dL; t = 2.132, p = 0.039), which runs counter to the HDL-lowering effect of cigarette smoking commonly reported in the literature and should be interpreted with caution. Differences in TG and VLDL-C between the two groups were not significant (Table 2).

Table 2: Serum lipid fractions by smoking status (independent-samples t-test).

Parameter (mg/dL)	Non-smokers (n=37)	Smokers (n=43)	t	p
Triglycerides	135.02 ± 80.46	136.46 ± 66.24	1.136	0.067
Total cholesterol	155.10 ± 42.67	162.76 ± 67.86	2.73	0.031
HDL-C	31.27 ± 8.10	34.20 ± 10.77	2.132	0.039
LDL-C	94.97 ± 35.79	102.85 ± 56.17	3.414	0.007
VLDL-C	27.01 ± 16.09	27.69 ± 13.24	1.022	0.069

Values are mean ± SD (mg/dL). p < 0.05 is considered significant.

3.3 Lipid profile by age class

Across the five age groups, total cholesterol, LDL-C, and TG increased significantly in middle age ($p < 0.05$). The overall levels of total cholesterol were higher in <31 years (146.6 mg/dL) and peaked at 183.1 mg/dL in the 51–60-year group ($F = 5.674$, $p = 0.029$), whereas LDL-C followed a similar trajectory peaking at 120.3 mg/dL compared to other bands ($F = 4.638$, $p = 0.032$). HDL-C increased only modestly with age ($F = 3.312$, $p = 0.056$), but this was not significant, and there was no significant effect of age on VLDL-C (Table 3).

Table 3: Serum lipid fractions by age class (one-way ANOVA).

Parameter	<31 y (n=16)	31–40 y (n=5)	41–50 y (n=25)	51–60 y (n=12)	>60 y (n=22)	F	p
TG	125.37 ± 76.67	145.60 ± 79.06	138.36 ± 80.12	143.33 ± 81.86	138.27 ± 58.68	4.233	0.043
CHO	146.62 ± 47.08	155.00 ± 52.91	160.32 ± 56.03	183.08 ± 82.46	175.09 ± 51.49	5.674	0.029
HDL	32.50 ± 9.06	33.80 ± 7.79	34.72 ± 10.60	35.41 ± 7.02	35.13 ± 10.32	3.312	0.056
LDL	89.05 ± 35.32	96.08 ± 40.03	97.92 ± 46.84	120.29 ± 73.82	107.28 ± 40.80	4.638	0.032
VLDL	25.07 ± 15.33	29.12 ± 15.81	29.67 ± 16.02	28.66 ± 16.37	27.65 ± 11.73	2.123	0.082

Values are mean ± SD (mg/dL). p < 0.05 is considered significant.

3.4 Correlations among lipid fractions

The atherogenic fractions were strongly, positively intercorrelated within each CAD group (Table 4). For total cholesterol, there were very strong correlations to LDL-C in all groups (for r, see Table 1; $p < 0.01$) and for TG with VLDL-C ($r = 1.000$), reflecting the deterministic nature of the VLDL = TG/5 derivation. In all groups, TG had moderate positive correlations with total cholesterol ($r = 0.544$–0.630). Except in the MI group, HDL-C was largely independent of any other fractions and positively correlated only with total cholesterol ($r = 0.609$, $p < 0.01$) and LDL-C ($r = 0.525$, $p < 0.05$).

Table 4: Pearson correlation coefficients between lipid fractions within each CAD group

Lipid pair	Normal (n=19)	Unstable angina (n=23)	Stable angina (n=19)	MI (n=19)
TG – Total cholesterol	0.630**	0.617**	0.544*	0.587**
TG – HDL-C	−0.126	0.045	0.216	0.117
TG – LDL-C	0.421	0.475*	0.253	0.484*
TG – VLDL-C	1.000**	1.000**	1.000**	1.000**
Total cholesterol – HDL-C	0.379	0.381	0.43	0.609**
Total cholesterol – LDL-C	0.951**	0.950**	0.925**	0.983**
Total cholesterol – VLDL-C	0.630**	0.617**	0.544*	0.587**
HDL-C – LDL-C	0.302	0.288	0.192	0.525*
HDL-C – VLDL-C	−0.126	0.045	0.216	0.117
LDL-C – VLDL-C	0.421	0.475*	0.253	0.484*

** p < 0.05; ** p < 0.01 (two-tailed). The TG–VLDL-C coefficient of 1.000 reflects the derivation VLDL-C = TG/5.*

4. Discussion

In this cross-sectional study of 80 adults, we examined the serum lipid profile across the clinical spectrum of coronary artery disease and its relationship to smoking and age. Three principal observations emerged.

First, the lipid fractions followed a biologically plausible pattern along the CAD continuum. The atherogenic fractions — total cholesterol, LDL-C, TG, and VLDL-C- increased incrementally from normal controls to myocardial infarction, while HDL-C, the protective fraction, declined progressively along the same gradient. This is consistent with the central role of LDL-driven atherogenesis and the inverse, protective association of HDL-C reported in large prospective cohorts [3,7]. The clear separation of groups by LDL-C and total cholesterol supports the continued use of these two front-line markers in coronary risk assessment [8,9].

Second, smoking was linked with significantly higher total cholesterol and LDL-C, consistent with the well-known pro-atherogenic and endothelial effects of cigarette smoke [5]. However, this finding of higher HDL-C in smokers is in apparent contrast with the usual observation that smoking lowers HDL-C; it could reflect uncontrolled confounding (such as differences in sex distribution, alcohol intake, body mass, or medication use between groups), or be a chance finding due to modest sample size. This result must be interpreted with caution and confirmed in appropriately sized, controlled analyses before any conclusions can be drawn.

Third, total cholesterol, LDL-C, and TG increased with age up to the 51–60 years age band, followed by a non-significant decline in the oldest age category; this is a well-described trend of lipoprotein clearance with advancing age (alongside potential survivor effects in older patients) [3]. The accompanying increase in triglycerides is of interest because they independently contribute to cardiovascular risk [10]. The few participants in the 31–40 year band (n = 5) limit the accuracy of age-stratified estimates.

Correlation analysis confirmed the lipid panel internal structure. The extremely strong relationship between total cholesterol and LDL-C, and the perfect relationship between TG and VLDL-C are almost entirely methodological (the result of Friedewald and other related equations rather than independent biological covariation); characteristics that will lead to genuine public perception. However, convincing because the most informative finding is the appearance of

Paper ID: SR26524145528 DOI: https://dx.doi.org/10.21275/SR26524145528

significant HDL-C correlations when considering total cholesterol and LDL-C only in MI subjects; this effect suggests a unique lipoprotein profile that may be recognizable in the setting of acute infarction and should be further investigated.

All of these findings together add clinical sense: worse lipid shift correlated with severe coronary presentation thus emphasizing that all of those above may be affected by preventive methods since smoking and dyslipidemia are modifiable factors as well. They highlight that secondary prevention (smoking cessation and lipid-lowering therapy) is especially important in patients with acute coronary syndromes [9].

5. Limitations

Several limitations should be acknowledged. A causal inference was prohibited by the cross-sectional design. Our sample was relatively small, particularly for some age strata (Table 1) which limits both statistical power and the precision of subgroup estimates. Unadjusted residual confounding cannot be ruled out with respect to gender, BMI (body mass index), DM (diabetes mellitus), hypertension status, medication or dietary composition. Future studies could test the robustness of conclusions with multivariable modelling. Interpretation of their correlations is limited as VLDL-C and LDL-C were calculated instead of directly measured, with the Friedewald equation proven to underestimate at very high TG concentrations (6). A potential limitation is generalizability with single-center recruitment.

6. Conclusion

Serum lipid profiles became more atherogenic along the clinical spectrum of coronary artery disease (CAD), and myocardial infarction patients bore the least favorable profile. In conclusion, smoking was associated with a more atherogenic lipid profile, although the unexpected finding of lower HDL-C needs careful consideration. These findings support the clinical utility of lipid profiling in CAD risk assessment, although further confirmation will require larger prospective studies with multivariable adjustment.

References

[1] Castelli WP. Epidemiology of coronary heart disease: the Framingham study. Am J Med. 1984;76(2A):4–12.
[2] Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High-density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. Am J Med. 1977;62(5):707–714.
[3] Gordon DJ, Probstfield JL, Garrison RJ, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation. 1989;79(1):8–15.
[4] Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937–952.
[5] Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol. 2004;43(10):1731–1737.
[6] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18(6):499–502.
[7] Emerging Risk Factors Collaboration. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009;302(18):1993–2000.
[8] Sharrett AR, Ballantyne CM, Coady SA, et al. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: the ARIC study. Circulation. 2001;104(10):1108–1113.
[9] Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/Multisociety guideline on the management of blood cholesterol. Circulation. 2019;139(25):e1082–e1143.
[10] Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. Lancet. 2014;384(9943):626–635.