

Plasma Lipid Profile and Apolipoproteins in Patients with Coronary Artery Diseases and Healthy Persons, in Sana'a City, Yemen

Abstract:

Background: Cardiovascular disease (CVD) is the primary cause of all disease loads and accounts for almost half of all fatalities. The early detection of coronary artery disease (CAD) has drawn a lot of attention because it is anticipated that the global burden of cardiovascular disease will rise by almost 75% by 2020. They are easily oxidized, which causes an increase in affinity for arterial proteoglycans and a decrease in affinity for LDL receptors. It demonstrates significant CAD importance. **Objective:** the measurement of plasma lipid profiles and apolipoproteins (ApoA-1, ApoB, and Apo B/A-1 ratio) in healthy individuals and patients suffering from coronary artery disease. **Methods:** In this cross-sectional comparative study, 90 Yemeni subjects aged 45 to 70 years were divided into three groups: Group I: 30 cases as CAD positive (CAD+). Group II: 30 cases CAD negative (CAD -). Group III: 30 healthy person was as control. A standardized questionnaire was administered to collect demographic and clinical data from participants. Venous blood (10 ml) was collected from each individual and divided into two portions. The first portion was 5 ml in plain tubes, ApoA-1 and Apo B vacuum tubes for freezing at -20°C until analysis. 5ml in a plain tube for measuring fasting blood glucose, and lipid profile. **Results:** ApoB and Apo B/A ratios were significantly higher in CAD+ and CAD- subjects compared to controls. In addition, ApoB and Apo B/A ratios were significantly higher in CAD+ subjects compared to CAD- subjects. (P .value=0.002). In contrast, Apo A-1 was significant in CAD+ compared to CAD- and controls, and not significantly different between CAD and controls (P .value=(0.001, 0.032). Furthermore, FBS and LDL-c were significantly higher in CAD+ compared to CAD subjects (P value=0.05). In contrast, HDL-c was significantly lower in CAD+ compared to CAD and controls, with no significant difference between CAD and controls (P value=0.038, 0.004, 0.70).

However, TG was not substantially different between CAD- and controls, but it was significantly greater in CAD+ compared to controls ($P.value=0.002, 0.09, 0.31$). Nevertheless, there was no difference in TC between study groups ($P.value = 0.08, 0.12, 0.98$). **Conclusions:** The degree of CAD is significantly positively correlated with WHR. More important than overall obesity, abdominal obesity is a risk factor for coronary heart disease (CHD). A significant positive connection has been observed between the Apo B/Apo A ratio and CAD. One thing to think about as a CAD risk factor is Apo B.

Keywords: Apolipoprotein, LDL, Cardiovascular disease, Yemen.

Introduction:

“Cardiovascular disease (CVD) is responsible for nearly 50% of all deaths and is the leading cause of all disease burdens in Europe”[1]. “Much attention has been focused on the early prediction of coronary artery disease (CAD), as it was well-predicted that the global burden of cardiovascular disease would increase by almost 75% by 2020”[2]. “CAD is also known as ischemic heart disease (IHD)”[3]. “A group of diseases includes stable angina, unstable angina, myocardial infarction, and sudden cardiac death”[4]. “It belongs to the group of cardiovascular diseases and is the most common type among them”[5]. “In 2015, CAD affected 110 million people and killed 8.9 million”[6]. “It is the leading cause of death worldwide, accounting for 15.9% of all deaths. Especially in developed countries, the risk of death from CAD decreased at specific ages between 1980 and 2010”[7]. “It is present in 7% of 45-64-year-olds and 1.3% of 18-45-year-olds, with a higher proportion in men than women at any given age”[8]. “Coronary artery disease has several well-defined risk factors. The most common risk factors include smoking, family history, hypertension, obesity, diabetes, physical inactivity, stress, and elevated blood lipid levels”[9]. “Smoking is associated with approximately 36% of cases and obesity with 20%”[10]. “Although some people have a genetic predisposition to develop atherosclerosis, it appears that most people can develop the disease, dietary fats, especially cholesterol, that are carried in the

blood. High levels of LDL cholesterol in the blood can cause and exacerbate atherosclerosis. Other factors that contribute to atherosclerosis include smoking, hypertension, type 2 diabetes, age, sex, sedentary lifestyle, and obesity”[11].“High blood cholesterol levels (especially serum LDL levels). HDL (high-density lipoprotein) has a protective effect against the development of coronary artery disease”[12].“Plasma lipids, particularly cholesterol, and triglycerides have long been implicated in the pathogenesis of coronary artery disease (CAD)”[13,14,15,16,17].“In vivo, water-insoluble cholesterol and other lipids form complexes with proteins (apoproteins) to form lipoproteins for transport and metabolism”[18,19].“Lipoproteins are classified into five main types according to their size and density. These are exogenous and endogenous triglyceride-transporting chylomicrons and very low-density lipoproteins (VLDL). VLDL remnant - intermediate density lipoprotein (IDL). The major cholesterol-transporting low-density lipoprotein (LDL). Hypothesized tissue cholesterol-scavenging high-density lipoprotein (HDL). Most epidemiological, experimental, clinical, and genetic studies have emphasized the role of elevated levels of LDL, or cholesterol contained in this lipoprotein fraction (LDL-C), in atherogenesis. Although the relatively high amount of cholesterol in the LDL fraction is generally thought to be an atherogenic factor, cholesterol in LDL in familial hypercholesterolemia or "familial" type 2 disease is associated with early CAD”[17,20,21,22].“Seems to have a causal relationship with From Fredrickson et al. Proposed diagnostic criteria”[23].“Type 2 disease, includes (1) Elevated LDL. (2) Enter 2 for first-degree relatives. Or (3) supple xanthomas. Moreover, these patients show no significant reduction in LDL-C levels on a standardized low-cholesterol diet”[24].“More recently, dysfunction of specific LDL cell receptors was reported by Brown and Goldstein”[25].“Familial type 2 patients. Given accelerated atherosclerosis in patients with well-defined metabolic abnormalities, lowering plasma LDL-C levels using effective therapeutic regimens may slow progression. Most people would agree that familial type 2 patients with CHD can be used to determine whether it is possible to induce regression.

CAD to ameliorate angina, prevent myocardial infarction and reduce death from CAD. Recently, there has been an increasing interest in HDL”[26].“Early observations showed that plasma alpha-lipoprotein (HDL) was lower in post-myocardial infarction patients than in healthy individuals. Suggesting that high HDL is an independent negative risk factor for CHD; epidemiological studies”; [27,28,29].“Clinical correlative studies show that CHD patients with normolipidemic often have low HDL”;[30].“Families with higher HDL levels live longer”[31].“Some experimental data suggest that HDL may facilitate the removal of cholesterol from tissues”[32,33].These observations made on LDL and HDL demonstrate that intracellular cholesterol can be regulated by developing intervention programs that can achieve significant reductions in atherogenic LDL and VLDL fractions. A program that increases the anti-atherosclerotic HDL fraction while reducing LDL and VLDL to normal levels would be highly desirable.

Materials and methods:

Study design:

A hospital-related cross-sectional comparative study.

Study area:

Cardiac Center, Al Thawra and General Military Hospital (Referral Hospital), Sana'a City, Yemen.

Sample size and subjects:

Sample size was 90, which calculated according to Pradeep, *et, al.* 2015.Using Open Epi program with 95% confidence level and mean \pm SD of Apo B of 95.2 ± 74.7 cases and mean \pm SD of controls of 25.3 ± 23.0 and a 2:1 case: control ratio using the Open Epi program. The validity is 80%. This study is a cross-sectional comparative study conducted between March 2018 and January 2019. Subjects were divided into three groups: CAD negative (CAD-) if no occlusion is detected by coronary angiography and healthy controls.

Group I: 30 examples. : CAD positive (CAD+). Group II: 30 cases of CAD negative (CAD -). Group III: 30 A healthy person is a control. Inclusion and exclusion criteria: Subjects were selected for coronary angiography based on one or more of the following criteria: chest pain, shortness of breath, and hypertension. A selected patient is considered CAD(+) if she has ≥ 50 stenosis in at least one of her coronary arteries.

Data collection and processing:

Each participant must complete the questionnaire by providing their age, sex, weight, height, blood pressure, and waist circumference. Waist circumference is measured at the waist, halfway between the iliac crest and the rib arch. Using a tape measure, measure the man's waist at the top of his hipbone. After ten minutes of rest, the systolic and diastolic blood pressure is measured using a mercury sphygmomanometer. Type I or type II diabetes, metabolic syndrome (classified as high triglycerides, low HDL, small high-density LDL, or high non-HDL cholesterol), and smoking. Sample collection and processing: From a fasting patient, he draws 10ml of venous whole blood into a scheduled tube and separates the blood sample in the scheduled tube to obtain the serum. There are two components to the serum. (1) The first part is frozen at -20°C until analysis of ApoA-1 and Apo B. (2) the second part measures fasting blood glucose and lipid profile.

Statistical analysis:

All statistical analyzes were performed by the Social Package of Statistical Science (SPSS) 20.0 (LEAD Technologies; Inc. USA). Missing data were removed list by list. If any variable was missing, the entire observation was removed from the analysis. The significance of all parameters in the three groups was assessed by ANOVA (used to account for anthropometric and biochemical parameters). Except for Apo A, Apo B, and BAR values assessed by univariate analysis (general linear model) and adjusted for age. And BMI as a covariate. Association of Apo A, Apo B, and BAR with risk factors for CAD parameters. (BMI, waist, SBP, DBP, TG, T-C, HDL-c, LDL-c, and FBS (dependent

variables) Correlations of Apo A, Apo B, and Apo B/Apo A-1 ratios across all participants were evaluated by linear regression controlling for age and weight. Were studied by linear regression adjusting for age and weight as covariates for all subjects. Mean differences were considered significant if the *P*.value was less than 0.05.

Results:

Anthropometric parameters by study group, during the analysis, waist, hip, and waist-to-hip ratio (WHR) were significantly higher in CAD⁺ and CAD⁻ subjects compared with controls. Furthermore, waist and hip were significantly higher in CAD⁺ compared to CAD⁻ subjects, and none were significantly higher in WHR. There were no significant differences between CAD and other groups. Nevertheless, there were no differences in age, weight, height, diastolic and systolic blood pressure between the study groups (**Table 1**). Biochemical parameters; fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol between groups. Results showed that FBS and LDL-c were significantly higher in CAD⁺ and CAD⁻ patients compared with controls. Furthermore, FBS and LDL-c were significantly higher in CAD⁺ subjects compared to CAD⁻ subjects. In contrast, HDL-c was significantly lower in CAD⁺ compared to CAD⁻ and controls, with no significant difference between CAD⁺ and controls. On the other hand, TG was significantly higher in CAD⁺ compared to controls, not significantly higher compared to CAD⁻; and not significantly different between CAD⁺ and controls. However, there was no difference in TC between study groups (**Table 2**). Comparison of the ratios of apolipoprotein A-1, apolipoprotein B, and apolipoprotein B/A in all groups. The ratios of apolipoprotein A-1, apolipoprotein B, and apolipoprotein B/A between study groups. In general, ApoB and ApoB/A ratios were significantly higher in CAD⁺ and CAD⁻ subjects compared to controls. In addition, ApoB and ApoB/A ratios were significantly higher in CAD⁺ compared to CAD⁻ subjects. In contrast, Apo A-1 was significantly higher in CAD⁺ compared to CAD⁻ and control groups, with no significant

difference between CAD and control groups (**Table 3**). Associations between ApoA-1, ApoB, and Apo B/A-1 ratios and coronary risk factor parameters. Apo B and Apo B/A-1 ratios were significantly positively correlated with WC, LDL-C, and FBS, and were independent of systolic and diastolic blood pressure. Furthermore, Apo B was significantly positively associated with BMI, HDL-C, TG, and total cholesterol. On the other hand, the Apo B/A-1 ratio was significantly negatively correlated with HDL-C, BMI, TG, and total cholesterol. However, there was no association between ApoA-1 and other parameters (**Table 4**).

The correlation between ApoA-1, ApoB, and Apo B/AI ratio in group studies. The ratios of apolipoprotein A-1, apolipoprotein B, and apolipoprotein B/A among the study groups. In general, the Apo B/A-1 ratio was significantly positively correlated between the Apo B/A-1 ratio and ApoB, and negatively significantly correlated with ApoA-1, whereas ApoB and ApoA-1 were significantly correlated (**Table 5**).

Table-1: Anthropometric parameters of control, negative and positive coronary artery disease.

<i>Parameters</i>	<i>Control</i>	<i>CAD⁻</i>	<i>CAD⁺</i>
Age (years)	56.90 ± 6.283	56.87 ± 7.171	55.87 ± 6.699
<i>P. value</i>		^a 1.0	^a 0.82 , ^b 0.83
Weight (kg)	60.90 ± 4.318	64.63 ± 7.604	64.90 ± 11.678
<i>P. value</i>		^a 0.20	0.16 , 0.99
Height (cm)	161.30 ± 6.396	162.33 ± 5.909	158.57 ± 6.377
<i>P. value</i>		^a 0.79	^a 0.21 , ^b 0.55
Body Mass Index (kgm²)	23.52 ± 2.511	24.62 ± 3.393	25.73 ± 3.796
<i>P. value</i>		^a 0.40	^a 0.028 , ^b 0.39
Waist Circumferences (cm)	79.47 ± 5.015	90.23 ± 7.486	95.03 ± 8.257
<i>P. value</i>		^a 2.0 × 10⁻⁷	^a 5.1 × 10⁻⁹ , ^b 0.027
Hip	78.23 ± 5.263	88.20 ± 7.170	92.50 ± 7.427

<i>P. value</i>		^a 3.6×10⁻⁷	^a 5.1×10⁻⁹, ^b0.039
Waist-to-Hip ratio	1.0134±.00694	1.020±.00643	1.0254±.01312
<i>P. value</i>		^a 0.021	^a 1.0×10⁻⁵, ^b0.069
Diastolic Blood pressure(mmHg)	78.00±6.103	81.33 ±9.371	79.00± 8.449
<i>P. value</i>		^a 0.25	^a 0.88, ^b0.50
Systolic Blood Pressure(mmHg)	118.00±8.052	122.00±12.704	121.33± 12.521
<i>P. value</i>		^a 0.36	^a 0.49, ^b0.97

Table-2: Comparison of fasting blood glucose and lipid profiles of all groups.

<i>Parameters</i>	<i>Control</i>	<i>CAD-</i>	<i>CAD+</i>
Fasting blood glucose (mg/dl)	85.67 ± 8.97	94.97 ± 12.66	104.13 ± 18.45
<i>P. value</i>		^a 0.03	^a 5.0×10⁻¹⁴, ^b0,033
Triglyceride (mg/dl)	96.57 ±14.46	101.33±11.94	108.23 ± 11.22
<i>P. value</i>		^a 0.31	^a 0.002, ^b0.09
Total-Cholesterol (mg/dl)	112.53± 17.260	113.17±16.735	121.47± 13.68
<i>P. value</i>		^a 0.987	^a 0.08, ^b 0.12
High Density Lipoprotein (mg/dl)	41.07±6.64	39.40±8.67	34.17±8.81
<i>P. value</i>		^a 0.70,	^a 0.004, ^b0.038
Low Density Lipoprotein (mg/dl)	59.07±8.00	64.67±9.73	74.80± 9.41
<i>P. value</i>		^a 0.05	^a 1.0×10⁻⁸, ^b1.2×10⁻¹⁶

Table-3: Comparison of apolipoprotein A-1, apolipoprotein B and apolipoprotein B/A ratio among in all groups.

<i>Parameters</i>	<i>control</i>	<i>CAD-</i>	<i>CAD+</i>
ApoA-1 (mg/dl)	101 (96-106)	96 (96-101)	87 (82-92)
<i>P. value</i>		^a 0.146,	^a 0.001, ^b 0.028
ApoB(mg/dl)	76 (70-82)	86 (80-91)	144 (138-150)
<i>P. value</i>		^a 0.032	^a 9.5×10⁻²⁷, ^b 1.3×10⁻²³
ApoB/A-1 ratio	0.72 (0.65-0.70)	0.88 (0.81-0.94)	1.63 (1.56-1.69)
<i>P. value</i>		^a 0.002	^a 3.6×10⁻³¹, ^b 1.5×10⁻²⁶

Table-4: Association of ApoA, ApoB, and ApoB/A-1 ratios with risk factors for coronary parameters in study groups.

risk factors of CAD	ApoA-1 b(P-value)	ApoBb(P-value)	ApoB/A-1 ratio b(P-value)
Body Mass Index (kg/m²)	-0.035 (0.70)	0.07(0.002)	-4.05 (0.02)
Waist circumference (cm)	0.024 (0.25)	0.84(6.4×10⁻⁵)	5.38(5.9×10⁻⁷)
Diastolic Blood Pressure (mmHg)	-0.37 (0.24)	0.26(0.54)	-23.4 (0.51)
Systolic Blood Pressure (mmHg)	-0.13 (0.95)	0.18(0.08)	-11.0 (0.17)
Triglyceride (mg/dl)	-0.18 (0.17)	0.17(0.006)	-5.85(0.005)
HDL- cholesterol (mg/dl)	-0.08 (0.23)	0.04(0.002)	-10.9(0.001)
LDL-cholesterol (mg/dl)	-0.03 (0.04)	0.06(2.4×10⁻⁴)	8.07(4.5×10⁻⁷)
Total - cholesterol(mg/dl)	-0.37 (0.16)	0.29 (0.02)	-17.6 (0.01)
Fasting Blood Sugar (mg/dl)	0.17 (0.61)	0.20(2.6×10⁻⁸)	4.19 (2.4×10⁻²⁰)

Table-5: Correlation of ApoA-1, ApoB, and Apo B/AI ratio in group studies.

Parameters	ApoA-1r(p.value)	ApoB r(p.value)	ApoB/A-1 ratiop(p.value)
ApoA-1 (mg/dl)		-0.100- (0.175)	-0.517(8.6×10⁻⁸)

ApoB(mg/dl)	-0.100- (0.175)		0.883(5.0×10³¹)
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Discussion:

Our study aimed to determine the lipid profiles, ApoB, ApoA-1, and ApoB/A-1 ratios of coronary artery disease and healthy subjects. In the present study, waist, hip, and waist-to-hip ratio (WHR) were significantly higher in CAD+ and CAD- subjects than in controls. Obesity or overweight is known to promote or exacerbate all the atherogenic risk factors that predispose individuals to all types of coronary events. Abdominal fat accumulation as measured by WC or WHR is associated with metabolic and CHD risk, type 2 diabetes mellitus, hypertension, coronary artery disease, and stroke, and is more associated with abdominal obesity than with all-cause obesity as measured using BMI. The current study showed that BMI was significantly higher in CAD+ compared to controls. This is consistent with previous results by Anand Sharma and workmates at 2014 [34]. However, our results are inconsistent with the study reported by Gregory and his colleagues at 2017 [35]. "There was no significant difference between BMI and CAD. This can be explained by the fact that BMI quantifies general obesity. Overweight or obese people may have excess fat, but BMI does not indicate how that fat is distributed throughout the body. However, fat distribution is an important determinant of CAD, independent of BMI and other classical risk factors for CAD" [36]. BMI is the most studied predictor of risk for obesity-related complications. Of note, some people within the normal BMI range may exhibit excessive central fat accumulation and increased metabolic risk, suggesting that central (visceral or intraperitoneal) obesity is more common than peripheral fat distribution is associated with the subsequent development of cardiovascular disease. [34]. "Since the central fat distribution is thought to be more atherogenic than peripheral fat, much attention has been focused on methods that can assess central fat

depots”[34].“Inthecurrent study,FBSwassignificantlyhigherinCAD+and CAD- subjectscomparedto controls, a result consistent with the study reportedbyNarimanMoradiand her colleagues at 2018”[37].In this study,significantlyhigher LDL-c levels were observed inCAD+and CAD- patients comparedto controls.Ourfunding yielded thesameresults as previously described [38].LDLcausesendothelialdysfunction through localinflammationandoxidative stress in the vessel wall, which leads to the attraction of monocytes from the bloodandmacrophages,andLDLinfiltratesthe intima-retained subendothelial space.Atherosclerosis occurs when oxidative LDLphagocytesbymacrophagesform a foamy matrix[39,40].Thepresent study showed that HDL-cwassignificantlylowerinCAD+comparedtoCAD-andnormal subjects. The role of HDLinreversecholesteroltransport is probably mostimportantin reducing plaquedevelopment[41].Inthepresentstudy,weobserved that TGwassignificantlyhigherinCAD+compared with normalsubjects. Our funding mentioned thesameresult done byPechlaner at 2017 with his colleagues[42].TG can represent residual cholesterol levels[43].And the smallerchylomicrons directly increase cholesterol accumulation as they penetrate thearterialwall[44].These residual TRLparticles directly contributetoplaqueformation [45].In this study,no differences inTC were found between study groups. Ourfunding yielded thesameresultsmentionedMashayekhi at2014[46].Inthe current study, ApoB values and ApoB/A ratios were generally significantlyhigherinCAD+and CAD-subjectscompared with controls. Our funding is the same results mentioned by Hem2014[47].ApoBisthe major apolipoproteinofchylomicrons,VLDL,IDL,andLDLparticles[48].Furthermore,highapoB levels indicate increased risk, even though LDL-Cornon-HDL-Clevels typically remain lowin severe atherogenic conditions suchasmetabolicsyndromeandtype2diabetes[49].The Apo B/Apo A-Iratiorepresentsthebalancebetween Apo B-rich and Apo A-I-rich anti-atherogenic particles andis more predictive ofcardiovascularriskthan lipid, lipoprotein,

and lipid ratios [50]. Apolipoproteins may be more informative risk markers than lipoproteins (such as LDL and HDL) [49]. In particular, the ratio of apolipoprotein B to apolipoprotein A-I (apoB/apoA-I) [51,52,53]. In the current study, apoA-I was observed to be significantly higher in CAD+ compared to CAD- and control studies. Apolipoproteins A-I and B/A-I are significantly higher in CAD+ than in CAD-. ApoB and the ApoB/A-I ratio were significantly positively associated with WC, LDL-C, and FBS in a series of studies. Higher values of WC, LDL-C, and FBS were associated with a higher risk in CAD. We demonstrate the importance of the ratio of ApoB to ApoA-I as a predictive marker. The same results are mentioned by Sheriff et al. 2013 and his colleagues [38]. Another finding was a significant positive association between Apo B and BMI, HDL-C, TG, and total cholesterol. The same results are mentioned by (Anand, 2014, Hem, 2014, and Pechlaner, 2017). [34,47,42]. Concentrations of lipid parameters can vary with diet. However, apolipoprotein levels are not affected by diet. Therefore, fasting blood samples are not required for apolipoprotein measurements. HDL cholesterol can lead to misleading results because HDL cholesterol composition can vary in response to different physiological and pathological conditions. Therefore, measuring the protein fraction of HDL, ApoA1, is a better predictor of CAD [54].

Conclusions:

The degree of CAD is significantly positively correlated with WHR. More important than overall obesity, abdominal obesity is a risk factor for coronary heart disease (CHD). A significant positive connection has been observed between the Apo B/Apo A ratio and CAD. One thing to think about as a CAD risk factor is Apo B.

Ethical approval and consent:

Ethical approval for the study was obtained by the Ethics Committee of the Sana'a University School of Medicine and Health Sciences. The written informed consent form was obtained from each guardian of the participant as well as from the subject himself

before recruitment into the study. All protocols in this study were done according to the Declaration of Helsinki (1964).

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