



RISK PREDICTION - APOLIPOPROTEINS IN CORONARY ARTERY DISEASE

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ABSTRACT

Coronary artery disease (CAD) is a major cause of morbidity and mortality in modern society. Known risk factors for coronary artery disease include dyslipidemia, hypertension, obesity, dysglycemia, insulin resistance, inflammation, arterial intimal thickening, development of vulnerable plaque and thrombosis. This study compared lipid parameters in CAD patients with healthy individuals to see the predictive power of lipid parameters. Results show that a significant number of CAD patients have abnormal lipid profile. LDL-Cholesterol and Apo-B were significantly higher in CAD patients compared to healthy controls. HDL-Cholesterol and Apo A-1 were significantly decreased in CAD patients. The ratio of Apo B/Apo A-1 is highly significant in CAD patients. To conclude Apo A-1 and Apo-B are better predictors of CAD risk in general, and Apo- B/Apo A-1 ratio seems to be a more powerful predictor of CAD risk than individual apolipoprotein and it can be measured routinely along with lipid profile in the screening of CAD risk.

KEY WORDS: Atherosclerosis, Coronary artery disease, Apolipoproteins, Risk Predictions, Apo A-1 and Apo – B.



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INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality in modern society. The cost of management of CAD is a significant economic burden and so prevention of CAD is very important step in the management. Prevention of CAD can be approached in many ways including health promotion campaigns, specific protection strategies, life style modification programs, early detection and good control of risk factors.¹ Known risk factors for coronary artery disease include dyslipidemia, hypertension, obesity, dysglycemia, insulin resistance, inflammation, arterial intimal thickening, development of vulnerable plaque and thrombosis. Dyslipidemia includes abnormalities of lipoprotein transport and hyperlipidemia. The definition of dyslipidemia has gradually evolved as a result of advances in the understanding of the underlying mechanism.² Approximately 70% of total cholesterol is in the LDL particles, 20% is in HDL particles and only 10% is in VLDL particles.³ Thus the greatest attention has been directed toward the determinant of LDL and HDL Cholesterol. Lipid lowering trails, as well as experimental studies confirm the importance of LDL-cholesterol as a cause of atherosclerosis in both men and women with or without symptoms of CAD.⁴

Many Indian studies shows a strong positive correlation between serum cholesterol and CAD risk and no threshold has been identified below which lower cholesterol is not associated with a lower risk of CAD. An elevated LDL-cholesterol level is the primary CAD risk factor and higher the total and LDL-cholesterol levels are the greater is the risk of an atherosclerotic event.^{5,6} A low level of HDL-cholesterol is a potent individual predictor for CAD in population having higher cholesterol levels. Thus, low HDL-cholesterol like other independent risk factors promote coronary atherosclerosis, when a high LDL-cholesterol is present.⁷ Hypertriglyceridemia due to VLDL and IDL are (normally VLDL carry most of plasma

triglycerides) atherogenic and are inversely associated with plasma HDL-cholesterol level. These factors explain hypertriglyceridemia as an important risk factor for CAD.⁸ The recognition of an association between deranged lipid transport and development of coronary atherosclerosis has led to a number of studies indicating a positive correlation between coronary artery disease and hyperlipidemia.^{9, 10, 11}

Plasma lipoprotein levels are closely related to arteriosclerosis leading to coronary artery disease. The two major apolipoproteins of HDL are Apo A-I and A-II. Apo B-48 and Apo B-100 are the principal structural apolipoproteins of Chylomicron, and Apo B-100 virtually the only apolipoprotein on LDL.¹² Apo A-I has a role in the activation of Lecithin Cholesterol Acyl Transferase (LCAT) and removal of free cholesterol from extra hepatic tissues. Apo A-II has also a role in catabolism of HDL perhaps by stimulating hepatic lipase. Defects in the structure or in the assembly of Apo-B containing lipoproteins results in the failure of intestinal and hepatogeneous triglyceride rich lipoprotein secretion which results in elevation in Apo-B concentrations leading to atherosclerosis.¹³ Several large multicenter prospective studies^{14,15,16} show the predictive ability of Apo-B in CAD. In Indian prospective there are few studies^{17, 18, 19} to show that measurement of plasma apolipoprotein is better in comparison to conventional lipid parameters in the screening of CAD patients. In this study we compared lipid parameters including apolipoproteins, in CAD patients with healthy individuals to see the predictive power of lipid parameters.

MATERIALS AND METHODS

The patients were selected randomly from the department of Cardiology, Sri Jayadeva Institute Cardiovascular Sciences and Research, Bangalore, who had come for cardiac evaluation. The study group consisted of 242

patients who had undergone coronary angiogram test, of which 117 had normal coronary arteries (control group) and 125 had stenosis (>50%) in one or more major epicardial coronary arteries (patients group). The study was approved from the ethics committee of the Institute and informed consent were obtained from patients.

Biochemical Methods

Blood samples were collected from the subjects after 10 hours of overnight fasting, sera were separated and analyzed for estimation of Cholesterol²⁰ HDL-Cholesterol²¹ LDL- Cholesterol²² and Triglycerides²³ using standard procedure with available reagent kits. Levels of Apolipoproteins A-I and apolipoproteins-B was estimated by the principle of immunoturbidometry method using antigen-antibody reaction.²⁴ All the estimations were done using Hitachi 912 analyzer.

Statistical analysis

All the values calculated as mean \pm standard deviation. The two groups were analyzed by comparing each parameter by students- t test. P values were computed using 'chi square' distribution.

RESULTS

The specific purpose of the study was to assess the predictive power of lipid parameters to discriminate between patients with CAD and those without CAD. Methods used to measure risk factors are standard established procedures. The basic characteristics of the CAD patients and controls were given in table 1. Results show risk factors like age, sex, hypertension, smoking show a significant association with CAD patients than controls. Table 2 shows the distribution of lipid parameters in controls and CAD patients. Table 3 shows the lipid values with their standard deviation in controls and CAD patients. Also the diagnostic values lipid parameters for CAD patients and controls were compared and statistically shown. The results show a significant number of CAD patients have abnormal lipid profile. LDL-Cholesterol and Apo-B were significantly higher in CAD patients compared to healthy controls. HDL-Cholesterol and Apo A-1 were significantly decreased in CAD patients. The ratio of Apo B/Apo A-1 is highly significant in CAD patients.

Table 1
Risk factors distribution in CAD patients and controls

Risk Factors	Controls (n=117)		CAD (n=125)		p value
	Number	%	Number	%	
Age in years (Mean \pm SD)	46.54 \pm 8.18		49.57 \pm 7.39		0.003
Male	74	63.25	101	81.27	0.003
Female	43	36.75	24	18.72	0.003
F/H of premature CAD	18	15.38	25	19.79	0.465
DM	32	27.35	53	42.40	0.021
HTN	38	32.48	79	63.25	0.000
Smokers	38	32.48	71	56.89	0.000

Table 2
Distribution of Lipid parameters between CAD patients and controls

Risk Factors	Controls(n=117)		CAD(n=125)		p value
	Number	%	Number	%	
Cholesterol >200 mg/dl	41	35.04	77	61.94	0.000
HDL <40 mg/dl	42	36.24	99	79.51	0.000
LDL >100 mg/dl	83	70.94	102	81.98	0.061
TGL >150 mg/dl	72	61.54	75	60.42	0.963
Apo A-1<123 mg/dl	34	29.51	82	66.27	0.000
Apo B >140 mg/dl	42	36.24	87	69.98	0.000
Apo B/Apo A-1 >0.9	23	19.85	91	73.45	0.000

Table 3
Comparative analysis of Lipid parameters between CAD patients and controls

Lipid parameters (mg/dl)	Controls (mean±SD) n=117	CAD Patients (mean±SD) n=125	Z - Value	P- value
Total Cholesterol (mg/dl)	195.52±43.07	226.31±38.20	5.87	0.000
HDL-Cholesterol (mg/dl)	39.38±6.01	33.10±5.28	8.61	0.000
LDL-Cholesterol (mg/dl)	101.91±35.34	139.38±37.19	8.04	0.000
Triglycerides (mg/dl)	164.37±86.78	186.31±79.44	2.05	0.041
Apo A-1 (mg/dl)	133.40±23.10	94.31±11.24	16.56	0.000
Apo B (mg/dl)	98.19±18.32	163.23±26.84	22.14	0.000
Apo B/Apo A-1	0.74±0.86	1.64±1.52	5.72	0.000

DISCUSSION

This study compares the association of lipid parameters in total of 242 subjects which included 117 age and sex matched healthy individuals and 125 patients with CAD. The age of these subjects varied from 30- 60 years but majority was between 35-50 years. CAD risk factors measured included total cholesterol, LDL-cholesterol, HDL- cholesterol, Triglycerides, Apo A-1 and Apo-B. The study shows though CAD patients were found to have abnormal lipid profiles the level of HDL, LDL,

Apo A-1 and Apo-B were more significantly associated with CAD risk. Apo-B is significantly elevated in CAD patients ($p>0.001$). Based on the results we observe the concentrations of Apo A-1 and Apo-B in plasma are more significantly associated with CAD patients than other lipid parameter. Though lipid parameters like LDL-cholesterol and triglyceride are associated to CAD, the association of Apo A-1 and Apo B is more significantly associated with CAD patients when compared to healthy

controls. Also a significant association of Apo-B/Apo A-1 ratio is seen with CAD patients when compared to healthy controls and concentrations of Apo A-1 and Apo-B in plasma are better discriminators than other lipid parameters for the identification of patients with CAD. Thus hyper Apo-B and Apo-B/Apo A-1 ratio seems to be more powerful predictor of CAD risk than individual lipid parameter.

A multicentre study conducted by Siderman et al²⁵ to assess a similar hypothesis concluded that elevated Apo B had higher CAD risk than elevated LDL-cholesterol. In another study Khan et al²⁶ shows enlarged Waist(EW) and elevated triglyceride (ET) levels are the predictors of CAD and metabolic syndrome, which also identifies that more persons who were younger and had greater LDL-Cholesterol and Apo-B. Kim et al²⁷ showed that measuring plasma apo-protein concentration routinely along with lipid profile in apparently healthy Asian adults is beneficial for assessing the CAD risk. Sherett et al²⁸ showed that measurement

of Apo A-1 and Apo B along with HDL – Cholesterol as the better predictor of CAD risk. Chennai Urban population study²⁹ showed age and LDL-cholesterol as risk factor for CAD and a multiple logistic regression analysis by showed age, BMI, Apo B and Apo A having a significant independent association with CAD. In another study Jadhav et al³⁰ shows a significant association between carotid intimal thickness and apolipoprotein in CAD patients.

CONCLUSION

To conclude though routine lipid profile is the primary biochemical investigation for cardiac evaluation, Apo A-1 and Apo-B are better predictors of CAD risk in general, and Apo-B/Apo A-1 ratio seems to be the more powerful predictor of CAD risk than individual apolipoprotein and it can be measured routinely along with lipid profile in the screening of CAD risk.

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