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Original Article

Cardiology # Biochemistry Section

Apolipoprotein B / Apolipoprotein A-I Ratio a better Diagnostic Marker of Coronary Heart Disease than Conventional LDL/HDL Ratio

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ABSTRACT

Introduction: Apolipoprotein B (Apo B) and apolipoprotein A-I (Apo-I) are cholesterol transporters playing an important role in lipid metabolism. Apo B and A-I represent the total atherogenic and non-atherogenic particles respectively. Hence, their ratio – Apo B/A-I has been strongly associated with various cardiovascular events.

Aim: To compare the diagnostic efficacy of apolipoproteins with conventional lipids for coronary heart disease.

Materials and Methods: There were 295 individuals with or without coronary heart disease were enrolled in the study. The demographic details along with clinical investigations of serum lipid parameters, Apo B and Apo A-I levels were obtained and recorded.

Study Design: It was a single centre, prospective observational study of 295 individuals of both the genders (235 males and 60 females) with or without coronary artery disease.

Statistical Analysis: A comparison of parametric values between two groups was performed using student's t-test. Non-parametric analysis of the continuous data was performed using Mann-Whitney U test. Significance was taken as two tailed $p<0.05$.

Results: In study population, 221(74.92%) had coronary heart disease (CHD) and 74(25.08%) were normal. Statistically significant differences were found in the levels of apo B/apo A-I ratio ($p=0.009$), and Apo A-I ($p\leq0.001$) between two groups. The other lipid parameters and ratios such as cholesterol, triglyceride, HDL-C, LDL-C, non-HDL-C cholesterol, VLDL, Total lipid, Apo-B, LDL-C/HDL-C and TC/HDL-C were not found to be significant.

Conclusion: The present study shows that Apo B/A-I possesses superior diagnostic efficacy for coronary heart disease as compared to conventional lipid parameters and could be effectively used in clinical practice.

Keywords: Coronary artery disease, Diagnostic efficacy, Lipids

INTRODUCTION

Incidence of coronary heart disease (CHD) has shown an upward trend in India in the last decade [1]. Each year there are about 5.8 million new CHD cases and about 40 million individuals with prevalent CHD are alive today [2]. Hypercholesterolemia, hypertriglyceridemia and other abnormalities in lipid metabolism constitute a major risk factor of CHD. However, several studies have reported a contraindication for this, suggesting a possible role of few atherogenic lipids in CHD, rather than the overall cholesterol level [3].

"Lipoprotein" - a biochemical assembly that contains both proteins and lipids are broadly classified under High density lipoprotein (HDL) and Low density lipoprotein (LDL). HDL particles, unlike the larger particles, transfer fats away from cells, artery walls and tissues (around the body, body wide) through the bloodstream. Increasing concentrations of HDL particles are strongly associated with decreasing accumulation of atherosclerosis within the walls of arteries [4]. Contrary to that, LDL particles often known as atherogenic cholesterol transfer lipid molecules into the artery wall and hence facilitating the process of atherosclerosis. Elevated LDL levels are associated with sudden plaque ruptures and clots formation within the artery lumen causing i.e. cardiovascular disease, stroke, and other vascular disease complications [5].

Different lipoprotein fractions can provide more information on cardiovascular risk than the isolated measurement of total cholesterol. The total blood cholesterol does not remain as free cholesterol, but it is the sum of several components

(LDL, VLDL and HDL), transported in respective lipoproteins, the LDL-C/HDL-C ratio had more prognostic value than LDL-C, HDL-C or cholesterol alone [6].

The ratio of Apo A-I to Apo B is a simple index reflecting the balance of cholesterol transport in a system. Apolipoprotein A-I (Apo A-I) is associated with cardio protective lipid (HDL-C) [7] and hence, plays a central role in the reverse cholesterol transport while apolipoprotein B (Apo B) is associated with atherogenic lipid (LDL-C and VLDL) [8]. Henceforth the lower the value of Apo A-I/Apo B ratio, the more cholesterol is likely to be deposited in the arterial wall and thereby provoking atherogenesis and also increasing cardiovascular risk [9]. The current study aims to evaluate and compare the diagnostic efficacy of LDL-C/HDL-C ratio to Apo B/Apo A-I ratio in coronary heart disease patients.

MATERIALS AND METHODS

This single centre, prospective observational study, conducted by U. N. Mehta Institute of Cardiology and Research Center was approved and cleared by institutional ethics committee. Written inform consent was obtained from all the patients. Total 295 individuals of both the genders (235 males and 60 females) were enrolled from January 2013 to November 2014. The patients admitted for CAG, hospitalized with first time chest pain, myocardial infarction patients, ECG showing changes and the patients admitted in emergency were included in the study. Exclusion criteria of the study were patients taking any lipid lowering drug (statin), recent major surgery and rheumatic heart disease. Demographic characteristics, echocardiographic measurements (ejection fraction grade), laboratory lipid profile findings and angiographic measurements were collected for all patients. The subjects were then divided into two groups depend¬ing on the findings of the coronary angiogram: positive for CHD (CHD+), if an occlusion of ≥50% present in any coro¬nary artery was detected; negative for CHD (CHD-), if no occlusion in coronary artery was detected by coronary angiography.

Sample Collection

Venous blood was collected from the antecubital vein of the subjects under sterile conditions after overnight fasting before blood investigations. Total cholesterol (TC), triglycerides (TG), total lipid (TL), and lipoproteins (low density lipoproteins cholesterol (LDL-C), high density lipoprotein (HDL-C) and very low density lipoprotein cholesterol (VLDL), lipoprotein (a), Apo A-I, Apo B were measured by International Federation of Clinical Chemistry (IFCC) approved enzymatic methods using commercially available kit on auto analyzer (ARCHITECH PLUS ci4100, Germany). Lipids levels were classified according to the classification recommended by National Cholesterol Education Program (NCEP) and Adult Treatment Panel III (ATP III) guidelines [10].

STATISTICAL ANALYSIS

The statistical studies were carried out using SPSS software v 20.0 (Chicago, IL, USA) Quantitative variables were expressed as mean ± standard deviation whereas qualitative variables were expressed as percentage (%). A comparison of parametric values between two groups were performed using student's t-test. Non-parametric analysis of the continuous data was performed using Mann-Whitney U test. Significance was taken as two tailed $p<0.05$.

RESULTS

The study included a total number of two ninety five (295) patients. Among them 221 (74.92%) patients had CHD and 74 (25.08%) had normal arteries. The clinical presentation and mean ± SD of the lipid profile are showing [Table/Fig-1]. Overall there were 235 males (79.7%) and 60 females (20.3%) patients showing mean age of 42.49(±10.76) years. Comparison between the lipid profiles of CHD and non-CHD patients are shown in [Table/Fig-2]. Apo A-I ($p\leq0.001$) and Apo B/Apo A-I ratio ($p=0.009$) was significantly higher in CHD patients than non-CHD patients. Apo B increased in CHD patients group and decreased in non-CHD group

Variables	Mean±SD / N (%) N=295
Age	42.49 ± 10.76
Male	235 (79.7)
Female	60 (20.3)
Cholesterol (mg/dl)	150.33 ± 45.99
Triglyceride (mg/dl)	133.91 ± 104.22
High Density Lipoprotein Cholesterol (mg/dl)	33.78 ± 9.68
Non-High Density Lipoprotein Cholesterol (mg/dl)	116.55 ± 44.09
Low Density Lipoprotein Cholesterol (mg/dl)	90.22 ± 38.16
Very Low Density Lipoprotein Cholesterol (mg/dl)	26.86 ± 20.88
Low Density Lipoprotein Cholesterol / High Density Lipoprotein Cholesterol	2.84 ± 1.27
Total Cholesterol/ High Density Lipoprotein Cholesterol	4.66 ± 1.61
Total lipids (mg/dl)	617.97 ± 131.44
Lipoprotein (a) (mg/dl)	35.03 ± 28.60
Apolipoprotein A-I (mg/dl)	1.17 ± 0.30
Apolipoprotein B (mg/dl)	0.83 ± 0.29
Apolipoprotein B/ Apolipoprotein A-I	0.76 ± 0.35

[Table/Fig-1]: Demographic and clinical characteristic of the population. Values are express as mean±SD and other number (%).

Variables	CHD(+ve) N=221	CHD(-ve) N=74	Sig.
Age	44.13±11.03	37.61±8.41	<0.001
Sex (Male: Female)	180:41	55:19	NS
Cholesterol (mg/dl)	149.86±46.90	151.76±43.44	0.63
Triglyceride (mg/dl)	135.92±107.59	127.89±93.88	0.29
HDL-C (mg/dl)	33.67±10.23	34.12±7.89	0.35
Non-HDL-C (mg/dl)	116.19±45.13	117.64±41.11	0.66
LDL-C (mg/dl)	89.29±38.79	93.02±36.33	0.3
VLDL (mg/dl)	27.28±21.56	25.58±18.78	0.28
LDL-C/HDL-C	2.81±1.34	2.82±1.14	0.54
TC/HDL-C	4.69±1.69	4.58±1.31	0.9
TL (mg/dl)	619±135.95	613.75±117.69	0.78
Apo A-I (mg/dl)	1.13±0.28	1.28±0.3	<0.001
Apo B (mg/dl)	0.84±0.3	0.81±0.25	0.66
Apo B/Apo A-I	0.78±0.35	0.69±0.34	0.009

[Table/Fig-2]: Level of lipids in CHD and non-CHD patients. Values are express as mean±SD, Level of significance accepted p≤0.05.

(p=0.66) however the difference was not significant. The other components of lipid profile including cholesterol (p=0.63), triglyceride (p=0.29), HDL-C (p=0.35), non-HDL-C cholesterol (p=0.66), LDL-C (p=0.3), VLDL (p=0.28), LDL-C/HDL-C (p=0.54), TC-HDL-C (p=0.9), total lipid (p=0.78), lipoprotein (a)(p=0.30) were found to be statistically insignificant.

DISCUSSION

Coronary heart disease remains the leading cause of death in developed and developing countries [11]. In the present study we tried to evaluate and compare the association of apolipoproteins and classical lipid profile parameters with CVD.The mean HDL-C values were 33.67±10.23 in CHD positive group and 34.12±7.89 in non-CHD group with p=0.35. On the contrary Apo A-I, a part of HDL-C was found to decrease significantly in CHD patients as compared to non-CHD patients (1.13±0.28 mg/dl vs 1.28±0.3 mg/dl; p<0.001). This indicates that Apo-A-I is better diagnostic marker than HDL-C which is in accordance to other studies. The comparison of present study and different studies of apolipoprotein mentioned in [Table/Fig-3]. In 2008, INTERHEART study McQueen MJ et al., [12] showed that Apo A-I measurements may provide more information than HDL-C levels in the assessment of CHD risk. Gerald Luc et al., [13] in PRIME study stated that among the parameters related to HDL-C, Apo A-I appears to be the strongest independent risk factor. In Atherosclerosis risk in the community (ARIC) study shows Apo B has been found to have a stronger relation with CV risk than LDL-C [14]. Agoston-Coldea et al., [15] shows the protective effect of ApoA-I in multivariate analysis. They concluded that the predictive value of the Apo-ratio is superior to that of serum lipid fractions and that the Apo-ratio therefore should be introduced in current clinical practice.

We have observed an increase in Apo B levels in CHD patients as compared to non-CHD patients, though statistically insignificant indicating poor diagnostic capacity of it in our population.

The ratio of Apo A-I and Apo B was found to be the most significant parameter in our study. It was 0.78±0.35 mg/dl in CHD patients against 0.69±0.34 mg/dl in non-CHD group, p = 0.009. The comparison of conventional lipid ratio (LDL-C/HDL-C) vs. novel lipid ratio (Apo B/Apo A1) for diagnosis of CHD, we found better efficacy of Apo B/Apo A1. Hence, Apo B/Apo A-I - a simple index reflecting a balance of atherogenic and non-atherogenic lipid could be effectively used in clinical practice. The finding of ratio of Apo A-I to ApoB in our study are similar to finding reported by Jadhav et al., [16]. The authors showed that in Western Indian population, along with traditional coronary riskfactors Apo B/Apo A-I plays a strong role in coronary artery disease.Tamang HK et al., [17] tried to evaluate and compare the predictive value of apo B/apo A-I ratio and classical lipid profile parameters for development of CVD., Goswani B et al., [18] also showed that Apo-B/Apo-AI ratio has a fairer association with CAD risk in Indians as compared to conventional lipids.

Goran Walldius et al., [19], Philippa J. Talmud et al., [8], Adnan Qureshi et al., [20] and Dawar et al., [21] shows in their study that Apo B/Apo A-I ratio has been reflected as marker for prediction of risk of myocardial infarction (MI) than

Sr. No	Type of study	Apo A1	Apo B	Apo B/ apo A1	LDL	HDL	LDL/HDL
1.	**Present Study (mg/dl)**						
	Case (n=221)	1.13±0.28	0.84±0.3	0.78±0.35	89.29±38.79	33.67±10.23	2.81±1.34
	Control (n=74)	1.28±0.3	0.81±0.25	0.69±0.34	93.02±36.33	34.12±7.89	2.82±1.14
2.	**Tamang et al., [17] [mmol/l]**						
	Case (n=45)	104.52±16.82	106.95±37.81	1.0±0.39	2.71±0.91	0.89±0.16	3.0±1.01
	Control (n=44)	105.54±9.05	91.06±22.64	0.84±0.18	2.52±0.49	0.99±0.16	2.79±0.77
3.	**Dawar et al., [21] [mg/dl]**						
	Case (n=60)	73.03±9.69	96.96±10.59	1.34±0.26	103.70±38.84	24.63±4.19	4.39±1.95
	Control (n=60)	99.8±7.71	73.92±14.25	0.75±0.17	80.84±27.55	35.82±7.81	2.37±0.98
4.	**Goswami et al., [18] [mg/dl]**						
	Case (n=100)	107±19.5	99.6±23.7	0.96±0.3	121.3±40.6	38.2±6.3	3.32±1.5
	Control (n=100)	109.1±18.8	76.9±22.7	0.71±0.2	77.7±27.2	43.2±5.6	1.84±0.78
5.	**Sharett et al., [14] [mg/dl]**						
	Case (Woman) (n=216)	1.33	1.01	0.76	3.89	1.30	2.99
	Control (Woman) (n=6691)	1.44	0.90	0.63	3.48	1.51	2.30
	Case (Man) (n=509)	1.17	1.03	0.88	3.91	1.07	3.65
	Contro (Man) (n=4923)	1.23	0.94	0.76	3.56	1.18	3.02

[Table/Fig-3]: Comparison of present study and different study of apolipoprotein.

traditional lipid ratios. In concordance to our results, Kim et al., also showed a superior risk association of Apo B/Apo A-I as compared to other lipids [22]. Goran Walldius et al., [19] in their study suggested that Apo B, Apo B/Apo A-I and Apo A-I should be regarded as highly predictive in evaluation of cardiac risk. Adnan I. Qureshi et al., [20] found that Apo A-I to B ratio was inversely associated with myocardial infarction and may be an important protective clinical marker for atherosclerosis. While evaluating the lipid related risk factors for development of CHD, major guidelines have proposed the diagnostic utility of HDL-C, non HDL-C, TG, and lipid ratios such as TC/HDL-C and LDL-C/HDL-C [23]. Apo B/Apo A-I showed a better prognostic value as compared classical lipid markers and Castelli index [19] and are more advantageous due to easy availability of well standardized assay systems having great accuracy [24,25].

Establishment of accurate prognostic and diagnostic markers of CVD would be of utmost important as it will help in primary and secondary prevention of the disease. Our findings showed that Apo B/Apo A-I ratio is a superior marker for diagnosis of CVD than classical lipid parameters. Studies published worldwide on favor of Apo B/Apo A-I ratio have increased the possibility that it may be introduced in routine laboratory investigation for cardiovascular risk assessment. Lack of follow-up is the major limitation of the present study.

CONCLUSION

The apolipoprotein profile, especially Apo B/A1 ratio is clearly a more valuable indicator of cardiovascular risk as compare to other conventional lipid fractions, and provides information that may be used to guide the treatment of patients in clinical practice. Based upon this study we may conclude that Apo B/Apo A-I ratio have better diagnostic efficacy than that of LDL/HDL ratio in cardiovascular risk assessment.

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