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Apolipoproteins: Risk Assessment Tools For Coronary Heart Disease.

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Abstract:*Myocardial Infarction (MI) is one of the major causes of morbidity and mortality in the world. Dyslipidemia is one of the important risk factor. It initiates atherosclerotic plaque formation, finally resulting in degeneration of endothelial cell function which enhances the coagulability of blood by activation of various factors for which apolipoproteins have been implicated. Apolipoprotein A-1 (apo A1) and apolipoprotein B (apo B) are the protein constituents of high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), respectively. Apo A-1 and HDL-C are antiatherogenic whereas Apo B and LDL-C are atherogenic.*

Objectives: *To evaluate and to compare the serum concentrations of apo A1, apo B and lipid profile between Coronary Heart Disease (CHD) patients and healthy subjects and to establish interrelationship if any, between apolipoproteins and lipid profile in CHD patients.*

Methodology: *In this study we have taken a group of 60 clinically proven CHD patients and an equal number of age and sex matched healthy subjects from whom blood was drawn for assay of apo A1, apo B by Immunoturbidimetric method and lipid profile by Enzymatic methods. Appropriate statistical analysis was done.*

Results: *A significant rise in serum apo B, total cholesterol, LDL-C, triglycerides and significant fall in serum apo A1, HDL-C was seen in CHD patients compared to normal subjects (p value < 0.05).*

Conclusion: *The results of the current study establishes apo A1and apo B are useful biomarkers as well as strongly related to CHD in addition to the levels of serum lipids.*

Key Words: *Coronary heart disease, apolipoprotein, lipid profile, dyslipidemia.*

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I. Introduction

Cardiovascular diseases are the major cause of death globally. About 29.2% of total global deaths result from various forms of cardiovascular disease of which about 50% are due to Coronary Heart Disease (CHD).

The cause of CHD is atherosclerosis. Atherosclerosis is a chronic inflammatory response of the arterial wall initiated by an injury to the endothelium by activation of various factors for which apolipoproteins have been implicated. Moreover, lesion progression is sustained by interaction between modified lipoproteins (e.g. oxidized low density lipoprotein), lipid laden macrophage (foam cells), T-lymphocytes and the normal cellular constituents of the arterial wall. Atherosclerosis is also characterized by thickening of the arterial wall, which protrudes into and obstructs the vascular lumen.[1]

Apolipoproteins are the protein components of lipoproteins.[2] Apolipoproteins are the key lipoprotein components that serve both as enzymatic cofactors, maintain structural integrity of lipoprotein complex and as recognition elements that bind to specific receptors on the peripheral tissues.[3,4] Initially the existence of three major groups of lipoproteins: apo A, apo B, apo C were reported, recently more apolipoproteins such as D, E, H and J have been characterized.[5] Apolipoprotein A-1 (apo A1) and apolipoprotein B (apo B) are the protein constituents of high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C),

respectively.[6] Apo B and LDL-C are atherogenic whereas Apo A-1 and HDL-C are anti-atherogenic. Each of the atherogenic particles in plasma [Very Low Density lipoprotein cholesterol (VLDL -C), intermediate density lipoprotein (IDL), LDL -C and lipoprotein (a)] contains one molecule of apo B and therefore, measurement of plasma apo B represents the total number of atherogenic particles.[7]

A great deal of research has been conducted in the use of apolipoproteins as biomarkers of CAD. Some investigators have found that the concentrations of apo A-1 and apo B are better predictors of CAD than the total plasma lipids or lipoproteins.[3]

Our objectives was toevaluate the serum concentrations of apo A1, apo B and lipid profile in CAD patients and healthy controls and to establish the interrelationships if any, between apolipoproteins and lipid profile in patients with CHD.

II. Material And Methods

A case control study of serum Apolipoprotein A1, B and lipid profile was carried out in patients with CHD and controls. After obtaining institutional ethical clearance the study was carried out in clinically proven cases of CHD and age and sex matched healthy individuals as controls. A total number of 60 patients with CHD and an equal number of controls were selected based on inclusion and exclusion criteria for the present study. The patients and controls voluntarily participated in the study.

Inclusion criteria:

- Clinically proven cases of CHD diagnosed either by electrocardiogram (ECG) and/or Troponin-I in the age group of 30-70 years and
- An equal number of age and sex matched healthy controls were included.

Exclusion criteria: CHD with

- Hepatic and renal disease,
- Anemia,
- Sepsis,
- Diabetes mellitus,
- Malignancy,
- Hypolipidemic drugs were excluded from the study.

Procedure methodology

After taking written informed consent about 5 ml of venous blood was drawn under aseptic conditions in a sterile vacutainer from selected subjects after a period of overnight fasting of 10-12 hours. Serum was immediately separated by centrifugation. The TC (CHOD-PAP method),[8] TGL (GPO-PAP method),[9] HDL-C (Phosphotungstic acid method, End point method)[10] were analysed by using semi auto analyzer. Apo A1 and apo B were analysed in Auto Analyzer using ERBA kits by immunoturbidimetric method.[11] LDL-C level was calculated by using Friedewald equation based on the levels of TC, TGL and HDL-C. VLDL-C is calculated by TGL/5.[12]

Statistical analysis

Descriptive data are presented as mean ± SD and range values. Student's unpaired 't'-test was used for comparing the means of two groups. Relationship between measurements was assessed by Karl Pearson's coefficient of correlation. For all the test, a p-value of 0.05 or less was considered as statistically significant.

III. Results

Table No 1: Shows comparison of Apo A1, Apo B, lipid profile and ratios in controls and in patients with CHD.

	CONTROLS	CASES	
Parameters	Mean ± SD	Mean ± SD	p*- Value
Apo A1 (mg/dL)	115.50±19.11	90.10± 20.45	p < 0.001
Apo B (mg/dL)	78.18±15.79	134.58±39.51	p < 0.001
TC (mg/dL)	145.28 ± 33.47	204.85 ± 32.23	p < 0.001
TGL (mg/dL)	125.88 ± 41.35	169.63 ± 72.27	p < 0.001
HDL-C (mg/dL)	43.43 ± 7.24	32.73 ± 6.74	p < 0.001
LDL-C (mg/dL)	109.26 ± 24.63	136.79 ± 33.86	p < 0.001
VLDL-C (mg/dL)	24.2 ± 8.17	36.24 ± 11.54	p < 0.001
Apo B / HDL-C	1.81 ± 0.47	4.04 ± 1.16	p < 0.001
Apo B/ Apo A1	0.67 ± 0.26	1.49 ± 0.20	p < 0.001

Student's unpaired t- test, p < 0.001 HS (Highly significant)

Table No 2: Shows karlpearson's coefficient (r) of correlation

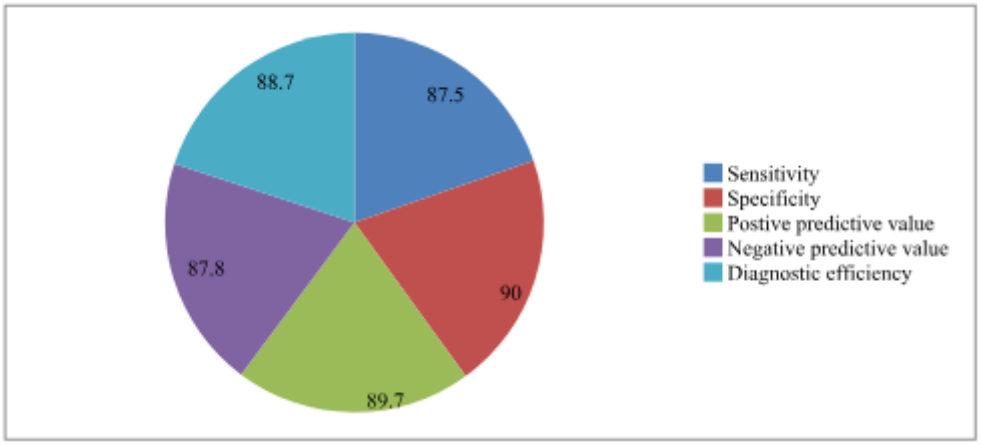
	Apolipoprotein A1			Apolipoprotein B		
Correlation between	r	p* value	Sig	r	p* value	Sig
TC	0.4	0.63	NS	-0.3	0.06	NS
TGL	0.14	0.24	NS	0.05	0.76	NS
HDL-C	0.30	0.04	S	-0.36	0.02	S
LDL-C	-0.26	0.03	S	0.37	0.02	S
VLDL-C	0.12	0.76	NS	0.09	0.56	NS

r = Karl Pearson's coefficient of correlation, $p < 0.05$ significant

Table No.3: Shows diagnostic validity of apo B and LDL-C for discrimination of CHD subjects.

Diagnostic test result	Apo B cut off value ≤105.5 mg/dL	LDL-C cut off value ≤ 116.6 mg/dL
Sensitivity	87.5	67.5
Specificity	90	65
Positive predictive value (PPV)	89.7	65.8
Negative predictive value (NVV)	87.8	66.6
Diagnostic efficiency	88.7	66.3

Figure No 1: Shows pie diagram showing Diagnostic validity of Apolipoprotein B for CHD.



IV. Discussion

CHD is one of the important causes of morbidity and mortality in most countries of the world. The debate on the value of lipids as a predictive risk factor for atherogenesis has centered for many years on TC, TGL and LDL. Recently the interest has been focused on role of apolipoprotein and inflammatory markers in atherogenesis.

Table 1 shows that the mean serum concentrations of TC, TGL, LDL-C and VLDL-C were higher in CHD subjects when compared to controls and thus had a positive correlation. The mean serum concentration of HDL cholesterol was lower in CHD subjects when compared to controls suggesting a negative association. These results were in accordance with the studies of Lhamo Y. Sherpa, et al[13] and M. Mohsen Ibrahim, et al.[14]

Table 1 shows that the apo 1 was decreased and apo B concentrations was increased in patients with CHD when compared to age matched healthy normal individuals. This study showed a positive association between CHD and apo B level and the results were in agreement with those of SamanMiremadi, et al,[7] Khadem-Ansari MH, et al,[15]VimalRamjee, et al[16] and Jae-Hong Ryoo, et al.[17]

The ratio of Apo B / HDL-C and Apo B/ Apo A1 are increased in CHD subjects when compared to controls and was statistically significant ($p < 0.001$).

Table 2 shows that there is a positive correlation between HDL-C and apo A1. Both of the variables are dependent on each other. As the concentrations of HDL-C decreases, there is a simultaneous decrease in apo A1 level thus suggesting that this correlation is statistically significant. There is a negative correlation between LDL-C and apo A1 and it is also statistically significant.

Although the inverse relationship between HDL cholesterol concentrations and risk of future CHD is well recognized and HDL cholesterol has been incorporated into various algorithms for calculating CVD risk, several studies have recently demonstrated that apoA-I might provide almost identical prognostic information as HDL, but several studies have suggested that apoA-I might even improve our ability to identify patients at risk for future CHD.[18]

Table 2 shows that there is a positive correlation between LDL-C and apo B. Both of the variables are dependent on each other. As the concentrations of LDL-C increases, there is a simultaneous increase in apo B level thus suggesting that this correlation is statistically significant. There is a negative correlation between HDL-C and apo B and it is also statistically significant.

Apo B synthesis is required for the hepatic secretion of VLDL and apo B remains associated with particle during the triglyceride hydrolysis and lipid exchange cascade until its clearance from the circulation as IDL or LDL particle. Measuring apo B in plasma is roughly equivalent to quantifying the number of apo B containing lipoproteins secreted by the liver because there is systematically only one apo B secreted. On the other hand, the cholesterol content of apo B containing lipoprotein may be highly variable. Thus, for a given cholesterol concentration, a high number of apo B containing lipoproteins will result in the large number of small dense LDL particles which have been associated with an enhanced risk of coronary artery disease.[6,19]

Table 3 and Figure 1 shows the diagnostic validity results with higher sensitivity, specificity, PPV, NPV and greater diagnostic efficiency for apo B when compared to LDL cholesterol suggesting superiority of apo B over LDL in predicting CHD and in discriminating CHD from normal healthy individuals.

Apo B has a role in the development of cardiovascular disease suggesting that the risk of cardiovascular disease is maximized if hypertriglyceridemia was associated with the high level of apo B as indicated by an increased number of LDL particles and density. It increases threefold rise in the risk of vascular events whereas hypertriglyceridemia with a normal apo B was not.[7,17,20.]

Strength and further scope of the study:

The concentrations of apo A1, apo B and lipid profile were significantly increased in patients with CHD as compared to control group except HDL which was statistically decreased in CHD subjects compared to controls. This study also proved that apo B is the better biomarker with high sensitivity and specificity of CHD than LDL cholesterol.

The diagnosis of IHD can be improved by measuring newer markers of CHD like Interleukin-6, oxidized LDL, Homocysteine levels.

V. Conclusion

The results of the current study support the concept that the levels of apo A1 and apo B are strongly related to CHD in addition to the conventional lipid profile. Our findings support the consideration of the measurement of serum Lp(a) as a screening tool for the risk of ischemic heart disease. Therefore, this study suggests the need for routine measurement of apo A1and apo B in the diagnosis of CHD and thus helps in early detection of myocardial damage which warrants timely intervention leading to lowered morbidity and mortality.

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References

[1]. Dutta S, Iqbal Z, Prasad KR. Comparison between serum hsCRP and LDL cholesterol for search of a better predictor for Ischemic heart disease. Ind J ClinBiochem 2011 Apr- June;26(2):210-13.
[2]. Rifai N, Warnick GR. Lipids, lipoproteins, apolipoproteins and other cardiovascular risk factors. In: Burtis CA, Ashwood ER and Bruns DA, editors. Tietz Text Book Of Clinical Chemistry and Molecular Diagnostics, 4th ed. New Delhi: Elsevier Co;2006:903-64.
[3]. Sharma R, Singh VS. Serum apolipoproteins in the patients of myocardial infarction in different age groups. Ind J ClinBiochem 2001;16(1):122-26.
[4]. Rifai N, Bachorik PS and Albers JJ. Lipids, lipoproteins, apolipoproteins and other cardiovascular risk factors. In: Burtis CA, Ashwood ER and Bruns DA, editors. Tietz Fundamentals of Clinical Chemistry, 5th ed. New Delhi: Elsevier Co;2006:903-64.
[5]. Irshad M, Dubey R. Apolipoproteins and their role in different clinical conditions: An overview. Indian Journal of Biochemistry & Biophysics 2005 April;42:73-80.
[6]. Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard PM, Dagenais GR et al. Apolipoprotein A-1 and B levels and the risk of ischemic heart disease during a five- year follow- up of men in the quebec cardiovascular study. Circulation 1996;94:273-78.
[7]. Miremadi S, Sniderman A, Frhlich J. Can measurement of serum apolipoprotein B replace the lipid profile monitoring of patients with lipoprotein disorders?.Cinical Chemistry 2002;48(3):484-88.
[8]. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. CLIN CHEM 1974;20(4):470-75.
[9]. McGowen MW, Artiss JD, Strandbergh DR, Zak B. A Peroxidase Coupled Method for the Colorimetric Determination Of Serum Triglycerides. CLIN CHEM 1983;29(3):538-42..
[10]. Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. Journal of Lipid Research 1970;11:583-95.
[11]. Naito HK. J Clin Immunoassay 1986;9.
[12]. Miremadi S, Sniderman A, Frhlich J. Can measurement of serum apolipoprotein B replace the lipid profile monitoring of patients with lipoprotein disorders?.Cinical Chemistry 2002;48(3):484-88.
[13]. Sherpa LY, Deji, Stigum H, Chongsuvivatwong V, Luobu O, Thelle DS, et al. Lipid profile and its association with risk factors for coronary heart disease in the highlanders of Lhasa, Tibet. HIGH ALTITUDE MEDICINE & BIOLOGY 2011;10(1):57-63.

[14]. Ibrahim MM, Ibrahim A, Shaheen K, Nour MA. Lipid profile in Egyptian patients with coronary artery disease. The Egyptian Heart Journal 2013;65:79-85.
[15]. Ansari KMH, Rasmi Y, Pour RA, Jafarzadeh M. The association between serum apolipoprotein A-1 and apolipoprotein B and the severity of angiographical coronary artery disease. Singapore Med J 2009;50(6):610-13.
[16]. Ramjee V, Sperling LS, Jacobson TA. Non-high-density lipoprotein cholesterol versus apolipoprotein B in cardiovascular risk stratification. Journal of the American college of cardiology 2011;58(5):457-63.
[17]. Ryoo JH, Ha EH, Kim SG, Ryu S, Lee DW. Apolipoprotein B is highly associated with the risk of coronary heart disease as estimated by the Framingham risk score in healthy Korean men. J Korean Med Sci 2011;26:631-36.
[18]. Walldius G, Jungner I: The apoB/apoA-I ratio: a strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy — a review of the evidence. J Intern Med2006; **259**:493–519.
[19]. Lamarche B, Chernof AT, Moorjani S, Cantin B, Dagenais GR, Lupein PJ, et al. Small, dense low-density lipoprotein particles as a predictor of the risk of ischemic heart disease in men. Circulation 1997;95:69-75.
[20]. Benn M, Nordestgaard BG, Jensen GB, Hansen AT. Improving prediction of ischemic cardiovascular disease in the general population using apolipoprotein B: The Copenhagen city heart study. Journal of the American Heart Association 2007;27:661-70.

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