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COMPARISON OF APO B/A-I RATIO WITH LDL-C/HDL-C RATIO IN PATIENTS OF ISCHEMIC HEART DISEASE WITH OR WITHOUT TYPE 2 DIABETES MELLITUS

Biochemistry

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ABSTRACT

Background: An early assessment of Coronary Artery Disease using valuable predictors can delay the onset of disease and improve the quality of life. Aim of the study is to determine the ratio of Apo B / A-I in patients of Ischemic Heart Disease with or without Diabetes and analyze the significance of this ratio over the conventional T.Chol/ **HDL-C** ration & **LDL-C/ HDL-C** ratios.

Methods: The study consists of 100 cases including 50 having Ischemic Heart Disease only & 50 having Ischemic Heart Disease with Diabetes as study group and 50 healthy individuals as control group conducted at Sir T. General hospital, Bhavnagar.

Results: Regarding results,Apo A-I ratio was elevated in group I & II and was found highly significant ($p < 0.0001$) as compare to the group III. There was positive correlation of Apo A-I ratio with **LDL-C/ HDL-C** ratio **($r=0.403$, $p<0.004$ in group I and $r= 0.433$, $p<0.002$ in group II)**

Conclusion: As the ratio covers both atherogenic and antiatherogenic lipid risk factor, it can be used as a better predictor of Ischemic Heart Disease than conventional risk factor.

KEYWORDS

APOLIPOPROTEIN B/A-I RATIO, ISCHEMIC HEART DISEASE, TYPE 2 DIABETES MELLITUS.

INTRODUCTION

"Ischemic Heart Disease" is a condition in which there is an insufficient supply of blood and oxygen to a specific part of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand.[1] In India, Coronary Artery Disease has increased more than 6 fold in the last 5 decades and reaches a prevalence of 10% among persons in the 35 to 65 years age group in last decade. Coronary Artery Disease is the most frequent cause of cardiovascular disease, and is expected to account for 40% of all deaths by 2020 and has become a global problem with the increasing prevalence of obesity, metabolic syndrome and diabetes.[2] The incidence of Coronary Artery Disease has halved in the West in the last 30 years, it has doubled in India with no signs of a downslide in spite of a lower prevalence of conventional risk factors amongst Indians.[3]

Among the various risk factors, Type 2 Diabetes Mellitus (T2DM), has a distinctive association with Coronary Heart Disease. In addition of it, certain other characteristic features which associated with T2DM like oxidative stress, enhanced atherogenecity of cholesterol particles, abnormal vascular reactivity, augmented haemostatic activation and renal dysfunction may confer excess risk of Coronary Heart Disease.[4]

An early assessment of Coronary Artery Disease using valuable predictors can delay the onset of disease and improve the quality of life.[5] Initially the estimation of serum lipids like cholesterol and triglycerides were used to assess the risk of Coronary heart disease. However, the inconsistency in the correlation between serum lipid profile and Ischemic heart disease, led to the development of better indicators.[6]

Apolipoprotein A-I and B are structural and functional components of lipoprotein particles which serve as transporters of cholesterol. Apolipoprotein-B (Apo B) is present as a single molecule in low, intermediate and very low density lipoproteins (LDL, IDL and VLDL respectively) and also transfers cholesterol and triglyceride from sites where it synthesized to tissues where it utilized for energy production, storage, membrane assembly or hormone synthesis. On the other hand, Apo A-I which is the major apolipoprotein associated with high density lipoprotein (HDL) plays an important role in the reverse cholesterol transport by transferring cholesterol from tissues back to the liver.[7, 8] Plasma Apo-B concentration reflects the number of atherogenic lipoprotein particles & quantisation of Apo-AI which is the main apolipoprotein in HDL in blood gives an indication of the number of anti-atherogenic particles.[3]

Based on these relations, cholesterol ratios such as total/HDL cholesterol and LDL/HDL cholesterol are considered by some investigators as a simple approach for lipid risk assessment.[5] In the current era, the ratio of Apo B & A-I (Apo B/ A-I) has been proposed to reflect the balance between the processes which opposes arterial internalization of cholesterol and the reverse transport of cholesterol back to the liver.[8]

The present study is designed as Apo-B/ Apo-AI ratio is a superior marker to elevated Ischemic Heart Disease risk amongst patients with or without Type 2 Diabetes Mellitus in comparison to conventional lipid profile ratios.

MATERIAL & METHODOLOGY

The study was conducted at Sir Takhtsinhji General Hospital, Bhavnagar. The study consists of 100 acute coronary syndrome cases as study group and 50 healthy individuals as control group. Of the 100 cases, 50 cases were IHD with Diabetes Mellitus and 50 were IHD without Diabetes Mellitus. All patients had a history of chest pain and ECG changes or raised CK-MB as evidence of acute coronary syndrome and further evaluated by biochemical investigations. The cases included in our study were patients admitted to intensive cardiac care units of Sir T. General Hospital, Bhavnagar and the control subjects were selected randomly. The inclusion & exclusion criteria for Group I & Group II are as below.

1. ***Inclusion criteria***

a) Patient age more than 30 years , both male and female included

b) Clinically diagnosed case of diabetes with duration more than 5 years.

c) Patient on oral hypoglycaemic drugs.

d)Patient with symptoms of Ischemic Heart Disease with electrocardiographic changes and elevated cardiac biomarkers

e) Patient who is able to give informed consent.

GROUP I: include criteria (d) and (e)
GROUP II: include criteria (b), (c), (d) and (e)

2. Exclusion criteria

a) Patient having H/O chronic alcohol consumption, hepatobiliary disorders or any other acute liver diseases like hepatitis.
b) Patients with coronary artery disease with atrial fibrillation or pacemaker
c) History of congestive heart failure
d) History of stroke, transient ischemia or carotid surgery
e) History of coronary artery bypass graft surgery or PTCA
f) History of intermittent claudication or PVD
g) Patient on insulin therapy.
h) Patients on lipid lowering agents.

Informed consent was taken from all the participants. The study was reviewed and approved by the human ethics committee of Govt. Medical College, Bhavnagar. To find out the significance of apolipoprotein B/ A-I ratio over traditional lipid profile ratios, subject underwent the following investigations:

Fasting samples were collected for estimation of Serum apolipoprotein A-I & B by Immunoturbidimetric method, serum total cholesterol by CHOD-POD method, serum triglyceride done by GPO PAP method, Serum LDL & serum HDL done by direct methods and fasting blood glucose levels done by GOD-POD method at NABL accredited Clinical Biochemistry Section, Laboratory Services Sir T Hospital, Bhavnagar.

In data analysis, the statistical studies were carried out using SPSS software v 23.0 (Chicago, IL, USA). A comparison of Apo B/A-I ratio with T. Cholesterol/HDL ratio & LDL/HDL ratio between control and study groups was carried out by applying ANOVA test and correlation of Apo B/A-I ratio with other lipid ratios were also studied by applying Pearson correlation test & Scatter plot with regression line. Significance was taken as two tailed $p<0.05$.

RESULTS & DATAANALYSIS:

The study include total 150 subjects, among them 50 subjects had IHD only (Group I), 50 subjects had IHD with Type II DM (Group II) & remaining 50 were healthy subjects (Group III).

Table 1: Descriptive data of biochemical parameters. (Apo B/A-I ratio, LDL/HDL ratio & T. Chol/HDL ratio). Data in Table-1 shows that mean value of Apo B/A-I, T.Chol./HDL-C & LDL-C/HDL-C in Study Group I and II are statistically higher than control Group III.

Descriptive Statistics																
	Group I					Group II					Group III				
	N	Mean ±SD	Range	Min.	Max.	N	Mean ± SD	Range	Min.	Max.	N	Mean ± SD	Range	Min.	Max.
Apo B/ A-I	50	1.17 ± 0.29	1.45	0.49	1.94	50	1.10 ± 0.29	1.73	0.66	2.39	50	0.69 ± 0.09	0.31	0.54	0.85
T. Chol/ HDL-C	50	3.61 ± 1.10	5.24	1.64	6.88	50	3.94 ± 1.28	6.96	1.79	8.75	50	3.41 ± 0.76	3.20	1.89	5.09
LDL-C/ HDL-C	50	2.07 ± 0.76	3.24	0.86	4.10	50	2.41 ± 0.86	4.34	0.66	5.00	50	1.68 ± 0.41	1.82	0.78	2.60

Table 2:Analysis of Variance between biochemical parameters. (Apo B/A-I ratio,LDL-C/ HDL-C ratio & T.Chol/HDL-C ratio) of Group I, II & III.

ANOVA							
Sr. no.	**Parameter**	**Sum of Squares**		**df**	**Mean Square**	**F**	**Significance**
1	Apo B/ A-I	Between groups	6.664	2	3.332	56.140	**0.000**
		Within groups	8.725	147	0.59		
2	T. chol./ HDL-C	Between groups	7.262	2	3.631	3.180	0.044
		Within groups	167.816	147	1.142		
3	LDL-C/ HDL-C	Between groups	13.164	2	6.582	13.453	**0.000**
		Within groups	71.923	147	.489		

Post Hoc						
		Mean Difference (I-J)	**Std. Error**	**Sig.**	**95% CI**	
					Lower	**Lower**
Apo B / Apo A-I						
Group III	Group I	-.47800	.04872	.000	-.5934	-.3626
	Group II	-.40800	.04872	.000	-.5234	-.2926
T. Cholesterol / HDL-C						
Group III	Group I	-.20960	.21369	.590	-.7156	.2964
	Group II	-.53480	.21369	.036	-1.0408	-.0288
LDL-C / HDL-C						
Group III	Group I	-.38460	.13990	.018	-.7158	-.0534
	Group II	-.72520	.13990	.000	-1.0564	-.3940

Table 2 shows the comparison of Apo B/A-I ratio, T.Chol./HDL-C ratio & LDL-C/HDL-C ratio in study groups (Group I & II) and control group (Group III). As per Table 2 values of Apo B/A-I ratio and LDL-C/HDL-C ratio is significantly higher ($p<0.0001$) in the cases compared to the controls.

Table 3: Correlation between Apo B/ Apo A-I & other parameters

Parameter	Two tailed p value	Pearson correlation (r)	R^2 Linear regression	Significance
Group I				
T.Chol / HDL-C	0.077	0.252	0.064	No
LDL-C/ HDL-C	**0.004**	0.403	**0.162**	**Yes**
Group II				
T.Chol / HDL-C	0.080	0.250	0.063	No
LDL-C/ HDL-C	**0.002**	0.433	**0.187**	**Yes**
Group III				
T.Chol / HDL-C	0.197	-0.186	0.034	No
LDL-C/ HDL-C	**0.009**	0.365	**0.133**	**Yes**

Table 3 shows that ratio of serum Apo B/A-I was positively correlated with ratio of LDL-C/HDL-C. (r=0.403, p=0.004 in Group I, r=0.433, p=0.002 in Group II & r=0.365, p=0.009 in Group III).

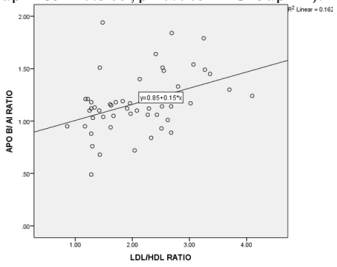

Figure 1: Scatter Plot with Regression Line (Apo B/A-I & LDL/HDL) in Group-I

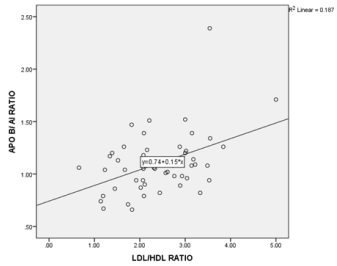

Figure 2: Scatter Plot with Regression Line (Apo B/A-I & LDL/HDL) in Group-II

DISCUSSION

Apolipoprotein B presents in LDL, IDL and VLDL particles, indicates the total number of potentially atherogenic particles which correlated with the non-HDL cholesterol levels. Apolipoprotein AI is strongly associated with HDL and its expression may be responsible for determining HDL plasma levels. Therefore, the ratio of Apo B & A-I reflects the balance between Apo-B-containing atherogenic cholesterol particles and Apo A-I containing antiatherogenic cholesterol particles.[9]

Researches associated with the predictive value of Apolipoproteins AI and B in atherosclerotic diseases was started approximately two decades ago. At present, plasma Apolipoprotein AI and B levels have been described as better predictors of atherosclerotic diseases than other lipid and lipoprotein concentrations. It has also been advised that the Apo B/Apo A-I. ratio represents a superior parameter for prediction of cardiovascular risk as compared to other lipid ratios, such as total cholesterol/HDL, LDL/HDL and non-HDL cholesterol/HDL. [9]

Our findings are in consensus with findings of the global INTERHEART study of risk factors for acute myocardial infarction in which 30000 patients from 52 countries were enrolled and they concluded that "the Apo B/A-I ratio was the most important risk factor in all geographic regions."[10]

In a study conducted by Binita Goswami et al. in Indian patients with acute myocardial infarction, it was observed that Apo B/ Apo-AI ratio in the patients with AMI was 0.96±0.30 and 0.71±0.20 in the control subjects ($p < 0.001$). In our study Apo B/ Apo-AI ratio was 1.17 ± 0.29 in patient with IHD and 0.69 ± 0.09 in the control subjects ($p<0.0001$) which correlate with present study.[4]

Sachu Philip et al. reported that Apo A-I ratio was 2.02 ± 0.96 ($p<0.0001$) in patient of CAD without DM and 2.02 ± 0.55 ($p<0.0001$) in patient of CAD with DM. Similar finding were also reported in present study.[2]

Rajni dawar et al. reported that the coefficient beta for Apo A-I was 0.691 with t value of 9.916 showing highly significant prediction of MI ($p<0.0001$). Present study correlates with this study.[11]

Moreover, recent reports from prospective risk studies, such as Apolipoprotein mortality risk study (AMORIS)[12], the European Prospective Investigation of Cancer-Norfolk study(EPIC Norfolk Study)[13], the Monitoring of trends and determinants in Cardiovascular disease Augsburg/cooperative Gesundheitsforschung in der Region Augsburg (MONICA/KORA Augsburg Study)[14], as well as from other studies on diseases related to atherosclerosis indicate that the ApoB/ApoA-I ratio is a useful risk predictor of both fatal and non-fatal MI.

CONCLUSION

The more accurately risk can be defined; the more cost effective primary prevention will be done. The clinical measurement of Apolipoproteins is standardized, simple, inexpensive and can be performed with random blood sample. Our data provide broad and straightforward support the hypothesis that ApoB and Apo A-I should be introduced into clinical practice for the assessment of the risk of cardiovascular disease in the larger interest of the patients. Furthermore fasting is not required for estimation of apolipoproteins, which is clearly an advantage over traditional lipid ratios. Also, apolipoproteins are better predictors of IHD risk and they are not altered in patients on lipid lowering agents.

To conclude, out of all the lipid parameters Apo A-I ratio was significantly increased in patients of Ischemic Heart Disease with or without DM. Though our study is a pointer in this direction but the patient group was small, suggesting further prospective population based research in this path for early and accurate prediction of IHD.

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