Association of Serum Apolipoprotein in Patients with Coronary Heart Disease – An Observational Study

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Research Article

Abstract: **Introduction:** Incidence of coronary heart disease (CHD) has shown an upward trend in Indian in the last decade. Estimation of serum lipids like Cholesterol and triglycerides were used to assess the risk of CHD. However, the correlation between serum Cholesterol and CHD is not ideal. Apoplipoprotein play an important role in many disorders of lipid metabolism. Indeed, it has become increasingly clear that while the lipids in lipoproteins are the transported moieties, the protein moieties of lipoproteins - the apoproteins - perform the crucial roles of transporting the lipids, and apoproteins can determine the levels of lipoprotein lipids. Therefore, attempts have been made to assess the relationships between plasma apoprotein concentrations and CHD. **Aim and Objectives:** To see the association of serum apolipoprotein A-I and B in patient with Coronary Heart Disease. **Materials and Methods:** The present study was conducted at Government Medical College and Hospital, Aurangabad. Levels of Apolipoprotein A-I and B in 60 Coronary Heart Disease patients admitted with first episode of coronary heart disease in ICCU were compared with 60 healthy apparently normal age, sex matched individuals. **Results**: it was observed that levels of apolipoprotein A-I and the ratio of apolipoprotein A-1 and B were decreased in CHD patients where as levels of apolipoprotein B was increased in CHD patients as compared to control group. And the difference was also statistically significant. **Conclusion:** concentration of apo A-I, apo B and its ratio can be a useful summary index of risk of CHD.

Keywords: Serum Apolipoprotein, Coronary Heart Disease.

Introduction

Incidence of coronary heart disease (CHD) has shown an upward trend in Indian in the last decade.[1] Atherosclerosis is the main cause of CHD. By the time the clinical manifestations of CHD including sudden death develop, the atherogenic process is far advanced. In 2001, Coronary Heart Disease caused 7.2 million deaths worldwide and accounted for loss of 59 million DALYs (Disability Adjusted Life Years). Each year there are about 5.8 million new CHD cases and about 40 million individuals with prevalent CHD are alive today.[2] It is thus imperative to identify and manage risk factors for coronary heart disease in order to prevent its development in asymptomatic individuals (primary prevention) as well as to avoid its recurrence in patient with established disease (secondary prevention).[3] Initially, estimation of serum lipids like Cholesterol and triglycerides were used to assess the risk of CHD. However, the correlation between serum Cholesterol and CHD is not ideal.[4] Inconsistency of such findings led to the development of better indicators like the lipoproteins for determining the risk. It is well documented that low HDL and high LDL levels are associated with higher risk for CHD.[5] But again, lipoprotein are not a sensitive index for determining the risk for atherogenicity.[6] In early seventies, Alaupovic[7] suggested that Apolipoprotein should also be considered when evaluating the contribution of lipids to presence of CHD. In addition, Onitri and Jover[8] suggested that Apoplipoprotein play an important role in many disorders of lipid metabolism. Indeed, it has become increasingly clear that while the lipids in lipoproteins are the transported moieties, the protein moieties of lipoproteins - the apoproteins - perform the crucial roles of transporting the lipids, and apoproteins can determine the levels of lipoprotein lipids. Therefore, attempts have be made to assess the relationships between plasma apoprotein concentrations and CHD.[9] Apolipoprotein B is present in very low density (VLDL), intermediate density lipoprotein (IDL), large buoyant LDL, and small dense LDL (sd-LDL), with one molecule of apo B in each of these atherogenic particles. Thus, total apo B reflects the total number of atherogenic particles. It is the apo B in the particle that leads to entrapment of these lipoproteins in the arterial wall. Apo B produced in the liver also stabilizes and allows the transport of cholesterol and triglycerides in plasma VLDL, IDL, large buoyant LDL, and sd-LDL. In addition, apo B serves as the ligand for the apo B and apo

B receptors thereby facilitating the uptake of cholesterol in peripheral tissues and the liver. Usually >90% of all apo B in the blood is found in LDL. In cases where LDL-C is in normal/low range, high apo B levels may indicate an increased number of sd-LDL particles, which are the most atherogenic particle because they are easily oxidized and promote an inflammatory response and the growth of plaques. Larger apo B containing particles, such as VLDL and IDL, can also enhance the risk of atherothrombosis by inhibiting the fibrinolytic system and by stimulating cytokine production and inflammatory reactions. Apo A-I is the major apolipoprotein in HDL particles and has a central role in the reverse cholesterol transport. Apo A-I can pick up excess cholesterol from peripheral cells and transfer it back to the liver in the HDL particles. The anti-atherogenic properties of apo A-I were recently documented. The ratio of apo A-I to apo B reflects the balance of cholesterol transport in a simple way. The lower the value of apo A-I/apo B ratio, the more cholesterol is likely to be deposited in the arterial wall thereby provoking atherogenesis and hence also increasing cardiovascular risk.[10]

Aim and objectives

To see the association of Associations of serum apolipoprotein A-I and B in patient with Coronary Heart Disease.

Materials and Methods

Study design: The present study was conducted at Government Medical College and Hospital, Aurangabad among the subjects those who were diagnosed of Coronary Heart Disease and admitted with either myocardial infarction or angina pectoris or ischemic Heart Disease in ICCU.

Type of study: case control study.

Study duration: January 2005 to January 2006.

Methodology:

Selection of cases and control:

Cases group: 60 patients with Coronary Heart Disease admitted to ICCU including male and female were taken with following inclusion and exclusion criterion.

Inclusion criteria

- Hospitalization with first time chest pain and fresh ECG showing sign of Ischemic changes.
- Patient between age group of 45-65 years.

Exclusion criteria

- Smoking
- Diabetes Mellitus
- Lipid lowering Drugs

Control Subjects: 60 healthy individuals with Age and sex matched were taken

Inclusion criteria

- Age and sex matched with patients
- No s/o ischemia or infraction like chest pain, sweating, vomiting etc.
- ECG not suggestive of myocardial infarction or ischemia.

Exclusion criteria

- Smoking
- Diabetes mellitus
- Lipid lowering Drugs (Statins)

All the details about the study were explained to the subject and informed consent was taken. Detail history of cases and controls was entered on proforma. Fasting blood sample were collected and analyzed for Apolipoprotein A-I and Apolipoprotein B. ratio of apolipoprotein A-I and B was also calculated. And the findings were also entered in proforma. The arithmetic mean (x), standard deviation (S.D.) were calculated for case and control group separately and compared by using unpaired t test.

Results

Table 1: Age and sex wise distribution of CHD patients and normal control subjects

Variable	CHD Patients (n=60)	Controls (n=60)
Male	39	42
Female	21	18
Age(yrs)	59.92 ± 5.40	55.18 ± 5.23

The study included a total number of sixty (60) coronary heart disease patients admitted in Medicine ICCU. Same number (60) age and sex matched apparently healthy normal subjects were studied as controls. It was observed there were 39 male and 21 female with an average age of 59.92 yrs suffering from CHD and control group of 42 male and 18 female with an average age of 55.18 yrs.

Table 2: Comparison Apolipoprotein A-I and B in CHD cases and control subjects

Parameters (mg/dl)	Cases (n=60) Mean ± S.D	Controls (n=60) Mean ± S.D	Unpaired t test	P value
Apo A-I	107.88 ± 13.33	133.07 ± 21.45	7.726	< 0.001
Apo B	128.12 ± 20.44	97.75 ± 13.989	9.497	< 0.001
Apo A-I/B Ratio	0.8567 ± 0.1365	1.3796 ± 0.2625	13.689	< 0.001

It was observed that level of apolipoprotein A-1 decreased in case group as compared to control group whereas level of apolipoprotein B increased in case group. Mean level of apolipoprotein A-1 in case group was 107.88 with SD 13.33 whereas mean level of apolipoprotein A-1 in case group was 133.07 with SD 21.45 and the difference was statistically significant. Level of apolipoprotein B in case group was 128.12 ± 20.44 whereas in case group it was 97.75 ± 13.989 and

the difference was statistically significant. When the ratio of apolipoprotein A-1 and B was compared, it was observed that the mean difference in the level of these two lipoporteins was statistically significant.

Table 3: Comparison Apolipoprotein A-I and B in Male CHD cases and control subjects

Parameters (mg/dl)	Cases (n=39) Mean ± S.D	Controls (n=42) Mean ± S.D	Unpaired t test	P value
Apo A-I	108.69 ± 12.99	133.98 ± 21.94	7.37	< 0.001
Apo B	126.97 ± 19.76	98.31 ± 14.69	7.36	< 0.001
Apo A-I/B Ratio	0.8726 ± 0.1454	1.3698 ± 0.2615	10.67	< 0.001

Comparison of level of apolipoprotein A-I and B in Male CHD cases and control subjects was done and it was observed that the difference in the level in these two groups was statistically significant. The ratio of apolipoprotein A-1 and B in case group was decreased as compared to control group. And the difference was also significant.

Table 4: Comparison Apolipoprotein A-I and B in female CHD cases and control subjects

Parameters (mg/dl)	Cases (n=21) Mean ± S.D	Controls (n=18) Mean ± S.D	Unpaired t test	P value
Apo A-I	106.38 ± 13.19	130.78 ± 19.07	4.57	< 0.001
Apo B	130.24 ± 20.62	96.44 ± 11.52	6.43	< 0.001
Apo A-I/B Ratio	0.8205 ± 0.1045	1.3743 ± 0.2617	8.42	< 0.001

The table no. 4 shows very high significant increase in level of Apolipoprotein B in case group. Whereas decrease in Apolipoprotein A-I / B ratio was observed in female case group with significant statistical difference.

Discussion

In the present study we compared apolipoproteins A-I and B in 60 Coronary Heart Disease patients admitted with first episode of coronary heart disease in ICCU of Government Medical College, Aurangabad with 60 healthy apparently normal age, sex matched individuals. There were 39 male and 21 female with an average age of 59.92 yrs suffering from CHD and control group of 42 male and 18 female with an average age of 55.18 yrs. It was observed that apolipoprotein A-I was decreased with very high statistical significance in CHD patients as total and also in male and female group. The values are 107.88 ± 13.33 mg/dl in total CHD group against 133.07 ± 21.45 mg/dl in matched control group with p<0.001. In male CHD patient apolipoprotein A-I was 108.69 ±12.99 mg/dl against 133.98 ± 21.94 mg/dl in controls, p<0.001 and in females it was 106.38 ± 13.19 mg/dl in CHD against 130.78 ± 19.07mg/dl, p<0.001. Transport of cholesterol and formation of HDL-cholesterol are the basic role of apolipoprotein A-I, low levels of this protein have been identified as a risk factor in the development and progression of coronary damage.[11] It was suggested by Avogaro P *et al* (1979)[6] that plasma apolipoprotein A-I measurements may provide more information than HDL levels in the assessment of CHD risk. Our findings correlates with the findings of Histoshi Kukita *et al* (1985)[12], Wolfgang Schwantzkopff *et al* (1990)[13], Peter Kwiterovich *et al* (1992)[14], V.K. Bahl *et al* (1994)[15], M.S. Graziani *et al* (1998)[16], Goran Walldius *et al* (2001)[17]. Gerald Luc *et al* (2002)[18] in PRIME study stated that among the parameters related to HDL, apolipoprotein A-I appears to be the strongest independent risk factor. P.P. Jadhav *et al* (1993)[4] and Johan Franzen *et al* (1986)[19] found significantly decrease levels of apolipoprotein A-I in survivors of myocardial infarction with normal levels of HDL. Apolipoprotein B in our study was increased in CHD patients as total group and also in male and female CHD group as compared with their age and sex matched controls, statistically showing very high significance. Serum apolipoprotein B levels in CHD patients were 128.12 ± 20.44 mg/dl as compared to 97.75 ± 13.98 mg/dl, p<0.001 and in males the values of apolipoprotein B in CHD cases were 126.97 ± 19.76 mg/dl against 98.31 ± 14.69 mg/dl in controls (p<0.001) and in females 130.24 ± 20.62 mg/dl in CHD patients against 96.44 ± 11.52 mg/dl in normal healthy controls (p<0.001). Apolipoprotein B is present in very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), LDL, small dense LDL (sd.LDL) with one molecule of apolipoprotein B in each of these atherogenic particles. Thus plasma apolipoprotein B concentration is equivalent to the number of atherogenic particles.[10] Our finding are well correlated with findings of Michael F.Reardon *et al* (1985)[20], Histoshi Kukita *et al* (1985)[12], Wolfgang Schwartzkopff *et al* (1990)[13], M.J. Stampfer *et al* (1991)[21], P.P. Jadhav *et al* (1993)[4], V.K. Bahl *et al* (1994)[15], Benoit Lamarche *et al* (1996)[22], Christa Meisinger e al (2004)[23], Tobais Pischon *et al* (2005)[31], all of whom found apo B as a strong predictors of CHD. Apolipoprotein B was found to be better index of risk in many prospective studies like AMORIS (2001)[12], Quebec (1996)[22], and EARS (1994)[24]. In P.N. Durrington's study (1988)[25] apolipoprotein B emerged as the main lipoprotein determinant of coronary disease risk. Peter O. Kwiterovich *et al* (1992)[14] concluded that 'nontraditional risk factors' (plasma apo A-I and B levels) are better predictor of premature coronary heart disease than are plasma lipoprotein. C. Snehalatha *et al* (2002)[26] found

that hyper apo B was more common than hyper LDL cholesterol in CAD subjects and apo B abnormalities exist in large percentage of CAD subjects despite having normal levels of LDL cholesterol. The ratio of apolipoprotein A-I and apolipoprotein B was found to be the most significant of all the parameters in our study. It was 0.8567 ± 0.1365 in CHD patients against 1.3796 ± 0.262 in controls, $p<0.001$. In male CHD patients the ratio was 0.8726 ± 0.145 and 1.369 ± 0.261 in male controls, $p<0.001$. In females 0.8205 ± 0.104 was the ratio of apolipoprotein A-I, B in CHD patients and 1.3743 ± 0.261 in normal matched controls with $p<0.001$. The ratio of apolipoprotein A-I to apolipoprotein B reflects the balance of cholesterol transport in a simple way. It is a useful summary index of risk and that it is at least as good as, and often better than, the conventionally used LDL-C. There are a number of user friendly reasons for adopting this ratio into clinical practice. Since the analyses can be made on non-fasting samples this is of great practical advantage for patients and physicians over the other methods, which usually need fasting. Furthermore, the results can be expressed as one number for the ratio only, rather than by many values for LDL, HDL, triglycerides and lipid ratio.[40] The finding of ratio of apolipoprotein A-I to apolipoprotein B in our study are similar to finding reported by G. De Baker *et al* (1982)[27], Steven P. Sedlis *et al* (1986)[9], Wolfgang Schwartzkopff *et al* (1990)[13], P.P. Jadhav *et al* (1993)[4], Sahi N. *et al* (1993)[28], Bahl V.K. *et al* (1994)[15], Goran Walldius *et al* (2001)[17], Philippa J. Talmud *et al* (2002)[29], Adnan Qureshi *et al* (2002)[30], Christa Meisinger *et al* (2004)[31]. Bahl V.K. *et al* (1994)[15] reported that apo B and triglyceride levels showed larger univariate difference between the normal group and the group with CAD. The variable with the strongest predictive power of CAD was the ratio of apolipoprotein A-I to B. Goran Walldius *et al* (2001)[17] in their AMORIS 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* (2002)[30] found that apo A-I to B ratio was inversely associated with myocardial infarction and may be an important protective clinical marker for atherosclerosis. At the same time apolipoprotein B concentration alone were not found associated with myocardial infarction by him. Christa Meisinger *et al* (2004)[31] stated that the result for apolipoprotein B levels and the apolipoprotein B/A-I ratio remained significant even when adjusted for age, smoking, alcohol, body mass index, diabetes and hypertension.

Conclusion

From the above discussion, it is clear that the concentration of apo A-I, apo B and its ratio can be a useful summary index of risk and that it is at least as good as, and often better than, the conventionally used lipid parameters.

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