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Body Mass Index, Blood Lipid and Apolipoprotein levels and Coronary Heart Disease among middle aged Punjabi Khatris of Northwest India

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ABSTRACT

Background: *Studies have suggested that an elevated plasma concentration of apolipoprotein (apo) B coupled with obesity may be considered as an important risk factor for coronary heart disease (CHD) than the traditional lipid factors. Coronary artery disease (CAD) is a multifactorial disease resulting from interaction among various hereditary, cultural and environment factors. Population specific studies are rare.*

Aim: *The aim of this study was to evaluate the association of body mass index (BMI), blood lipids and apolipoproteins with the CAD among the Khatri caste, which is an indigenous population of Northwest India.*

Materials and Methods: *The study was carried on 150 CAD patients and 150 normal controls belonging to the Punjabi Khatri caste ranging in age from 35–45 years. Height and body weight was measured using standard techniques. Blood was drawn from each subject to analyze serum concentrations of lipids and apolipoproteins.*

Results: *The study demonstrated that CAD patients had elevated BMI in both males and females than normal controls. Apo B levels were an important predictor of CAD. ApoA/ApoB ratio among CAD patients was 0.74 compared with 1.53 in normal subjects; controls had 105.79% higher ApoA/ApoB ratio than CAD subjects. Total cholesterol, LDL-C, triglycerides, LDL-C/HDL-C ratio of the two groups also showed significant differences. Prevalence of obesity in CAD patients was 70.7% compared with 10% in normal controls.*

Conclusions: *Apo B levels were found to the best predictor of CAD, even though significant differences were also found between CAD and normal subjects for other lipoprotein traits. Obesity was high CAD patients than normal controls.*

Keywords: *CAD, Body Mass Index, lipid profile, apolipoproteins.*

INTRODUCTION:

Asian populations have experienced spurt in chronic diseases later than the western populations. South Asia, where infectious diseases are still highly prevalent, has suffered much more after this transition, as the prevalence, incidence and mortality from coronary artery disease (CAD) among them have been reported to be higher than among the western and other Asians, irrespective of whether they live in India or abroad (Reddy 2007, Gupta 2008, Murthy et al. 2012). The prevalence of CAD doubled to 3 to 4% in rural India and quadrupled to 9 to 11% in urban India over the past four decades (Reddy 2007, Gupta 2008). Heart diseases are rising in Asian Indians 5–10 years earlier than in other populations around the world with the mean age for first presentation of acute myocardial infarction in Indians is 53 years (Sharma and Ganguly 2005). This increasing burden of chronic diseases may be attributed to demographic transition coupled with unplanned urbanization, food habits, lifestyle changes and genetic factors.

Epidemiologic studies have shown that an increased risk of coronary artery disease exists with elevated level of total cholesterol, very low density lipoproteins (VLDL), low density lipoproteins (LDL) and lower levels of high density lipoproteins (HDL)(Arsenault et al. 2009).However, it is yet difficult to define the independent contribution of several interrelated abnormalities in lipoproteins to atherogenesis. In this context, Lamarche et al. (1997) argue that despite the association between LDL levels and CAD is well accepted but yet a relatively high proportion of cases with CHD have LDL in the normal range. There are several possible explanations for the absence of a positive association between total cholesterol and vascular mortality. For example, the total cholesterol level in the elderly people may not represent their lifetime exposure, because of many lifestyle factors and diseases that may modulate it with advancing age (Lindberg et al. 1995).

Several additional components of the lipoprotein system have been identified and are under evaluation. These components include apolipoprotein subclasses, HDL subclasses, small dense LDL particles, remnants of chylomicrons and VLDL, IDL and Lp (a). Apolipoproteins binds lipids to form lipoproteins. Lipoproteins particles contribute to overall metabolic homeostasis by transporting hydrophobic lipids in the blood plasma to and from different tissues in the body;

very-low-density lipoprotein (VLDL) is the principal vehicle for the transport of endogenous triglyceride (TG), and its metabolic product, low-density lipoprotein (LDL) transports cholesterol(Mason 1998).The main structural protein of VLDL is called apolipoprotein (apo) B-100 (Apo B). Apo B formation and degradation are two major points of regulation of VLDL secretion (Mason 1998). Numerous epidemiological studies have shown that plasma LDL and high density lipoproteins (HDL) cholesterol are important risk factors for CAD. The indices such as totalcholestrol/HDL and LDL/HDL cholesterol ratios; and apolipoprotein B, the protein moiety of LDLmay also be relevant predictors of CAD (Reviewed in McGrowder et al. 2011, Bambauer et al. 2012). Apolipoprotein A-I (Apo-A1) has molecular mass of 28 kDa and it is the major structural HDL apolipoprotein and accounts for 70% of total HDL protein, whereas the second major HDL apolipoprotein, apoA-II, represents the 20% that constitutes approximately 70% of the protein in HDL (Superko2009). ApoA contains domain that are very similar to plasminogen. The main function of plasminogen is to dissolve fibrin blood clots.

Increased body weight has been associated with an increased risk of morbidity and mortality from coronary artery disease in several populations (Ford et al. 2007, Beaglehole and Bonita 2008, WHO 2009). Body mass index (BMI), expressed as body weight in kilograms divided by height in square meters (kg/m^2), is highly correlated with body weight and poorly correlated with height (Willett 1990) and is frequently used as a measure of obesity in large epidemiological studies. Lamon-Fava et al. (1996) studied the distribution of BMI in men (mean age, 49 ±10 years) and women (mean age, 49 ± 10 years) and the association of BMI with known CHD risk factors. They found in men, BMI increased with age until age 50 years, when it reached a plateau. In women, there was a trend toward an increase in BMI with age up to the seventh decade of life. Seventy-two percent of men and 42% of women had a BMI ≥25.00, the cutoff point for the definition of overweight. They further found in age-adjusted analyses that BMI was significantly and linearly associated with systolic blood pressure, fasting glucose levels, plasma total cholesterol, VLDL cholesterol, and LDL cholesterol levels and was inversely and linearly associated with HDL cholesterol levels ($P < .001$) in nonsmoking men and women. The association between BMI and apolipoprotein B and A-I was similar to that of LDL and HDL cholesterol, respectively. LDL size was also linearly associated with BMI: subjects with higher

BMI had smaller LDL particles. However they did not find association of Lipoprotein (a) levels with BMI in this population.

The present study was undertaken to compare blood lipid profile, apolipoproteins and BMI of coronary artery disease patients with normal controls drawn from an endogamous caste group of Khatris of Northwest India and to analyse whether apoA/ apo B ratio be used as a more accurate lipid risk factor.

MATERIALS AND METHODS

This cross sectional study was carried out on 150 diagnosed cases of CAD (75 males and 75 females) and 150 normal controls CAD (75 males and 75 females) belonging to Khatri caste of Punjab. The study sample was drawn from the department of Biochemistry and department of Cardiology, Christian Medical College and Hospital, Ludhiana and G. B. Pant Hospital, New Delhi. The controls were drawn from those who had visited for routine and normal checkup and had no history of CAD**.** Each subject was administered a health and lifestyle questionnaire schedule, which included questions on weight, height, socio-demographic details, medical history, and lifestyle habits. All participants gave their written consent voluntarily to take part in the study. The inclusive criterion was that the subjects should be belonging to Khatri caste and between 35 -45 years of age. The subjects younger than 35 and older than 45 years and not belonging to Khatri caste, and those who refused to participate in the study were excluded. Apart from these the exclusion was made if the patient suffered from any of the following conditions: congenital heart disease, valvular heart disease, dilated cardiomyopathy, recent myocardial infarction of less than 6 weeks duration prior to admission. Levels of educational attainments and yearly family income were comparable among CAD patients and controls and there were no statistically significant differences.

Their height was measured in centimeters and weight in kilograms. BMI was calculated by the following formula: BMI = Body Weight in Kilograms / Height (square meters). Five milliliter of blood was drawn from each subject, after a 12- to 14-hour fast, in 0.1% EDTA tubes. Lipid Profile estimation was done on automated analyzer — Hitachi – 902. Total cholesterol was estimated by colorimetric analysis. The other components of lipid profile were estimated as follows:

TRIGLYCERIDES**:** Triglycerides levels were estimated using GPO-PAP enzymatic colorimetric analysis in human serum on Roche autoanalyzer (Hitachi – 902).

HDL-CHOLESTEROL**:** HDL - C was measured directly by homogeneous enzymatic colorimetric test in human serum on Roche autoanalyzer (Hitachi-902).

LDL-CHOLESTEROL**:** LDL- Cholesterol was estimated by using Homogeneous Enzymatic Colorimetric assay for its direct quantitative determination in human serum on automated analyzer-Roche (Hitachi 902).

APOLIPOPROTEIN B**:** It was quantitatively estimated by Immunoturbidimetric immunoassay with Randox kit in serum on semiautomated analyzer — Clima Plus. (Cat. No. LP 2117) (Labeur et al, 1990)

APOLIPOPROTEIN A-1**:** It was quantitatively estimated by Immunotrubiditnetric Immunoassay with Randox kit in serum on semiautomated analyzer Clima Plus. (Cat. No. LP 2117) (Labeur et al, 1990).

VLDL-Cholesterol was calculated by TG/5.

Statistical Analysis

Data was recorded on a predesigned proforma and managed in a Microsoft Excel spreadsheet. All the entries were double checked for any possible keyboard error. The data was subjected to statistical analysis using Stata software. The descriptive data is presented as mean and standard deviation for the continuous variables and as absolute quantities and percentages for the discrete parameters. The correlation coefficient was worked out to find out the degree of association between anthropometric parameters on the one-side and lipid fractions on the other.

RESULTS

Table 1 summarizes the results of descriptive analysis t-tests comparing means of body mass index and various characteristics of the of plasma lipid and apolipoprotein levels (mg/dl) of men and women CAD subjects and controls. CAD subjects (both males and females) had significantly higher body mass index (BMI), blood levels of total cholesterol, triglycerides, low density lipoproteins (LDL), very dense lipoproteins (VLDL) and Apo B levels than controls. CAD subjects had 27% triglycerides, 24% total cholesterol, 25% VLDL, 47.5% LDL and 68.4% Apo B than normal controls. On the contrary, normal subjects had 27% higher blood levels of high density cholesterol (HDL) and 23% of Apo A than CAD patients. ApoA/ApoB ratio among

CAD patients was 0.74 compared with 1.53 in normal subjects; normal controls had 105.79% higher ApoA/ApoB ratio than CAD subjects.

The frequency distribution of the subjects according to different categories of BMI is shown in Table 2. The proportion of the normal controls having normal BMI value (ranging18.0-22.99 kg/m^2) was much greater (20%) than that of CAD patients (1.3%). As expected, the prevalence of obesity in CAD patients was much higher (70.7%) compared with 10% in normal controls. The differences were statistically significant. Prevalence of obesity grade II was low (0.7%) in CAD patients, and zero in normal controls. Among Asian Indian subjects, escalating population-wide generalized obesity correlates strongly with increasing cardiovascular risk factors (Gupta and Gupta 2008).

DISCUSSION

The present study finds significant differences between CAD subjects and normal controls for various lipoprotein traits and BMI. ApoB level was significantly higher in CAD subjects than normal and so also ApoA/ApoB ratio. It has now been widely argued that Apo B plays important roles for the hepatic secretion of VLDL and metabolism and clearance of triglycerides from the circulation (Young1990). Thus, for a given cholesterol concentration, a high number of apo B - containing lipoproteins will result in the presence of an elevated number of small, dense LDL particles, which have been associated with an enhanced risk of IHD (Austin et al. 1990). Patients with CAD may be characterized by increased transport rates of LDL apo B (Kesaniemi1985).Our results are consistent with other such case-control reports that supported the role of apo B as an important risk factor for CAD (Genest et al. 1992, Olofson et al. 2007, Philip et al. 2011).

According to World Health Organization (1998) and National Institutes of Health (1998) have set normal range of BMI at 19–24·9 kg/m^2, overweight at 25–29·9 kg/m^2, and obese at $\geq$ 30 kg/m^2. Japan Society for the Study of Obesity (JASSO) decided to define BMI $\geq$ 25 as obesity (Kanazawa et al. 2002). The findings of the present study are on the expected lines. Prevalence of obesity was higher in CAD patients than controls among middle aged adult *Khatris* of Punjab. When compared with other Indian studies, prevalence of obesity was lower in the present sample of normal controls (10%) than that reported among urban females (25.3%) by Sidhu and Tatla

(2002), but prevalence of overweight and obesity put together was higher in the present sample (80%) than urban females (45.3%). Gopalan (1998) found The Nutrition prevalence of overweight and obesity as 50% and 14%, respectively. Among Asian Indian subjects, generalized obesity correlates strongly with increasing cardiovascular risk factors (Gupta and Gupta 2008).

Conclusion

Apolipoproteins are the significant predictors of the coronary artery disease. The predictive ability of ApoA/ApoB ratio was also better than ApoB, apoA values. Thus ApoA/ApoB ratio is a better marker of cardiovascular risk and their inclusion in further clinical guidelines should not be discarded.

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Table 1: Mean standard deviation of plasma lipid and apolipoprotein levels (mg/dl) of men and women CAD patients and controls

		FEMALES		t-test	**MALES**			t-test	**OVERALL**			t-test
	N	Mean	σ	p	N	Mean	σ	p	Total	Mean	σ	p
Triglycerides (TG) (mg/dl)												
CAD	75	144.940	57.553		75	178.027	57.615		150	161.487	59.742	
CONTROL	75	113.040	25.233	0.000	75	141.013	27.702	0.000	150	127.027	29.905	0.000
Total	150	128.993	47.091		150	159.520	48.729		300	144.257	50.221	
Total cholesterol (TC) (mg/dl)												
CAD	75	194.560	43.507		75	199.813	41.810		150	197.187	42.605	
CONTROL	75	157.760	22.664	0.000	75	159.173	20.953	0.000	150	158.467	21.763	0.000
Total	150	176.160	39.192		150	179.493	20.953		300	177.827	38.944	
High-density lipoproteins (HDL) (mg/dl)												
CAD	75	40.200	15.848		75	34.160	9.632		150	37.180	13.416	
CONTROL	75	48.770	7.404	1.000	75	45.520	5.967	1.000	150	47.147	6.898	1.000
Total	150	44.480	13.056		150	39.840	9.810		300	42.163	11.761	
Low-density lipoproteins (LDL) (mg/dl)												
CAD	75	125.596	42.134		75	131.240	40.260		150	128.418	41.166	
CONTROL	75	88.236	22.165	0.000	75	85.849	16.870	0.000	150	87.042	19.667	0.000
Total	150	106.916	38.431		150	108.545	38.274		300	107.730	38.297	
Very-Low-density lipoproteins (VLDL) (mg/dl)												
CAD	75	28.989	11.511	0.000	75	39.963	8.362	0.000	150	34.476	11.438	0.000
CONTROL	75	22.608	5.046		75	32.448	5.300		150	27.528	7.139	

Total	150	25.798	9.418		150	36.205	7.930		300	31.002	10.134	
APO A (mg/dl)												
CAD	75	101.848	14.590		75	97.997	9.347		150	99.923	12.363	
CONTROL	75	125.691	17.151	1.000	75	120.317	18.818	1.000	150	123.004	18.145	1.000
Total	150	113.769	19.872		150	109.157	18.564		300	111.463	19.336	
APO B (mg/dl)												
CAD	75	131.622	26.635		75	149.299	17.209		150	140.461	24.043	
CONTROL	75	84.977	16.538	0.000	75	81.809	15.934	0.000	150	83.393	16.262	0.000
Total	150	108.300	32.183		150	115.554	37.677		300	111.927	35.167	
APO A/B ratio												
CAD	75	0.822	0.291		75	0.665	0.102		150	0.743	0.231	
CONTROL	75	1.547	0.408	0.000	75	1.512	0.296	0.000	150	1.529	0.356	0.000
Total	150	1.18	0.507		150	1.089	0.391		300	0.028	0.494	
BMI(kg/m^2)												
CAD	75	31.145	2.126		75	30.262	1.516		150	30.703	1.893	
CONTROL	75	26.431	2.667		75	27.707	1.624		150	27.069	2.292	
Total	150	28.788	3.372	0.000	150	28.984	2.024	0	300	28.886	2.778	0.000

Table 2 Comparison of BMI categories between CAD patients and controls

BMI category		**CAD**		**Controls**		**X^2 value**	**p**
BMI		**N**	**(%)**	**N**	**(%)**		
18.5-24.9	Normal	2	1.3	30	20		
25.0-30.0	Overweight	42	28	105	70		
30.0-35.0	Obesity (Grade I)	105	70	15	10		
35.0-40.0	Obesity II (Grade II)	1	0.7	0	0		
Total		150	100	150	100	120.00	0.000