Original Article

HYPERTRIGLYCERIDEMIA AND LOW HDL-CHOLESTEROL ARE THE MAJOR LIPID ABNORMALITIES IN NORMAL PAKISTANI ADULTS:

Are these contributing to the high rates of coronary artery disease in this population?

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ABSTRACT

Objective: Lipid abnormalities are related to enhanced risk of developing cardiovascular disease. The objective of the study was to investigate variability in lipid profile in Pakistani normal adults (from the personnel of 4 tertiary care hospitals) by age, gender, body mass index (BMI) and smoking, and to determine the prevalence of hypertriglyceridemia, hypercholesterolemia, "low HDL-cholesterol" and "isolated low HDL-cholesterol" in this population.

Method: Serum samples from 323 normal healthy subjects (236 males and 87 females, age 30-70 years) from the personnel of the Aga Khan University, Civil Hospital, Karachi, Armed Forces Institute of Cardiology and Military Hospital, Rawalpindi were analyzed for total cholesterol, HDL-cholesterol and triglycerides using kit methods. LDL-cholesterol was determined using the Friedewald formula.

Results: Mean ± SD concentrations of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides were found to be 165±37 mg/dl, 37±11.5 mg/dl, 98±34 mg/dl and 155 ± 88 mg/dl, respectively. Mean levels of total cholesterol were found to be significantly higher in hypertriglyceridemia (>200mg/dl) than normotriglyceridemia (181±30 mg/dl vs 160±38 mg/dl; p=0.001). Mean concentration of HDL-cholesterol in the younger age group (<50 years) was found to be significantly higher than the value in the older (>50 years) group (39.6±11.7 mg/dl vs 33.4±9.7 mg/dl; p=0.001). Similarly, mean concentration of HDL-cholesterol in females was significantly higher compared to males (44.3±14 mg/dl vs 34.9±9.1 mg/dl; p=0.001). In hypertriglyceridemia (>200 mg/dl), mean HDL-concentration was significantly lower compared to normotriglyceridemia (33.4±8.3 mg/dl vs 38.9±12 mg/dl; p=0.001). The combined effect of age, gender and triglyceridemia was found to be significantly associated with HDL-cholesterol concentration ($p<0.001$; $R^2=0.202$). Mean triglyceride levels among males were significantly higher than among females (166±88 mg/dl vs 127±83 mg/dl; p=0.001). Similarly, among overweight/obese individuals (BMI>25), triglyceride levels were significantly higher compared to those with BMI<25 (180±107 mg/dl vs 144±71 mg/dl; p=0.001). Levels of triglycerides were, therefore, significantly associated with gender and BMI ($p<0.001$; $R^2=0.076$). LDL-cholesterol levels were not found to be significant by age, gender, smoking, BMI and triglyceridemia. Smoking had no significant effect on lipid levels of male healthy subjects. Frequencies of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" and "isolated low HDL-cholesterol" were found to be 17.6%, 26.9%, 45.8% and 29.4%, respectively. High prevalence values of "low HDL-cholesterol" and "isolated low HDL-cholesterol" are reported for the first time in Pakistani normal adults and require further studies at the community level.

Conclusion: High levels of triglycerides and low levels of HDL-cholesterol are the most prominent abnormalities in Pakistani adults working in tertiary health care centers.

KEY WORDS: Total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, normal adults, low HDL-cholesterol, isolated low HDL-cholesterol, lipid profile, Pakistani

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INTRODUCTION

Pakistanis belong to an ethnic group, which has the highest rates of coronary heart disease (CHD).[1] According to the official estimates, cardiovascular disease (CVD) results in more than 100,000 deaths every year[2,3], however, the actual figure may be much higher than that.

Risk factor studies have shown that urban Pakistanis have a unique dyslipidemia characterized by hypercholesterolemia.[4] A number of studies carried out overseas on South Asians revealed high levels of triglycerides and low levels of high density lipoprotein (HDL)-

cholesterol in this ethnic group.[5-10] With the exception of a couple of reports[11,12], no detailed studies have been published on variability in lipid profile in Pakistani normal healthy adults due to age, gender, body mass index (BMI) and smoking. Moreover, no studies have been carried out to determine the prevalence of "low HDL- cholesterol" and "isolated low HDL-cholesterol" in Pakistani population.

The present study was undertaken to investigate the changes in lipid profile in Pakistani normal adults (working in 4 tertiary health care centers) due to age, gender, BMI, smoking, and triglyceridemia and also determine the prevalence of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" & "isolated low HDL-cholesterol" in this population.

METHODS

In this cross-sectional study, three hundred and twenty three normal healthy subjects (age, 30-70 years) were selected from the personnel of the Aga Khan University, Karachi, and Civil Hospital, Karachi, (from January 2003 to December 2003), and Armed Forces Institute of Cardiology, Rawalpindi and Military Hospital, Rawalpindi (August – September 2003) by convenience sample design. This population included the doctors, nurses, teaching faculty, technicians and nonmanagement nontechnical staff of the hospital / institute.

Exclusion Criteria

On the basis of history, those suffering from diabetes mellitus, hypertension, liver disease, malabsorption syndrome, uremia, cancer, tuberculosis or having pregnancy were excluded from the study. The study was approved by the Ethical Committee of the institution.

Sample collection

Five ml venous blood was collected from subjects and immediately transferred to plain tubes. After clotting, the serum was separated by centrifugation and stored at -60°C until analysis. Total cholesterol, high density lipoprotein (HDL)-cholesterol, and triglycerides were analyzed using colorimetric kit methods (RANDOX, UK). The concentration of low density lipoprotein (LDL)-cholesterol was calculated using the formula by Friedewald *et al.*[13]

Statistical analysis

Frequencies of all variables were generated. Means and standard deviation (SD) values of all quantitative variables like total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides were computed. Independent samples t-test, chi-square test and simple linear regression were used to test the significance at the univariate level. Multiple linear regression was used to test the significance at multivariable level. All variables with p-value <0.20 were considered for multivariable analysis. SPSS® (statistical package for social sciences) Software version 10 for Windows® was used for this purpose. The variable of smoking status was only considered for males as there were only 3 female smokers in the study subjects. For comparison of lipid levels in younger and older groups, the subjects were divided into those above 50 years and those below 50 years. This cut-off age of 50 years was chosen to exclude the effect of female sex hormones on lipid levels in older females because the usual age of menopause in female population is considered to be ~49 years. In all the analyses, a p-value of <0.05 was considered significant. All mean values were presented as means ± SD.

Table I: Demographic and clinical characteristics of normal healthy subjects (n=323)

Variable	*Value (mean ± SD)*	*Subjects (%)*
Age (years)	46±11.1	
Gender Male		236(73.1)
Female		87(26.9)
BMI (kg / m^2)	23.8± 4.8	
Smoking Yes		49(15.4)
No		270(84.6)
Glucose (mg / dl)	92 ± 25	
Cholesterol (mg / dl)	165 ± 37	
Triglycerides (mg / dl)	155± 88	
HDL-cholesterol (mg / dl)	37±11.5	
LDL-cholesterol (mg / dl)	98 ± 34	

Definition of variables:

* Body mass index (BMI): A BMI greater than 25 was classified as overweight and greater than 30 as obese.
* Hypercholesterolemia: Serum cholesterol level > 200 mg / dl.
* Hypertriglyceridemia: Serum triglyceride level > 200 mg / dl.
* Low HDL-cholesterol: Serum HDL-cholesterol level < 35 mg / dl.
* Isolated low HDL-cholesterol: Serum HDL-cholesterol level < 40 mg / dl and serum triglyceride level < 150 mg / dl.
* Smoking: Smoking cigarettes or "beerri" (one or more per day).

RESULTS

Table-I shows the demographic and clinical characteristics of normal healthy subjects. There were 236 males and 87 females. Mean age of the group was 46±11.1 years. Mean BMI was 23.8±4.8, while mean fasting level of serum glucose was 92±25 mg / dl. 15.4% of them were smokers. Among 49 smokers, only 3 were females. Mean values of serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides were 165 ± 37 mg / dl, 37±11.5 mg / dl, 98±34 mg / dl and 155±88 mg / dl, respectively.

Table-II shows the effect of age, gender, smoking, BMI and triglyceridemia on lipid levels of

Table II: Effect of age, gender, smoking, body mass index (BMI) and triglyceridemia on serum levels of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides in normal healthy subjects

Mean ± SD

Factors	*Number (n)*	*Lipid concentration (mg/dl)*			
		Total Cholesterol	*HDL-cholesterol*	*LDL-cholesterol*	*Triglycerides*
Age (years)					
<50	206	165±37	39.6±11.7	96±34	155±89
≥50	116	166±38	33.4±9.7	102±34	156±87
		(p value=0.692)	*(p value=0.001)**	*(p value=0.111)*	*(p value=0.893)*
Gender					
Female	87	169±34	44.3±14	102±37	127±83
Male	236	64±38	34.9±9.1	97±32	166±88
		(p value=0.307)	*(p value=0.001)**	*(p value=0.227)*	*(p value=0.001)**
Smoking**					
Yes	46	161.5±42	33.6±8.88	93.8±35.4	172±112.4
No	191	164.5±37.7	35.2±9.14	97.1±31.8	164.4±81.7
		(p-value=0.642)	*(p-value=0.289)*	*(p-value=0.538)*	*(p-value=0.603)*
BMI (kg / m^2)					
<25	186	163±38	37.8±11.4	98±33	144±71
>25	125	169±37	36.3±11.4	97±35	180±107
		(p value=0.140)	*(p value=0.261)*	*(p value=0.710)*	*(p value=0.001)**
Triglyceridemia(mg / dl)					
<200	237	160±38	38.9±12	99±34	-
>200	86	181±30	33.4±8.3	94±32	-
		*(p value=0.001)**	*(p value=0.001)**	*(p value=0.201)*	

* Significant at $p<0.05$

** Among males only (n=237)

normal healthy adults. Mean total cholesterol concentration was found to be significantly higher (p=0.001) in hypertriglyceridemia (triglyceride levels >200 mg/dl) compared to normotriglyceridemia (triglyceride levels <200 mg/dl). Mean HDL-cholesterol concentration was significantly higher among the younger age group (<50 years) compared to the older (>50 years) group (p=0.001). Similarly, mean HDL-cholesterol levels were also found to be significantly higher among females as compared to males (p=0.001). In hypertriglyceridemia, mean concentration of HDL-cholesterol was, however, significantly lower than the concentration in normotriglyceridemia (p=0.001). Combined effect of age, gender and triglyceridemia was found to be significantly associated with HDL-cholesterol concentration (p<0.001; R^2=0.202; Table III). LDL-cholesterol levels were not found to be significant by age, gender, smoking, BMI and triglyceridemia. However, mean triglyceride levels were significantly higher among males compared to females (p=0.001) and among overweight/obese vs those with BMI<25 (p=0.001). The combined effect of gender and BMI on triglyceride levels yielded significant association by multivariable analysis (p<0.001; R^2=0.076; Table-III).

Prevalence of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol", "isolated low HDL-cholesterol" is shown in Table-IV. The frequencies of hypercholesterolemia, hypertriglyceridemia, "low HDL-cholesterol" and "isolated low HDL-cholesterol" were found to be 17.6%, 26.9%, 45.8% and 29.4%, respectively. A comparison of percentages in male and female groups using chi square test revealed the prevalence of hypertriglyceridemia and "low HDL-cholesterol" to be significantly higher in males compared to females (p= 0.0002).

Table III: Effect of factors (age, gender, BMI and triglyceridemia) on lipid levels in normal healthy subjects using crude and adjusted regression coefficients

Factors	*Lipid concentration (mg/dl)*			
	HDL-cholesterol		*Triglycerides*	
	Crude slope (SE)	*Adjusted slope (SE)*	*Crude slope (SE)*	*Adjusted slope (SE)*
Age (years)				
<50	-	-	-	-
≥50	-6.24(1.28)	-5.54(1.20)	-	-
Gender				
Female	-	-	-	-
Male	-9.45(1.34)	-8.02(1.33)	39.44(10.83)	39.30(11.09)
BMI (kg/m^2)				
<25	-	-	-	-
≥25	-	-	35.68(10.05)	37.28(9.88)
Triglyceridemia (mg/dl)				
<200	-	-	-	-
≥200	-5.42(1.41)	-3.48(1.33)	-	-
Constant	-	46.17	-	113.9
R^2	0.202		0.076	

SE= Standard Error

Table IV: Prevalence of hypercholesterolemia, hypertriglyceridemia, low HDL-cholesterol and isolated low HDL-cholesterol in normal healthy subjects

Variable	*Frequency (%)*			*P-value**
	Males (n=236)	*Females (n = 87)*	*Total (n=323)*	
Hypercholesterolemia (<200 mg/dl)	43 (18.2)	14(16.1)	57(17.6)	0.68
Hypertriglyceridemia (>200 mg/dl)	77(32.6)	10(11.5)	87(26.9)	0.0001
Low-HDL-cholesterol (<35 mg/dl)	123(52.1)	25(28.7)	148(45.8)	0.0002
Isolated low-HDL-cholesterol (HDL<40 mg/dl and TG< 150 mg/dl)	71(30.1)	24(27.6)	95(29.4)	0.69

* P-value compares percentages in male and female groups and is based on test of association using chi square.

DISCUSSION

Abnormality in lipid levels is one of the major risk factors for coronary artery disease (CAD). Since it is a modifiable risk factor, monitoring and treating lipid abnormalities in normal adults will have a bearing on reducing the rates of CAD in Pakistani population. There have been only few reports on the detailed analysis of lipids in normal healthy Pakistani subjects.[11,12] In a study recently carried out at the Family Medicine Department of the Aga Khan University, the mean values of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides in ambulatory Pakistanis were found to be 209±179 mg/dl, 40±8 mg/dl, 125±54 mg/dl and 166±50 mg/dl, respectively.[4] Our values for these parameters (Table-I) compare well with those mentioned above with the difference that the mean levels of total cholesterol, HDL-cholesterol and LDL-cholesterol in our study were some what on the lower side. This could be due the fact that the normal healthy subjects in our study belonged to a relatively lower socioeconomic strata of the population compared to the population studied by the investigators in the Family Medicine Department of the Aga Khan University (subjects visiting the general preventive checkup clinics at the Aga Khan University Hospital) and, therefore, might have been consuming diet low on saturated fats.

Raised mean triglyceride levels in our study population (155±88 mg/dl) are in conformity with those reported by Salahuddin *et al* (141±9 mg/dl)[14], Iqbal *et al* (166±50 mg/dl)[4], Jabeen *et al* (145 ± 33 mg/dl)[11] and Shahid *et al* (131±3 to180±7 mg/dl).[12] These levels, when compared with triglyceride levels in Caucasians (86 mg/dl)[12] were found to be significantly higher. However, when compared with triglyceride levels in Indians, as reported by Gupta *et al*[15], these were not found to be significantly different, indicating that high levels of triglycerides is a common feature among Pakistanis and South Asian Indians. This could be due to their similar genetic makeup and nutritional habits involving high consumption of saturated fats.[16]

William Castelli has presented data from Framingham suggesting that the blood triglyceride level is an independent risk factor for CHD.[17] This may explain why South Asians have a greater risk of developing CHD. Moreover, Pakistani males have significantly higher levels of triglycerides and lower levels of HDL-cholesterol than females (Table-II). This inverse relationship between serum levels of triglycerides and HDL-cholesterol is in line with other published reports.[18]

Mean HDL-cholesterol value in our study (37±11.5 mg/dl) compares well with the mean value reported by Iqbal *et al* (40 ± 8 mg/dl) in 370 ambulatory Pakistanis.[4] However, significantly higher levels of HDL-cholesterol in females compared to males (Table II) indicate a positive influence of female sex hormones on HDL-cholesterol levels.[19] Although smoking has been shown to decrease levels of HDL-cholesterol[20], yet in the present study we could not find any association between smoking (in males) and HDL-cholesterol levels.

It is important to mention that the baseline mean HDL-cholesterol levels in our normal healthy subjects are well below the normal levels (40 mg/dl) recommended by the National Cholesterol Education Program[21] indicating that "low HDL-cholesterol" in our population may have been one of the factors contributing to high rates of CAD. In fact, the prevalence of "low-HDL-cholesterol" (<35 mg/dl) in our population is 45.8% (Table IV) which is among the highest reported in the literature. For example, Azizi *et al* have reported a prevalence of 31% in men and 13% in women in Tehran's urban population.[22] Gupta *et al* have reported a prevalence of 9.5% in Indian females and 6.5% in Indian males.[15] Large scale population based studies will be required to have an accurate assessment of the frequency of "low HDL-cholesterol" in our population. Similarly, the prevalence of "isolated low HDL-cholesterol" (HDL< 40 mg/dl and triglycerides < 150 mg/dl) in our normal healthy subjects was found to be 29.4%. Again, this frequency is very high compared to the values reported in the literature. Lamarche *et al*, for example, have reported its prevalence in a male population in Quebec city suburb to be 13.4%.[23] Since triglyceride levels were found to be associated with BMI (Table II) it is suggestive that weight control measures would have a most profound effect on decreasing hypertriglyceridemia.

Despite the limitation of this study that its normal healthy subjects do not represent the general population, it definitely points towards the very high prevalence of hypertriglyceridemia and low HDL-cholesterol in Pakistani adults and could be considered as one of the major risk factors for CAD in this part of the world. Our dietary habits and sedentary life style, in addition to the genetic make up, may have been contributing to these lipid abnormalities. These two lipid abnormalities constitute "atherogenic dyslipidemia" which is one of the 6 components of "metabolic syndrome"[24]. This syndrome poses a significant health risk to individuals and is a growing health problem of this country. Media campaign for preventive health measures which lead to decreasing the levels of triglycerides and increasing the levels of HDL-cholesterol, such as, engagement in healthy physical activity, cessation of smoking[25] and use of low fat diet which is rich in polyunsaturated fatty acids[18,26] would be required to contain the epidemic of CVD in our urban population.[27]

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