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CORONARY HEART DISEASE;
LIPID ABNORMALITIES AS PREDICTOR IN OFFSPRING OF PREMATURE CORONARY HEART DISEASE PATIENTS.

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ABSTRACT ... Objectives: This study was conducted to perform serum lipid profile in off springs of premature coronary heart disease (CHD) patients and age and sex matched normal controls and compare the results of two groups. **Study design:** A cross sectional study. **Patients and methods:** 250 off springs of diagnosed premature CHD patients were selected from Punjab institute of cardiology, Lahore and Services hospital, Lahore. 50 age and sex matched normal controls were selected from different areas of Lahore. Serum total cholesterol (TC), serum triglycerides (TG) serum low density lipoprotein-cholesterol (LDC-c) and serum high density lipoprotein cholesterol (HDL-c) was performed. **Results:** Serum TC, TG, LDL-c of off springs of premature CHD patients was increased as compared with normal controls. Serum HDL-c of all the subjects of off springs of premature CHD patients was decreased as compared with normal controls. **Conclusion:** Off springs of premature CHD patients are more prone to develop lipid abnormalities as compared with normal controls.

INTRODUCTION

Coronary heart disease (CHD) is considered as plague of modern society[1] . It is a complex multifactorial disorder that results from interaction between the individual's genetic background and various environmental factors like obesity, smoking and sedentary lifestyle[2].Abnormal lipid levels contribute significantly to risk of CHD which increases further in the presence of other factors[3]. The presence of familial predisposition to CHD is seen in substantial number of patients[4] . Hypercholesterolemia is an important risk factor for development of CHD[5].CHD is characterized by fibrofatty plaque formation along coronary endothelium and low density lipoprotein cholesterol (LDL-c) concentrations accelerate this process. Increased plasma triglycerides (TG) concentration is also a risk factor for the development of CHD. Epidimiological studies have shown that there is direct relationship between TG level and CHD risk[6]. High density lipoprotein cholesterol (HDL-c) has inverse relationship with risk of developing CHD[7].

This study was undertaken in an attempt to prove on scientific basis that the offsprings of premature CHD patients with significantly elevated serum lipids levels must be advised to consult the physician to avoid serious complications resulting from elevated serum lipid levels in future and to live a CHD free life.

PATIENTS & METHODS

The present study of the serum lipids was undertaken on 300 subjects. 250 offsprings of diagnosed premature CHD patients (Group B) were selected from Punjab institute of cardiology (PIC), Lahore and Services hospital, Lahore. 50 normal controls (Group A) were

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selected from different areas of Lahore. CHD was diagnosed on the basis of clinical findings, electrocardiography and biochemical findings including creatine kinase (CK), creatine kinase-MB isoenzyme (CK-MB), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH). Parents age was 45 years for males and 50 years for females i.e upper limit to designate CHD as premature[8] . Offsprings belong to adolescent age group i.e from 11-21 years[9]. Subjects suffering from diabetes mellitus, thyrotoxicosis, hypertension and hepatitis were excluded from study. Five ml blood was drawn aseptically avoiding stasis after overnight fast. Blood was clotted and centrifuged to obtain serum. The serum was analyzed in the laboratory on FP901 analyzer using commercially purchased kits. The serum TC was estimated by cholesterol oxidase (CHOD) method, serum TG was estimated by glycerophosphate oxidase method, serum LDL-c was estimated by CHOD method after heparin precipitation while HDL-c was estimated by CHOD method after precipitation with phosphotungstic acid and Mg chloride[10].

Arthmatic mean and standard deviation were calculated. Data analysis was done by student's 't' test. 'P' value was read from specific tables.

RESULTS & OBSERVATIONS

Serum lipids determination of 250 offsprings of premature CHD patients and 50 normal controls was done. Sex distribution is given in table I and Fig.1. Age range was from 11-21 years. Age distribution is given in table II and fig-2. Age has been expressed as mean $\pm$ SD. Age was comparable (P>0.05) between males of two groups, between females of two groups and between all subjects of two groups.

Comparison of serum TC between group A and group B is given in table III and fig-3. Results are given in mg/dl as mean $\pm$ SD. Serum TC was increased statistically highly significantly (P<0.01) in males, females and all subjects of group B as compared with males, females and all subjects of group A.

Table-I. Sex distribution

	Males	Females
Group A (Normal controls)	25 (50%)	25 (50%)
Group B (Offsprings of premature coronary heart disease patients)	137 (54.8%)	113 (45.2%)

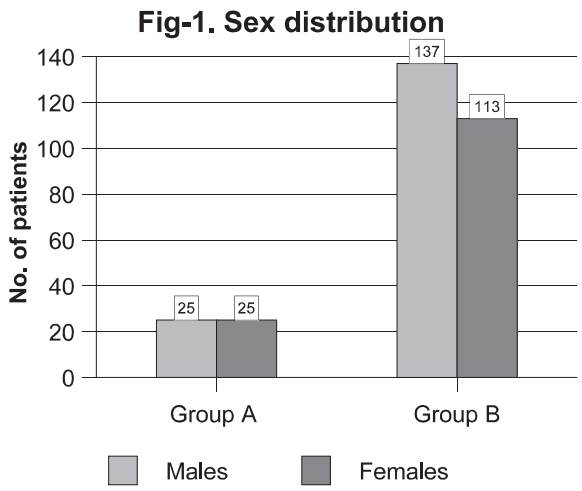


Table-II. Age distribution

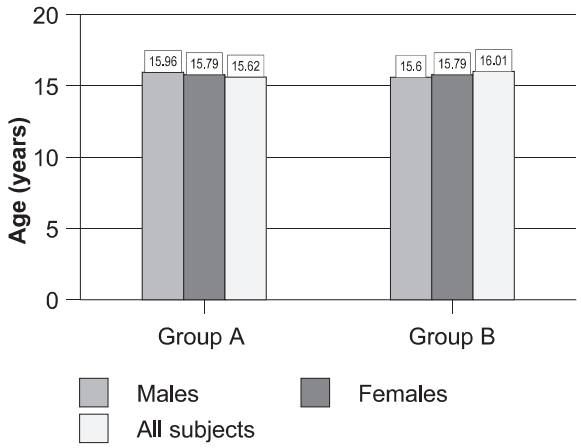
	Males	Females	All subjects
Group A (Normal controls)	15.96 ± 3.0 (n=25)	15.79 ± 2.92 (n=25)	15.62 ± 3.11 (n=50)
Group B (Offsprings of premature coronary heart disease patients)	15.60 ± 3.09 (n=137)	15.79 ± 3.6 (n=113)	16.01 ± 2.89 (n = 250)
Statistical analysis	(P>0.05) NS	(P>0.05) NS	(P>0.05) NS

n = number or subjects *NS = Non significant*

Comparison of serum TG between group A and group B is given in table-4 and fig-4. Results are expressed in

mg/dl as mean±SD. The serum TG of males, females and all subjects of group B was increased as compared with males, females and all subjects of group A. Difference was statistically highly significant (P<0.01) in all three comparisons.

Fig-2. Age distribution



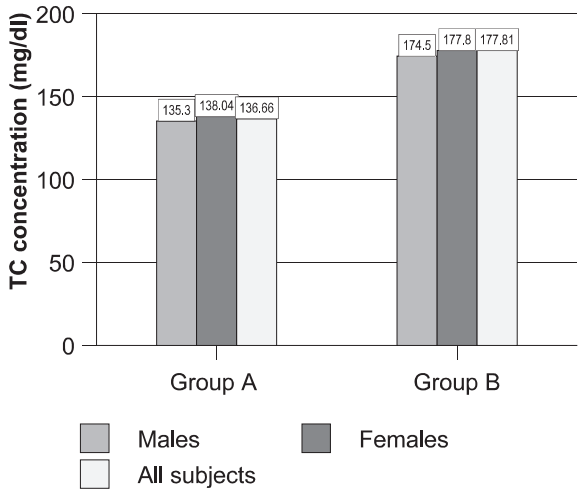
Group-A Normal controls
Group-B Offsprings of premature Coronary heart disease patients

Table-III. Comparison of serum cholesterol of group A and group B

	Males	Females	All subjects
Group A (Normal controls)	135.3 ± 22.1 (n=25)	138.04 ± 35.3 (n=25)	136.66 ± 25.37 (n=50)
Group B (Offsprings of premature coronary heart disease patients)	174.5 ± 30.46 (n=137)	177.8 ± 30.0 (n=113)	177.81 ± 29.85 (n = 250)
Statistical analysis	HS (P<0.01)	HS (P<0.01)	HS (P<0.01)

n = number or subjects *HS = Highly significant*

Fig-3. Comparison of serum total cholesterol of Group A and Group B



Group-A Normal controls
Group-B Offsprings of premature CHD patients

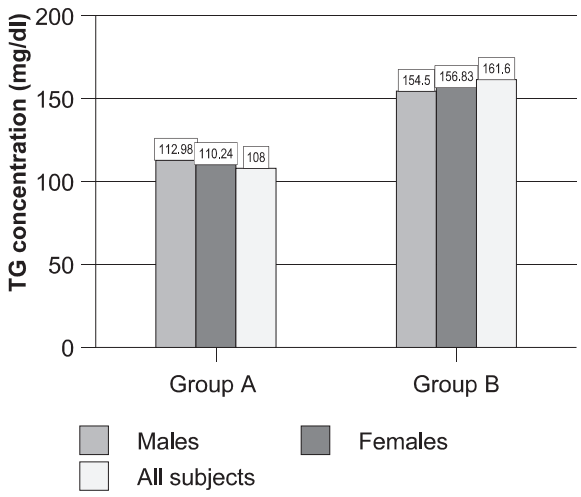
Table-IV. Comparison of serum TG of group A and group B

	Males	Females	All subjects
Group A (Normal controls)	112.98 ± 34.85 (n=25)	110.24 ± 38.8 (n=25)	108 ± 35.65 (n=50)
Group B (Offsprings of premature CHD patients)	154.5 ± 49.57 (n=137)	156.83 ± 51.6 (n=113)	161.6 ± 47.07 (n = 250)
Statistical analysis	HS (P<0.01)	HS (P<0.01)	HS (P<0.01)

n = number or subjects *HS = Highly significant*

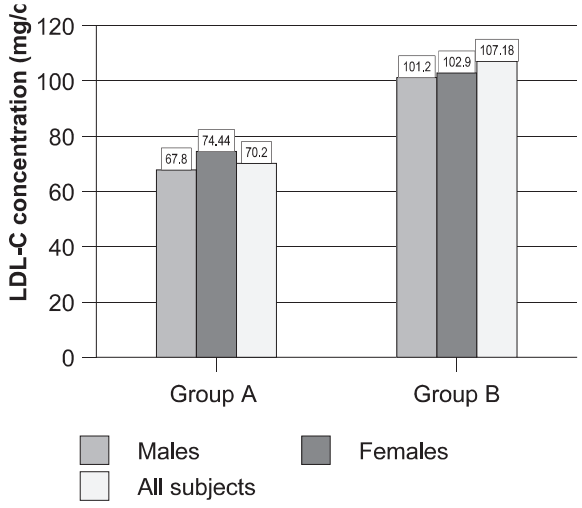
Comparison of serum LDL-c between group A and group B is given in table V and figure 5. Results are expressed in mg/dl as mean ± SD. The serum LDL-c of males, females and all subjects of group B was increased as compared with males, females and all subjects of group A.

Fig-4. Comparison of serum TG of Group A and Group B



Group-A Normal controls
Group-B Offsprings of premature CHD patients

Fig-5. Comparison of serum LDL-C of Group A and Group B



Group-A Normal controls
Group-B Offsprings of premature CHD patients

The difference in all three comparisons was highly significant statistically (P<0.01).

Comparison of serum HDL-c between group A and group B is given in table VI and figure-6. Results are expressed as mean ± SD. Serum HDL-c of males and females of group B was decreased as compared with males and females of group A.

Table-V. Comparison of serum LDL-C of group A and group B

	Males	Females	All subjects
Group A (Normal controls)	67.8 ± 22.12 (n=25)	74.44 ± 32.5 (n=25)	70.2 ± 25.67 (n=50)
Group B (Offsprings of premature coronary heart disease patients)	101.2 ± 39.19 (n=137)	102.9 ± 24.65 (n=113)	107.18 ± 28.5 (n = 250)
Statistical analysis	HS (P<0.01)	HS (P<0.01)	HS (P<0.01)

n = number or subjects *HS = Highly significant*

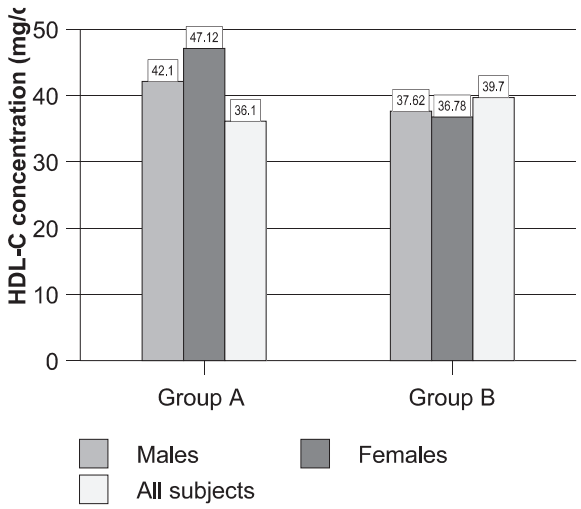
Difference was highly significant statistically (P<0.01). Serum HDL-c of all subjects of group A was decreased as compared with all subjects of group B. Difference was significant statistically (P<0.01).

Table-VI. Comparison of serum HDL-C of group A and group B

	Males	Females	All subjects
Group A (Normal controls)	42.1 ± 7.53 (n=25)	47.12 ± 7.8 (n=25)	36.1 ± 11.76 (n=50)
Group B (Offsprings of premature coronary heart disease patients)	37.62 ± 8.20 (n=137)	36.78 ± 10.18 (n=113)	39.7 ± 8.87 (n = 250)
Statistical analysis	HS (P<0.01)	HS (P<0.01)	HS (P<0.01)

n = number or subjects *HS = Highly significant*

Fig-6. Comparison of serum HDL-C of Group A and Group B



Group-A Normal controls
Group-B Offsprings of premature CHD patients

DISCUSSION

Coronary heart disease (CHD) is a leading cause of mortality and morbidity all over the world. It is a global epidemic increasing faster in developing countries than the developed[11]. There has been constant increase in the incidence of CHD in Pakistan[12]. Atherosclerosis (AS) an important cause of CHD originates as early as in the first decade of life, therefore much attention has been focused on serum lipids in children and adolescents. The serum TC and LDL-c level of Pakistani children are comparable with north American children reported by Lipid Research Clinic (LRC) population studies in United States and Canada[13].

The serum TC level results of this study are consistent with results of laur et al[14] (1990) and sesso et al[15] (2001) whom described that family history affects lipid levels. The serum TC level may be high primarily due to some inherited defects or secondary to other causes like diet rich in saturated fatty acids[16] The relationship between cholesterol and atherosclerotic coronary disease is curvilinear[17.] According to Multiple Risk Factor Trial (MRFIT) if risk ratio of 1.0 is arbitrarily assigned at a cholesterol level of 200 mg/dl the risk ratio increases to 2.0 at 250 mg/dl and 4.0 at 350 mg/dl[18]. Families consuming diets rich in cholesterol e.g. eggs, milk, chees, are at higher risk of developing hypercholesterolemia.

The serum TG results of this study are consistent with report of Sesso et al[15] (2001) whom reported that family history affects serum lipid levels. Hypertriglyceridemia in families occurs in familial hypertriglyceridemia (FHTG), in familial combined hyperlipidemia (FCHL)[10] and in association with various life styles like smoking and use of diets rich in saturated fatty acids.[19] Metabolic syndrome is a familial disorder characterize by obesity, hypertension, diabetes mellitus (DM) and lipid abnormalities like hypertriglyceridemia, low HDL and CHD, according to Adult Treatment Panel III (ATPIII) these abnormalities track from childhood to adulthood[20]. Obesity is strongly associated with dyslipidemias. It leads to hypertriglyceridemia and hypercholesterolemia because of decreased very low density lipoprotein (VLDL) catabolism, a particle containing higher levels of cholesterol and fatty acids[21].

LDL-c results of present study are in agreement with Genest et al[23] (1992) whom reported aggregation of elevated LDL-c levels in families. Austin et al[24] (2000) have also similar report. There is a linear relation between LDL-c levels and coronary events. LDL particle has been proved to be the main cause of CHD[25] .Familial hypercholesterolemia results from an absent or defective receptors responsible for internalization of LDL particle, particularly in hepatocytes[26], caused by LDL receptor gene mutations. Affected persons have markedly increased LDL from birth[22]. According to the third report of National Cholesterol Education Programme (NCEP) ATP III increased LDL-c level is one primary factor of CHD and LDL-c lowering is considered a primary goal of the CHD treatment[27].

HDL-c results of present study are in agreement with study of orford et al (2002)[28] whom reported that people not suffering from CHD have high HDL-c levels. HDL-c is concerned with reverse transport of cholesterol towards liver[26] and has inverse relationship with CHD risk[7.]

The findings of this study are throwing light on

importance of family history while considering coronary heart disease resulting from atheroselerosis. Elevation of serum TC, TG and LDL-c in children of fathers and mothers having CHD at a relatively young age indicates importance of compulsory assessment of serum lipids in such children. The need of lipid profile in children is strengthened because lipid abnormalities have been shown to track from childhood to adulthood.[20,23,24.]

CONCLUSION

Identification and treatment of children who may be high risk of development of CHD offers the possibility of preventing and delaying of this disease. It is concluded in the light of findings of this study that offsprings of premature coronary heart disease (CHD) patients are more prone to develop lipid abnormalities as compared with offsprings of people not suffering from CHD. Such children must be advised measures to maintain lipid levels in control, to avoid risk of having CHD in future.

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