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Studies on the Lipid Profile in Relation to Sex, Age in Non-obese and Non-diabetic Patients with Essential Hypertension among Human Population of Multan, Pakistan

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Abstract: The present study was carried out to assess the lipid profile in relation to sex, age in non-obese and non-diabetic patients with essential hypertension among human population of Multan, Pakistan for a period of 24 months from June 2001 to May 2003. The study revealed that there was a highly significant effect of age on total cholesterol of both hypertensive and normotensive individuals. The highest level of total cholesterol was present in hypertensive patients of 41-45 age group. The normotensive had low level of total cholesterol than hypertensive. There was no effect of age on triglycerides and HDL cholesterol. Hypertensive patients had higher level of LDL cholesterol than normotensive. The male had significantly higher level of total cholesterol than female and higher LDL cholesterol. The male had marginally higher level of triglycerides than females. There was no effect of sex on HDL cholesterol. When comparison was made between mild, moderate and severe hypertensive patients, it was found that severe hypertensive patients had significantly higher level of total cholesterol and triglycerides than mild and moderate hypertensive patients. There was no effect of severity of hypertension on HDL cholesterol and LDL cholesterol.

Key words: Hypertension, lipid profile, fatty acids, obesity, diabetes

INTRODUCTION

An elevated blood pressure is a very important public health problem with prevalence of 15% in different parts of world population. (Christopher *et al.*, 1991). Systemic hypertension is usually asymptomatic, readily detectable, usually easily treatable and leading to lethal complications such as coronary artery disease, stroke, renal failure and congestive cardiac failure, if untreated (Petersdar *et al.*, 1983). Hyperlipidaemia and hypertension are major risk factors for coronary heart disease and arteriosclerosis (Kannel, 1987). Moreover when they occur together, risk factor increases sufficiently. Stamler *et al.* (1986) and Castelli (1986) in separate studies found the prevalence of hypertension in hyperglyceridaemic and hypercholesteroleamic subjects. Williams, in 1988 conducted a study on 38 Utah families to detect a common disorder responsible for both hyperlipidaemia and hypertension. In the preliminary studies conducted at national level prevalence of hyperlipidaemia in hypertension was observed (Haider, 1980). Essential hypertension is thought to be a heterogeneous group of disorders (Clegg *et al.*, 1986). Specific sub types could be related to sodium sensitivity (Luft *et al.*, 1982), renin angiotension imbalance and specific defects of membrane cation transport (Canessa *et al.*, 1980), calcium intake and

metabolism (Resnick *et al.*, 1982), obesity (Stunkard *et al.*, 1986) and diabetes. Essential hypertension aggregates in families (Staessen *et al.*, 1985). Pathological syndromes leading to hypertension may therefore involved shared genes, shared environmental factors or combination of both. Now there are reports of disturbances at cellular levels. So the presence of sodium potassium ATPase inhibitors in essential hypertension have been found by Hamlyn *et al.* (1982), as they have been identified as unsaturated fatty acids i.e oleic acids and linoleicacids (Phosphatidylcholine a constituent of cell wall, a precursor of these substances), the link between the disturbed lipids and hypertension. There are also reports of insulin resistance in essential hypertension in non-obese and non-diabetic subjects (Ferrannini *et al.*, 1987). As insulin lowers levels of free fatty acids and directly stimulates sodium potassium ATPase (Clausen *et al.*, 1986) in contrast to unsaturated fatty acids which have been implicated as inhibitors of sodium pump (Ahmad *et al.*, 1971), it is conceivable that the link between insulin resistance, lipid disturbance and hypertension may be at the level of cellular cation transport. So the link between the disturbed lipids is a matter of consideration and to be viewed independently of secondary causes of disturbed lipids and hypertension. The study of association of hypertension and lipid abnormalities is also important in

view of the metabolic changes caused by many of the commonly used anti hypertensive drugs (Pollare *et al.*, 1989).

This research work also merits importance as the control of hyperlipidaemia and hypertension with control of smoking has produced drastic reduction in coronary heart disease in America and Scandinavia (Kannel *et al.*, 1989). So the results of this study may influence the attitude of physician as well as society towards control of these factors.

MATERIALS AND METHODS

The present study was carried out to assess lipid profile in relation to sex, age in non-obese and non-diabetic patients with essential hypertension from human population in Multan, Pakistan. The study period was from June 2001 to May 2003. The present study was based on the data, collected from the patients which were non-diabetic, non obese with essential hypertension. Efforts were made to include samples of only those patients who were untreated and freshly diagnosed. Patients suffering from secondary hypertension, myocardial infarction, congestive cardiac failure, renal failure, diabetes mellitus, hypothyroidism, nephrotic syndrome, obese and biliary obstruction were excluded from the study. Male patients and female patients of different age groups were analyzed. The male patients were divided into three age groups i.e. (age 35-40 years), (age 41-45 years) and (age 46-50years). The female patients were also divided into similar three groups. Body mass index was noted by using the formula.

Weight in Kg /Height in m²= B.M.I. (Christopher *et al.*, 1991)

Male patients with B.M.I. greater than 27 and female patients with B.M.I. greater than 25 were excluded. Triceps skin fold thickness was measured with vernier calipers. The patients with triceps skin fold thickness greater than 20 mm in male and 28 mm in female were excluded from the study. Patients with the positive results of the urine glucose and elevated blood glucose, both fasting and random were excluded from study. The presenting complaints and the history of the subjects with a special emphasis on personal past history and family history was noted. Blood pressure was measured with standard mercury sphygmomanometer. The measurement of blood pressure was carried out when patient was comfortable in a quiet room with arm's muscles relaxed and fore arm supported and positioned at heart level. They had not smoked or ingested caffeine within 30 minutes prior to measurement. Blood pressure of newly

diagnosed patient was taken at 3 or more occasions in a month's time before they were registered for evaluation. The patients with diastolic pressure more than 95 mm Hg. and /or with systolic blood pressure 155 mm Hg. were included in study. The patients with hypertension were marked mild, moderate and severe in other three different groups with different age and sexes according to the following:

Diastolic blood pressure 95-104 mm Hg = Mild Hypertension.
Diastolic blood pressure 105-114 mm Hg = Moderate Hypertension
Diastolic blood pressure more than 115 mm Hg = Severe hypertension.

To exclude secondary hypertension cases history of the patients was assessed along with clinical examination and laboratory investigations. Patients with intake of oral contraceptives, renal hypertension, presence of protein urea, urinary tract infections, tuberculosis, renal colic haematuria, polyurea, dysurea, were excluded. Urea and creatinine levels were assessed and patients with normal levels of both were included in the study. For exclusion of patients with acute myocardial infarction, stroke, congestive cardiac failure and renal failure, history was assessed along with E.C.G., laboratory investigations. Patients with chest pain, heaviness and tightness in chest, history of palpitation, enlarged heart and enlarged liver were excluded. For exclusion of patients with diabetes mellitus along with history, blood glucose levels, urine glucose levels, glycated hemoglobin levels were assessed. The patients with positive laboratory findings suggesting diabetes were excluded from the study. For exclusion of the patients with biliary obstructions history for jaundice and Ultra sonography was done to check the liver size and enlargement in gall bladder. The estimation of lipid profile was carried out in laboratory after getting fasting blood samples immediately after the collection of blood samples. The venous blood was collected via venipuncture with the help of disposable syringe (B.D).

RESULTS

The results from the present study suggested that there was highly significant effect of age on total cholesterol of both hypertensive and normotensives individuals (df = 5,194, F= 6.10; P.<0.001). The highest level of total cholesterol was present in hypertensive patients of age group 41-45. The normotensive patients had low level of total cholesterol than hypertensive patients of all age groups. There was no effect of age on triglycerides and HDL cholesterol (P>0.5). Hypertensive patients had significantly higher level of LDL cholesterol than normotensive (df =5,194; F= 6.38; P<0.001) (Table 1).

There was highly significant effect of sex on total cholesterol (df =1,198; F=8.90; P = 0.003) and LDL

Table 1: Total Lipid contents (mg dl⁻¹) according to age. Standard deviation is given in parenthesis. T.C.= Total Cholesterol, TG. = Triglycerides, H.D.L. = High Density Lipo proteins, L.D.L. = Low Density Lipo proteins

Age T	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
35-40 H.	38	192.11 ^b (42.23)	197.79(87.65)	42.279(11.791)	107.39 ^{ab} (37.91)
41-45 H.	20	242.45 ^a (120.89)	229.35(116.68)	38.630(10.593)	120.20 ^a (39.76)
46-50 H.	42	210.48 ^{ab} (66.66)	198.64(73.04)	41.574(7.761)	124.87 ^a (43.88)
35-40 N.	40	170.48 ^b (29.95)	183.47(70.57)	41.615(12.095)	86.60 ^b (28.48)
41-45 N.	16	170.50 ^b (34.00)	207.12(71.42)	37.413(6.901)	89.49 ^b (25.13)
46-50 N.	44	176.80 ^b (39.30)	178.80(73.24)	40.116(7.716)	97.71 ^b (32.99)

Note: Letters indicate results of multiple range tests (LSD) procedure. Mean with same letters are not significantly different from each other at 0.05 level

Table 2: Total Lipid contents (mg dl⁻¹) according to sex. Standard deviation is given in parenthesis

Sex	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
Male	100	209.89 ^a (75.15)	204.46(88.60)	41.253(10.014)	117.29 ^a (41.25)
Female	100	173.26 ^b (34.77)	185.20(71.85)	40.283(9.631)	91.95 ^b (30.25)

Table 3: Total Lipid contents (mg dl⁻¹) according to hypertensive and normotensive condition. Standard deviation is given in parenthesis

Type	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
Hypertensive	100	204.24 ^a (76.27)	217.00 ^a (97.61)	41.253(10.014)	109.45 ^a (36.37)
Normotensive	100	178.91 ^b (37.32)	172.66 ^b (51.76)	40.283(9.631)	99.79 ^b (39.64)

Table 4: Total Lipid contents (mg dl⁻¹) according to age in hypertensive patients. Standard deviation is given in parenthesis

Age	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
35-40	32	193.16(100.15)	194.06(71.79)	38.938(9.705)	110.03(36.82)
41-45	33	201.42(84.89)	192.36(43.61)	40.848(8.074)	108.58(41.85)
46-50	32	234.72(94.87)	222.38(101.83)	41.375(7.143)	112.31(34.50)

Table 5: Total Lipid contents (mg dl⁻¹) according to sex in hypertensive patients. Standard deviation is given in parenthesis

Sex	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
Male	48	230.27 ^a (96.30)	227.10 ^a (110.17)	41.188(8.507)	123.67 ^a (40.06)
Female	49	175.94 ^b (33.21)	192.61 ^b (72.50)	39.612(8.205)	97.18 ^b (29.85)

Table 6: Total Lipid contents (mg dl⁻¹) according to severity of hypertension. Standard deviation is given in parenthesis

Type	N	T.C.(mg dl ⁻¹)	TG.(mg dl ⁻¹)	H.D.L.(mg dl ⁻¹)	L.D.L.(mg dl ⁻¹)
mild	32	198.75 ^a (42.39)	182.75 ^a (59.33)	41.063(10.386)	121.31(40.17)
Moderate	34	183.62 ^b (39.79)	200.82 ^b (81.31)	39.265(8.225)	101.82(39.55)
Severe	31	228.10 ^a (118.25)	247.19 ^a (123.12)	40.935(5.916)	108.19(30.06)

(DF = 1,198; F = 24.54; P < 0.001). The male had higher level of total cholesterol and LDL cholesterol than females (df = 1,198; F = 2.85; P = 0.093). The age had no effect on HDL cholesterol (Table 2). ANOVA suggested that hypertensive patients had significantly higher level of total cholesterol (df = 1, 198; F = 19.57; P = 0.003) and triglycerides (df = 1,198; F = 16.11; P < 0.001). The hypertensive patients had marginally higher level of LDL cholesterol than normotensive (df = 1,198; F = 3.22; P = 0.074). The level of HDL cholesterol was found to be similar in hypertensive and normotensive individuals (P > 0.5) (Table 3).

There was no effect of age on total lipids contents of only hypertensive patients (Table 4). In Hypertensive patients sex had significant effect on levels of total cholesterol, triglycerides and LDL cholesterol. The male had significantly higher level of total cholesterol than female (df = 1,95; F = 13.91; P < 0.001) and higher LDL cholesterol (df = 1,95; F = 13.67; P < 0.001). The male had marginally higher level of triglycerides than females (df = 1,95; F = 3.33; P = 0.071). There was no effect of sex on HDL cholesterol (P > 0.5) (Table 5). When comparison was

made between mild, moderate and severe hypertensive patients. It was found that severe hypertensive patients had significantly higher level of total cholesterol (df = 2,94; F = 2.93; P = 0.058) and triglycerides (df = 2,94; F = 4.18; P = 0.018) than mild and moderate hypertensive patients. There was no effect of severity of hypertension on HDL cholesterol (P > 0.5) and LDL cholesterol (P > 0.1) (Table 6).

DISCUSSION

The present study comprised of a random sample of population, which has been selected on strict criteria based on including non obese non diabetic hypertensive and normotensive patients. The patients were without complications in the range of 35-50 years of both sexes.

A strong clustering of risk factors for coronary artery disease has been observed in hypertensive subjects in this study. The results from the present study suggested that there was highly significant effect of age on total cholesterol of both hypertensive and normotensive individuals. The highest level of total cholesterol was

present in hypertensive patients of age group 41-45. The normotensive patients had low level of total cholesterol than hypertensive patients of all age groups. There was no effect of age on triglycerides and HDL cholesterol. Hypertensive patients had significantly higher level of LDL cholesterol than normotensive individuals. The male had higher level of total cholesterol and LDL cholesterol than females. The age had no effect on HDL cholesterol. The level of HDL cholesterol was found to be similar in hypertensive and normotensive individuals. In hypertensive patients sex had significant effect on levels of total cholesterol, triglycerides and LDL cholesterol. The male had significantly higher level of total cholesterol than female and higher LDL cholesterol. The male had marginally higher level of triglycerides than females. There was no effect of sex on HDL cholesterol. When comparison was made between mild, moderate and severe hypertensive patients, it was found that severe hypertensive patients had significantly higher level of total cholesterol and triglycerides than mild and moderate hypertensive patients. There was no effect of severity of hypertension on HDL cholesterol and LDL cholesterol. The increase in values of cholesterol, LDL cholesterol, triglycerides and a decrease in values of HDL cholesterol have been observed. These trends have been observed not only in mean values but also in the number of subjects. Similar results have been observed in other studies (Salonen *et al.*, 1981; Kaare *et al.*, 1991). Kaare *et al.* (1991), tromso study, observed the same type of correlations in a population of 8081 male 20-54 years old and 7663 female 20-49 years old. In his study he detected an increase in total and non HDL cholesterol levels with increasing systolic or diastolic blood pressure in both sexes. In male association of blood pressure and total cholesterol decreased with age whereas in women it increased. The positive association of serum triglyceride levels with hypertension was also found. So the results of the study corroborate with the present study, so far as the increase in triglycerides are concerned. The levels of cholesterol and LDL cholesterol, however, did not relate with the present study. The age related differences cannot be detected in the present study, perhaps, because of the smaller sample size and a strict criteria was followed in case of selections. A much pronounced correlation of triglycerides and blood pressure were detected in by (Assmann *et al.*, 1987). The prevalence of hypertension in hyper-triglyceridaemics were found twice that was found in normotensives (triglycerides less than 150 mg dl^{-1}). In our study the prevalence of hypertension in hypertriglyceridaemics were found thrice than was found in normotensives (triglycerides less than 200 mg dl^{-1}). The difference in the findings of present study from study of (Assmann *et al.*, 1987) is due to the fact that later study

was primarily designed to identify risk factors for coronary artery disease among a population without a strict criteria of excluding obesity, diabetes, complications and not selecting the specific age range of subjects. Secondly, there may be some environmental, racial and dietary factors which are underlying these differences. The study conducted on families by (Williams *et al.*, 1988) found a strong correlation of dyslipidaemia and hypertension. Among 131 hypertensive subjects in 58 siblings similar abnormalities in fasting serum lipid concentrations were observed in two or more siblings in 48% of sib ships. More than one lipid levels were abnormal in almost all concordant sib ships, suggesting an association between hypertension and a syndrome of mixed lipid abnormalities probably Familial Combined Dyslipidaemia. The lipid abnormalities were higher cholesterol, higher triglycerides, higher L.D.L. cholesterol and lower H.D.L. Although our study has not been conducted in this pattern, but about 55% of subjects gave a family history of hypertension and as about 49% of subjects gave a family history of hypertension; Hypertensive individuals in our study showed abnormalities in lipid patterns, so the familial dyslipidaemia may be very strong finding in our population.

At national level, in a study conducted by Haider (1980) hyperlipidaemia was found in 48% of patients with hypertension. The type IV lipoprotein abnormalities was found in 32% of hypertensive subjects as compared to 39% of hypertensive subjects in the present study with the same abnormality. Type IIB abnormality was found in 10% of hypertensive subjects, the results of which are very similar to the present study. However, type IIA abnormality was found in 6% of the hypertensive subjects as compared to one percent of hypertensive subjects in the present study. The criteria of selection was nearly similar. However, in the present study the criteria of age and the measurement of HDL cholesterol has also been made. The association of hypercholesterolaemia and increased LDL cholesterol with hypertension has been observed in the present study. The increased association of cholesterol and blood pressure has also been observed in high risk population such as Eastern Thailand than in low risk population such as in South California (Graundy *et al.*, 1990). A higher trend towards LDL cholesterol has been observed in case of hypertensive group in the above study. Another research work by (Ekelund *et al.*, 1988) observed the lowering of LDL cholesterol levels with lowered incidence of hypertension. Still another research has shown that LDL cholesterol level may blunt endothelium dependent vasorelaxation (Henry *et al.*, 1990). The understanding of metabolism of lipoprotein by

artery wall have yielded new insights into the factors that may be involved in arterial response (Piper, 1956). It has been reported in certain studies (Henriksen *et al.*, 1981) that LDL when incubated with cultured endothelial cells for 12-18 hours underwent striking series of modifications both physical and chemical. These changes oxidize lipids exclusively (Morel *et al.*, 1984). These oxidized lipids have also been shown to cause vasoregulatory impairment (Kugiyama, 1990). So the association of cholesterol and non HDL cholesterol seem to be anticipatory. The present study demonstrates a much pronounced correlation of triglycerides and blood pressure. The increased mean concentration of triglycerides in hypertensives as well as the increased number of subjects with hypertension with hypertriglyceridaemia have been demonstrated. The results of present study coincide with the results of (Zavaroni *et al.*, 1989), so far as the plasma concentration of hypertriglyceridaemia and lower HDL cholesterol concentrations are concerned. The study was primarily conducted for detection of risk factors for coronary artery disease in healthy persons with hyperinsulinaemia and normal glucose tolerance. Association of lipid and insulin abnormalities with hypertension have been detected by many other studies (Reaven *et al.*, 1989 and Fuh *et al.*, 1987).

In the present study 39% of individuals with hypertension as compared to 12% normotensive subjects have been found having type IV lipoprotein abnormality (as classified by Fredrickson, 1967). So the abnormality is pronounced one. The other abnormality observed in this study is a trend towards a decrease in HDL cholesterol levels in hypertensive group. There are several studies describing an inverse relationship between HDL cholesterol and insulin levels (Zavaroni *et al.*, 1985) and that higher the plasma triglyceride concentration, greater the fractional catabolic rate of HDL and lower the plasma HDL cholesterol concentration. Consequently, there is considerable evidence that an increase in plasma triglyceride concentration and a decrease in plasma HDL cholesterol concentration are the expected results of insulin resistance and hyperinsulinaemia. As has been described in the introduction of this study that the lipids may affect blood pressure by altering the ion transport of cells (Gray *et al.*, 1986; Dahi, 1986) and the configuration of cell wall lipids are further evidences for correlation of blood pressure with insulin resistance (Zavaroni *et al.*, 1989), so in the present study the changes in lipids in hypertensives give a strong evidence for the presence of some common mechanism of hypertension and lipid abnormalities.

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