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Study of Serum Lipoprotein (a) and Lipid Profile in patients with untreated essential hypertension in North Indian population

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Abstract:
Aim: Aim of the study was to find out the serum lipoprotein(a) in healthy and essential hypertensive subjects along with the lipid levels in them to assess that lipoprotein(a) measurement could help in risk stratification in these newly diagnosed essential hypertensive group. Material &Method: Eighty newly diagnosed essential hypertensive patients and seventy healthy subjects were included in the study. Sera were collected from them and lipid levels and serum Lipoprotein(a)were estimated in both groups. Result: It was observed that mean level of total cholesterol, Triglyceride, Very Low Density Lipoprotein-Cholesterol and Low Density Lipoprotein-Cholesterol were significantly elevated in hypertensive subjects as compared to controls. Taking 30 mg/dl as the cut off value of Lp(a),majority of the cases had levels more than 30mg/dl($p<0.001$) when compared to controls. Conclusion: This study indicates that significantly elevated serum Lp(a) level can be included along with lipid profile for risk stratification in newly diagnosed essential hypertensive patients.
Key words*: cholesterol, essential hypertensive, lipoprotein(a),lipid*

I. Introduction

Hypertension is an important medical and public health problem both in developed and developing countries and a major risk factor for cardiovascular diseases, stroke and chronic renal disease. It has been deemed the "biggest single risk factor for deaths worldwide" causing around 7 million deaths each year. With the current rates of this disease, India is projected to have the largest number of people with hypertension in the world and has a potential to become the 'Hypertension capital of world'. [1]

Essential hypertension has been appropriately called as a Silent Killer because it is usually asymptomatic and untreated. Abnormalities in Serum lipid levels (dyslipidemia) are recognized as a major risk factor for cardiovascular disease and essential hypertension.[2]Lipid profile is the earliest marker for coronary heart disease and includes total cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglycerides and VLDL.

The role of Lp(a) [lipoprotein(a)] as an independent biomarker of vascular disease risk has been investigated for more than 20 years, but recently the European Atherosclerosis Society (EAS) has issued a new consensus statement endorsing routine measurement of Lp(a) among patients with moderate to high risk of cardiovascular disease[3]. Many prospective epidemiological studies have reported positive associations of baseline Lp(a)concentration with coronary heart disease (CHD) risk[3], but very limited case-control studies studied the association between elevated Lipoprotein (a) and essential hypertension [4]. The Lp (a) was described for the first time in 1963 by Berg.[5] It consists of a set of lipoproteins with different molecular weights (from 350 to 900 KD) [6], in which particles of Low density lipoprotein(LDL) are bonded to apoprotein(a) (apo(a)), which has a Cringle structure with a high level of homology to plasminogen [5].The physiological function of this lipoprotein is still unknown but the importance attributed to it has increased considerably in the light of the evidence that high plasma concentrations of Lp(a) are not only associated with an increased risk of vascular diseases such as CHD and the restenosis of coronary bypass but are also considered an independent risk factor.

The objectives of this study was to compare the blood lipid levels and lipoprotein(a) in Essential hypertensives and normotensives by making the association of hypertension with lipid profile and lipoprotein(a) .

II. Material &Methods

This case-control study was carried out in the Department of Biochemistry, Rama Medical College, Hospital &Research Centre,Ghaziabad. The total number of subjects in our study was 150 and were divided into two groups. The case group consists of 80 newly diagnosed stage 1 essential hypertensives according to JNC-6 criteria and whose systolic blood pressure (SBP) / diastolic blood pressure (DBP) mmHg were in range of 140-159/ 90-99 mmHg. The control group consists of 70 subjects who were healthy and normotensive (B.P < 120/80mmHg) with no past / present and family history of hypertension. Subjects with cardiovascular disease, (CVD), renal disease, stroke, endocrine and thyroid disorders were not included for the study. Subjects were selected after filling the informed consent form. Records of E. Hypertensive patients diagnosed by the attending

physician and medical history and life style information were maintained on a pretested performa. Blood pressure readings were obtained using a mercury sphygmomanometer. Three readings each of systolic blood pressure (SBP) and diastolic pressure (DBP) were taken after 2 minutes interval from the seated subjects and were averaged. Hypertension was diagnosed based on the JNC-**6** Criteria.[6]Anthropometric measurements (height, weight) were taken for each participant . Fasting venous blood sample was collected from the subjects in a plain vacutainers and was centrifuged at 3000 rpm for 10 minutes for the estimation of serum lipid profile . Serum levels of TG, TC, HDL-C,blood urea, serum creatinine and lipoprotein(a) were measured in an automated analyzer (EM 200)) using commercial kit and LDL-C and VLDL was calculated using the standard formula (Friedwaldet. al. 1972). Lp (a) levels were estimated by in vitro turbidometric immunoassay using a kit (AGAPPE DIAGNOSTIC Ltd).Elevated Lp(a) were defined as more than 30mg/dl [7].
Stastistical analysis was done by using student's t test and p value calculated.

III. Results

The clinical and biochemical characteristics of 80 essential hypertensive cases and 70 controls are presented in table 1 and 2. The essential hypertensives are in the age group of 18-45 years and the mean age is 33.42±0.88 years whereas among the controls the age group is 18-40 years and the means age is 33.99±1.06 years. The blood pressure is calculated separately as systolic blood pressure and diastolic blood pressure. The mean SBP is 159 ± 9.18 mm Hg among essential hypertensives and 113.8 ± 5.94mm Hg among healthy controls. The mean DBP is 94.98 ± 4.12mm Hg among cases and was 76.51 ± 4.71mmHg among healthy controls. The mean value of total Cholesterol in essential hypertensive cases were 210± 9.77mg/dl which was significantly higher ($p<0.001$)than controls (124±4.37mg/dl). The mean HDL of essential hypertensive cases are 43.76 ± 0.49 mg/dl and that of controls is 49.25 ±1.20 mg/dl. The decrease in mean value of HDL among essential hypertensive than in the controls was significant ($p<0.05$). The mean value of LDL in essential hypertensive cases were 81.22 ±0.48 mg/dl and in the controls was 67.94 ± 1.08 mg/dl. The mean values of LDL in cases were higher than controls ($p<0.001$). The mean value of triglycerides in essential hypertensive subjects were 172.9 ±1.09 mg/dl and in controls was 86.07+0.96 mg/dl. The mean value of triglyceride in cases is significantly higher than the controls ($p<0.001$). The mean value of VLDL in essential hypertensive subjects were 34.57±2.08 mg/dl and in the controls was 17.21±1.66 mg/dl. The mean values of VLDL in cases were higher than controls ($p< 0.001$). In the present study majority of the patients had Lp(a) levels more than 30 mg/dl($p<0.01$) when compared to controls.

Table1. Comparison of Clinical/Biochemical parameters of hypertensive and non-hypertensive subjects**.**
*Significant difference between groups.

Parameters	**Controls(m±SD)**	**Cases(m±SD)**	**p value**
Numbers	70	80	
Age (years)	33.99 ± 1.06	33.42 ±0.88	0.6780
BMI (Kg/m2)	23.93 ± 0.78	25.36 ± 0.76	0.1958
Systolic BP (mm Hg)	113.8 ± 5.94	159 ± 9.18	<0.01*
Diastolic BP(mm Hg	76.51 ± 4.71	94.98 ± 4.12	<0.01*
Total cholesterol(mg/dl)	124±4.37	210± 9.77	<0.001*
HDL cholesterol(mg/dl)	49.25 ± 1.20	43.76 ± 0.49	<0.05*
Triglyceride (mg/dl)	86.07 ± 0.96	172.9 ± 1.09	<0.001*
VLDL(mg/dl)	17.21±1.66	34.57±2.08	<0.001*
LDL cholesterol (mg/dl)	67.94 ± 1.08	81.22 ± 0.48	<0.001*
Lipoprotein(a) (mg/dl)	21.6±11.9	30.3 ±13.6	<0.001

Interpretation was done according to p-value as follows:
$p<0.05$—significant ; $p<0.001$—highly significant; $p<0.01$—very significant; $p>0.05$ — not significant

Table 2: Distribution of controls and cases according to serum Lp(a) levels

Lp(a) mg/dl	**Controls (n=70)**	**Cases (n=80)**
≥ 30 mg/dl (High)	9(12.8%)	42(52.5%)
< 30 mg/dl (Normal)	61(87.14)	38(47.5)
Inference	Percentage of patients with Lp(a) of >30.0 mg/dl is significantly larger in cases when compared to controls (52.5% vs. 12.8% with $p < 0.001$)	

IV. Discussion

Hypertension already affects one billion people worldwide and the prevalence of hypertension between three and six decades in India has increased by about 30 times among urban residents and by about 10 times among the rural residents.[8] Whatever the precise mechanism of the underlying pathophysiology it is generally thought to be a combination of genetic and environmental factors. Changes in the environment of modern society have allowed the expression of genetic susceptibility in populations with physical inactivity and weight gain.[9] In our study serum TC, TG and LDL-C concentrations are significantly higher in essential hypertensive patients than among normotensive controls. This observation may be due to common risk factor for essential hypertension in the young population. The exact pathogenetic mechanisms underlying the CVD risk mediated by dyslipidemia are not fully elucidated but high levels of serum cholesterol are known to increase the risk of developing macrovascular complications such as coronary artery disease (CHD) and stroke.[10]A study conducted on hypertensive persons in Nigeria found a significantly higher lipid profile except HDL-Cholesterol and the findings were similar to the observations of our study.[11] Serum HDL-C level in hypertensive patients was found to be lower than the findings of Shahadat et al. (1999) Castilli et al. (1977), Wilson et al. (1980), Person et al. (1979) and Miller et al. (1977) but serum LDL Cholesterol level corroborated with the all above studies and the Framingham offspring study and the cooperative phenotyping study in USA, who demonstrated a positive correlation between the levels of LDL- Cholesterol and Coronary risk.[12]Epidemiological studies shows that the TC levels were very high in CHD patients.[13] It is thus generally recognized and recommended that treatment of hypertension should in addition to lowering blood pressure, target correction of dyslipidemia if present, to reduce overall CVD risk and increase the cost effectiveness of therapy. The exact mechanism by which a low HDL-C increases CVD risk has not been fully elucidated, though experimental studies suggest a direct role for HDL-C in promoting cholesterol efflux (reverse cholesterol transport) from foam cells in the atherosclerotic plaque depots in blood vessels to the liver for the excretion.[14] In the present study it was found that the hypertensive patients had higher plasma

concentrations of Lp (a) than in the controls. In a similar study, Catalano et al [15]reported significantly elevated levels of plasma Lp(a) in 123 Caucasian essential arterial hypertensive patients (47 men and 76 women). The pathogenicity and atherogenic role of Lp (a) is greatly influenced by the concentration of other serum lipids and lipoproteins. Several investigators reported correlation between Lp(a) and other lipid variables.. Mechanism of pathogenicity of Lp(a) excess includes destabilization of plaque, increased smooth muscle cell proliferation and migration, inhibition of transforming growth factor β, formation of occlusive thrombus, impaired formation of collateral vessels, enhanced oxidation uptake and retention of LDLc and up regulation of expression of the plasminogen activator inhibitor- 1 (PAI-I). The striking homology of apo(a) with plasminogen causes impaired fibrinolysis by competing with plasminogen and enhances thrombogenesis. So Lp(a) modulates thrombosis and fibrinolysis. In our study higher mean Lp(a) levels were observed in cases than controls and the difference was statistically significant ($p<0.001$). Percentage of essential hypertension patients with Lp(a) $\geq$30.0 mg/dL is significantly larger in cases when compared to controls (52.5% vs. 12.8% with $p<0.001$) in our study.

V. Conclusion

We conclude that the increase in systolic blood pressure was more significant than the diastolic blood pressure with increasing age groups. Based on the results obtained from the present study, we concluded that serum cholesterol, triglycerides , LDL Cholesterol and Lp(a)levels are positively correlated with high blood pressure, whereas HDL Cholesterol has less significant changes with hypertension. These observations taken together with the data demonstrating the importance of lipid profile and Lp(a)level in patients risk stratification imply that patients who have high blood pressure and impaired lipid profile and high Lp(a)level are at high risk and should be the target of aggressive primary preventive strategies to reduce the burden of hypertension and subsequent CVD.

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