STUDY OF LIPOPROTEIN (A) LEVELS AS A RISK FACTOR IN PATIENTS WITH ESSENTIAL HYPERTENSION IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND
Lipoprotein (a) has been identified as an important, independent, causal risk factor for various cardiovascular diseases, but its association with hypertension has shown differing results. The studies regarding this association are limited.

AIMS AND OBJECTIVES
In the present study, the levels of Lp (a) and other lipid parameters like Serum Total Cholesterol, Serum LDL Cholesterol, Serum HDL Cholesterol, serum triglycerides have been studied in hypertensive and non-hypertensive patients to investigate any significant relationship between the same.

MATERIALS AND METHODS
30 essential hypertensive patients were selected and were compared with 30 controls matched in terms of age and sex. Lipid profile including Total cholesterol, LDL- Cholesterol, HDL- Cholesterol, Triglycerides and Lp (a) were studied in both groups.

RESULTS
Hypertensive patients were observed to have higher levels of Serum Total Cholesterol, Serum Triglycerides, Serum LDL cholesterol, but it was not found to be significant. But lipoprotein (a) was found to be significantly higher ($p<0.01$) in cases than in controls.

KEYWORDS
Lipoprotein (a), Essential Hypertension, Cardiovascular Disease, Atherogenesis.

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INTRODUCTION: Essential Hypertension is a major public health concern in the society because of its high prevalence and its complications. The prevalence of hypertension in India is stated to be around 29.8%.[1] With this high prevalence, it not only becomes important to screen and treat the disease in an enthusiastic way, but also to find the pathogenesis for the same so that newer screening and treatment modalities can be found for the same. Although many research works have been done in the past, the basic cause for the same remains unclear. Plasma lipoprotein (a) is a complex lipoprotein particle which is heterogenous and is homologous to plasminogen and hence has ability to modulate fibrinolytic system which can lead to thrombus formation.[2] Many studies have shown that lipoprotein (a) can be used as a marker for vascular injury. Not much is known about association of serum Lp (a) with essential hypertension. But certain experiments have shown that oxidised Lp (a) impairs endothelial dilatation.[3]

It has been found that Lp (a) is not essential in lipoprotein metabolism as it is found to be present only in a few animal species.[4] The levels of lipoprotein (a) are genetically determined, are associated with cardiovascular diseases and are not affected by lifestyle modifications or drug intake.[4] Almost all the parameters of lipid profile are known to get affected by lifestyle and drugs and hence non-dependence on the same makes Lp (a) a very attractive parameter for screening or prognostic use. Plasma Lp (a) is also found to be constant in an individual.[5]

In the present study, the possible relationship between serum Lp (a) and hypertension is studied along with other lipid parameters.

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MATERIALS AND METHODS: This cross-sectional study was done on 30 cases of essential hypertension and age and sex matched 30 controls from December 2015- March 2016 in PK Das Institute of Medical Sciences. Essential hypertension diagnosis was defined by need for chronic antihypertensive treatment or in untreated patients by a diastolic blood pressure greater than 90 mmHg or a systolic blood pressure greater than 140 mmHg or both on three different occasions at least 1 week apart.[6]

Essential hypertensive patients who were on drug treatment with beta blockers or who had history of diabetes, family history of hyperlipidaemia, renal failure, endocrinopathies**,** patients on lipid lowering drugs and smokers and alcohol users were excluded from the study. Also recent MI/vascular diseases or presence of acute or chronic infections were other exclusion criteria.

The laboratory tests were a panel of lipid profile which consisted of total cholesterol (TC), High Density lipoprotein–cholesterol), Low Density lipoprotein–cholesterol (LDL-C) and triglycerides (TG) in serum were measured using enzymatic methods by commercially available kits. Lp (a) was estimated by in vitro turbidimetric immunoassays using kit by Agappe Diagnostics Ltd. Elevated Lp (a) was defined as serum Lp (a) > 30 mg/dL.[7]

Venous blood samples were obtained from all patients and controls after taking informed consent.

For statistical analysis, descriptive data are expressed as Mean ±SD. Students t test has been used to find significance. All statistical analysis was performed after entering data into SPSS 15.0, statistical significance was inferred at p value <0.05.

RESULTS: The cases and controls were found to have no statistically significant difference between them in terms of age, male-female ratio (p>0.05). Significant differences were found in case of diastolic and systolic blood pressure between both the groups.

In case of lipid profile and Lp (a) in cases and controls, it was found that although the TC, LDL-C, TG were raised in Cases compared to controls, but it was not found to be statistically significant (p>0.05). But in the same place, a statistically significant difference was found between cases and controls in levels of Lp (a) levels (p<0.01).

	Controls	**Cases**
Age (yrs.)	50.24±9.6	51.82±8.2
Male: female	0.6	0.6
Systolic BP (mmHg)*	110±8.81	148±18.21
Diastolic BP (mmHg)*	71±10.08	95±7.95

Table 1: Baseline Characteristics of Study Population

*p<0.01

Biochemical parameter	**Control (Mean±SD)**	**Cases (Mean±SD)**
Total cholesterol (mg/dL)	170.02±40.02	184±30.76
Triglyceride(mg/dL)	125.23±45.81	160±65.54
HDL-C (mg/dL)	40.21±10.99	35.14±5.77
LDL-C(mg/dL)	110±35.54	130.98±30.02
Lp (a) (mg/dL)*	20.21±6.45	33.95±8.22

Table 2: Mean Distribution of Lipid Profile and Lp (a) in Study Population

*p<0.01

DISCUSSION: In the present study, it was found that the hypertensive patients had higher plasma concentrations of Lp (a) than in the controls.

Lipoprotein (a) {Lp (a)}, belongs to a subclass of low density lipoprotein (LDL) which contains a single additional apolipoprotein, apo (a). The apo (a) chain is made of five cysteine-rich domains known as "kringles", which are coded by a gene in the long arm of chromosome 6 (6q26-27). It is known to show multiple polymorphisms, especially in kringle IV.[8,9] It is this polymorphism which gives rise to various isoforms of plasma Lp (a). It is found that these isoforms are different in different races and the levels of Lp (a) are also found to be different according to the different isoforms. For example, plasma Lp (a) is found to be remarkably higher in Afro-descendants.[10] Various epidemiological studies have shown that there is a link between plasma Lp (a) and risk of vascular diseases in the form of cardiovascular diseases, peripheral vascular diseases, premature atherosclerosis in children and adolescents. [11,12]

Although Lp (a) was originally described as a blood group antigen,[13] current interest in the lipoprotein relates to its association with vascular disease, for which it appears to be an independent risk factor.[14] Apo (a) has considerable, structural homology to plasminogen, although its protease domain is enzymatically inactive, in vitro studies; however, suggest that apo (a) may interfere with fibrinolysis.[15]

Lp (a) have both a thrombogenic potential due to its apo (a) moiety and an atherogenic potential due to LDL moiety.[16] Apart from its role as a recognised independent CVD biomarker, the physiological function of Lp (a) is not completely understood.[17,18,19,20] Because of its structural similarity to plasminogen and tissue plasminogen activator, it competes with plasminogen for its binding site, leading to reduced fibrinolysis, and as a result of the stimulation of secretion of plasminogen activator inhibitor-1, Lp (a) leads to thrombogenesis.[17,18,19] Lp (a) also carries cholesterol and binds atherogenic proinflammatory oxidised phospholipids, which attract inflammatory cells to vessel walls and leads to smooth muscle cell proliferation. Hence, Lp (a) strongly contributes to the process of atherogenesis. [17,18,19,20]

Elevated serum Lp (a) levels are associated with an increased risk of cardiovascular disease and renal failure in hypertensive patients, only if LDL levels are found to be on the higher side.[21,22] The pathogenicity and atherogenic role of Lp (a) is highly influenced by the concentration of other serum lipids and lipoproteins.[23,24,25] Several investigators reported correlation between Lp (a) and other lipid variables. In the present study, a significant correlation was observed between HDL and LDL cholesterol levels and Lp (a). In a similar study done by Catalano et al,[26] significantly elevated

levels of plasma Lp (a) was found in 123 Caucasian essential arterial hypertensive patients (47 men and 76 women). Studies in Indian population have shown that Lp (a) levels are significantly higher among pulmonary arterial hypertension[27] (mean 31.6 mg/dL). Recent report from Fytili et al[23] suggested that arterial hypertension is associated with elevated Lp (a) levels in patients with end-stage renal disease. In their study, it was observed that Lp (a) levels were significantly higher in the hypertensive patients, but that difference was not significant among non-renal failure patients. Studies in Indian population prove that Lp (a) levels are significantly higher among coronary artery disease (CAD) patients as compared to controls.[28,29]

However, there is considerable evidence which shows that multiple metabolic cardiovascular risk factors, including dyslipidaemia, often co-exist with hypertension.[30] In addition, the relationship between hypertension and lipid abnormalities may be causally related to insulin resistance, as part of Reaven's syndrome.[31]

As suggested earlier Lp (a) levels are genetically determined and hence can be used to screen asymptomatic individuals to look for risk of developing cardiovascular disease in the future.[32] There are very few studies suggesting association between essential hypertension and plasma Lp (a).

According to a study done by Chien KL et al in Taiwan which observed the relationship between Lp (a) and socioeconomic and atherosclerotic risk factors, it was found that plasma Lp (a) was positively correlated with age, LDL-cholesterol, HDL-cholesterol and negatively correlated with serum triglycerides, obesity and insulin resistance. The factors which did not significantly correlate with plasma Lp (a) were found to be socioeconomic status, smoking, alcohol consumption, systolic and diastolic blood pressure and apoprotein A1.[33]

In particular, genetic, rather than acquired, factors have the major influence on plasma Lp (a) concentrations. According to Sechi et al, there was a significantly higher frequency of low molecular weight apo (a) isoforms with increasing severity of hypertensive target organ damage, the latter being associated with higher serum Lp (a) levels.[34] Lp (a) also behaves as an acute phase reactant.[35] It is therefore possible that despite a hypertensive cohort being apparently 'healthy', that the presence of inter-current and subclinical illness can affect Lp (a) levels. The strongest evidence that is suggestive of Lp (a) as a cardiovascular risk factor applies to plasma levels 30 mg/dL, and not to concentrations within the conventional reference range.

Although there is a prominent role shown to be played by Lp (a), but it still remains to be controversial because of the absence of proper guidelines for selection of patients who require the same. Further experimental studies are required for proper clarification of Lp (a) as a risk factor for cardiovascular diseases including essential hypertension.[36]

In conclusion, the increasing mortality due to hypertensive end-stage organ damage, emerging as an epidemic among the population of India is greatly debatable. There is a need to identify susceptible individuals and adopt preventive measures. Newer therapeutic methods can also be identified to reduce Lp (a) levels, which may prove to be useful in patients with essential hypertension.

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