Original Research Article

A comparative study of lipoprotein (a) level in young adults with and without family history of hypertension/diabetes mellitus

Muhammed Ashraf K[1], Pradeep Kumar K M[2], Geetha P A[3*], Bhaskaran Chalil[4]

[1,2,3]Department of Biochemistry, [4]Department of Medicine, Government Medical College Kozhikode, INDIA.
Email: drgeethapa10@gmail.com

Abstract

Non communicable chronic diseases like diabetes mellitus (DM), hypertension and cardio vascular diseases are increasing among the adult population all over the world. In India there is increased susceptibility to diabetes mellitus and these patients are at increased risk to develop coronary heart disease (CHD). Hypertension is also one of the major cause for myocardial infarction and congestive heart failure and cerebrovascular accidents. Dyslipedimia is one of the strong risk factor for CHD. Among the dyslipidemia, lipoprotein (a) [Lp (a)] is strongly associated with myocardial infarction and it is genetically linked also. In this study serum Lp (a) level was compared in 50 young adults with family history of hypertension /diabetes mellitus (group 1) and 50 young adults without family history of hypertension /diabetes mellitus (group 2). **Result:** Lp(a) level was significantly elevated(p value = 0.000) in group 1 subjects when compared to group 2. **Conclusion**: This present study indicates the importance of lipoprotein (a) estimation and follow up study to identify the risk of dyslipidemia and development of CHD in our population.

Key Words: Diabetes mellitus, hypertension, coronary heart disease, dislipidemia, lipoprotein (a).

[*]**Address for Correspondence:**
Dr. Geetha P. A., Department of Biochemistry, Government Medical College Kozhikode, INDIA.
Email: drgeethapa10@gmail.com
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INTRODUCTION

Non-communicable chronic diseases like diabetes mellitus (DM), obesity, hypertension, cardiovascular, renal and nervous diseases are increasing among the adult population all over the world. Most of these are characterized by multifactorial causation and long latent period[1]. Hypertension, cardiovascular diseases, diabetes, obesity and dyslipidemia are closely interrelated. Hypertension and diabetes account for about 40% of all coronary heart disease (CHD). Hypertension accelerates the atherosclerotic process, especially if hyperlipidemia is also present. The relationship between habitual diet, blood cholesterol-lipoprotein levels and coronary heart disease are judged to be causal[2]. DM is a metabolic disease due to absolute or relative insulin deficiency. It is a common clinical condition affecting about 10% of the population[3]. It is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. The effects of diabetes mellitus include long term damage, dysfunction and failure of various organs, especially the eyes, kidney, heart and blood vessels[4]. The population in India has an increased susceptibility to diabetes[5]. Diabetes is listed among the five most important determinants of the cardiovascular disease epidemic in Asia. Hypertension is the commonest cardiovascular disease. It is the major risk factor for cardiovascular mortality, which accounts for 20-50 % of all deaths. It is also one of the most common complex genetic disorders, with genetic heritability averaging to 30 %. Blood pressure levels are determined in part by genetic factors and inheritance is polygenic. Hypertension is one of the major cause for myocardial

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infarction and congestive heart failure, cerebrovascular accidents and chronic kidney disease[6]. In non-diabetic populations, the risk of coronary heart disease (CHD) increases in continuous and graded fashion with increasing blood pressure[7]. Obesity, diabetes mellitus, thyroid diseases, renal disorders, liver disorders, glycogen storage diseases, Cushing syndrome etc. are seen associated with dyslipidemia[8]. Among the dyslipidemia, lipoprotein (a) level is gaining more importance now a days.

Lipoprotein(a): Lipoprotein (a) [also called LP (a) and Lp-a] is a lipoprotein subclass. It is strongly associated with myocardial infarction and is sometimes called as "Little rascal". Lp-a has 2 alleles, 11 phenotypes and 19 genotypes [9]. Lp-a is a risk factor for CHD and other vascular diseases. Lipoprotein (a) consists of two components, the low-density lipoprotein (LDL) and a glycoprotein, the apo lipoprotein (a) [Apo (a)], which are linked by a disulfide bridge. Numerous epidemiological studies have shown that elevated concentrations of Lp (a) is a risk factor for coronary heart disease and stroke. Most in vitro functions that have been attributed to Lp (a) have also been suggested as an explanation for the pathophysiological properties of Lp (a) and may be responsible for the fatal consequences of excessive Lp (a) levels in human subjects. One is the modulation of the balance between clotting and fibrinolysis at the endothelial cell layer of the blood vessel wall, which results in a prothrombotic state. In vitro studies also suggest that a forming fibrin thrombus at a damaged vessel wall has the capacity to bind Lp (a). This may not only inhibit thrombus degradation but may also result in the trapping of the Lp (a) particle by cross-linking with fibrinogen. High homocysteine concentrations enhance fibrin binding of Lp (a) and might accelerate thrombus formation[7]. Lp-a is genetically linked with concentrations varying over one thousand fold, from <0.2 to> 200 mg/dl. African populations have Lp-a concentrations several fold higher than Caucasians and Asian populations[10]. In 40 % population, there is no detectable level of Lp-a in serum. In 20 % population Lp-a concentration is more than 30 mg/dl. Indians have a higher level of Lp-a than Europeans[9]. Lipoprotein (a) recruits inflammatory cells. In this study, lipoprotein (a) are determined in subjects selected depending on the major risk factor i.e., off springs of diabetic and/or hypertensive parents and compared with those off springs of non-diabetic /non-hypertensive parents.

MATERIALS AND METHODS

50 subjects with family history of diabetes or hypertension (Group 1) and 50 subjects without family history of diabetes or hypertension (Group 2) in the age group of 18 - 25 years were selected for the study and Serum Lipoprotein (a) was estimated and compared between the two groups. The period of study was one year.

Inclusion Criteria and Exclusion Criteria: Students admitted to Calicut Medical College with documented family history of having or not having diabetes or hypertension were included in the study. For assessing the family history, disease status of father and mother only is considered. Subjects who fail to give a written informed consent or having already diagnosed diabetes or hypertension were excluded from the study.

Study Methods: Serum Lipoprotein (a) was estimated by automated analyzer by multipoint calibration with fix time mode[20].

Statistical Analysis: Statistical comparison of socio-demographic and biochemical features between study groups was done. Results are expressed as mean and number (proportion) of subjects. The results were considered significant at the level of $P < 0.05$. The results were analyzed statistically using chi square and T-test.

RESULTS

100 subjects of age group 18-25 years were included in the study. They were grouped into two - Group I include children of either mother or father diagnosed of having diabetes mellitus or hypertension or taking medicines for either. Group 2 subjects does not have their parents diagnosed having diabetes or hypertension. There were 60 males and 40 females with mean age of 19.18 in both groups. Group wise details of demographic features are given in table 1-2. In group I, 16 % of subjects' mother have diabetes and 16 % have hypertension; 62 % of subjects' father have diabetes and 28 % have hypertension.

Table 1: Sex distribution of study group

Sex	Group I	Group II	Total
Male	28	32	60
Female	22	18	40
Total	**50**	**50**	**100**

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Table 2: Family history of diabetic mellitus/hypertension in study subjects

	Maternal diabetic status		Total	Maternal hypertension status		Total	Paternal diabetic status		Total	Paternal hypertension status		Total
	Yes	No	Total	Yes	No	Total	Yes	No	Total	Yes	No	Total
G I	8	42	50	8	42	50	31	19	50	14	36	50
G II	0	50	50	0	50	50	0	50	50	0	50	50
Total	**8**	**92**	**100**	**8**	**92**	**100**	**31**	**69**	**100**	**14**	**86**	**100**

Serum lipoprotein (a) was analyzed in both groups (Table 3) Mean Lipoprotein (a) level of the Group I subjects is 25.62 + 19.16 mg/dl. Mean Lipoprotein (a) level of the Group II subjects is 11.14 + 7.43 mg/dl. Mean Lipoprotein (a) is significantly elevated in the Group I subjects (P = 0.000). 17 subjects have elevated Lipoprotein (a) level (above 30 mg/dl). Among these 15 subjects belongs to Group I and 2 belongs to Group II.

Table 3: The mean values of lipoprotein (a) in the study subjects

	Group I	Group II	Significance
Lp (a) (mg/dl)	25.616 + 19.16	11.136 + 7.43	P =0 .000

DISCUSSION

Non-communicable chronic diseases viz. diabetes mellitus, obesity, hypertension, cardiovascular, diseases are assuming importance among the adult population in both developed and developing countries. Hypertension, cardiovascular diseases, diabetes and obesity are closely interrelated. Among these, diabetes mellitus, hypertension, hypercholesterolemia etc. have strong hereditary component. In these circumstances, a comparative study was done in which serum lipoprotein (a) level was determined and compared among young adults in the age group of 18 to 25 years belonging to two groups ie. Group I, consisting of subjects with family history of diabetes or hypertension and Group II of subjects without family history of diabetes or hypertension. Lipoprotein (a) level was significantly elevated (P = 0.000) in the Group I subjects when compared to group II (mean being 26.62 + 19.16 mg/dl and 11.14 + 7.43 mg/dl respectively). Diabetes mellitus have a strong family tendency. Chance of type 1 diabetes in siblings and offspring are 20 times that of general population [13-15]. Cumulative risk of diabetes in siblings of index case with no diabetic parents, one diabetic parent and two diabetic parents are 14%, 29.2% and 41.9% respectively[16, 11]. It is a well-established fact that a persistently high cholesterol level can almost certainly can precipitate a cardiac event. Risk factors for coronary artery disease are elevated cholesterol level (above 200 mg/dl), elevated LDL cholesterol level (above 130-160 mg/dl), lower levels of HDL cholesterol (30-60 mg/dl), elevated Lipoprotein (a) (above 30 mg/dl), cigarette smoking, hypertension, diabetes mellitus, elevated levels of homocysteine (above 15 micromol/L), sedentary life style and obesity[17]. Family studies have shown that children of two normotensive parents have 3% possibility of developing hypertension, whereas this possibility is 45% in children of two hypertensive parents. Although there are variations in findings among prospective studies of Lp (a) as a risk factor for coronary heart disease (CHD), which may in part be attributed to methodological differences, several studies, including a recent meta-analysis, have demonstrated that CHD risk is increased as Lp (a) concentration increases[18-20]. Significant relationship of Lp (a) with CHD is reported in South Indian studies[21,22]. Lp (a) levels correlate with both early and advanced atherosclerosis, severity, extent and progression of atherosclerosis and all complications of CHD including re-stenosis following percutaneous transluminal angioplasty, stent and bypass surgery[23]. Lp (a) excess increases the risk of premature CHD 3 to 100 fold depending on the absence or presence of concomitant risk factors[24]. Our study also revealed that there is a significant increase in LP (a) level in group I subjects. The distribution of Lp (a) levels showed skewed distribution in Chinese, Malays, Asian Indians, whites, blacks and Indians[24-27]. In many studies, distribution of Lp (a) levels showed skewness. Plasma Lp (a) levels are highly heritable. Mechanism of pathogenicity of Lp (a) excess include enhanced thrombogenesis and impaired fibrinolysis by competing with plasminogen, inhibition of transforming growth factor β, destabilization of plaque, increased smooth muscle cell proliferation and migration, formation of occlusive thrombus, impaired formation of collateral vessels, enhanced oxidation uptake and retention of LDL-C and up regulation of expression of the plasminogen activator inhibitor (PAI-I). Our study showed higher mean Lp (a) levels in group 1 subjects than in group 2 subjects, and difference was statistically significant (P<0.01). This is in agreement with earlier studies conducted in India and abroad[28]. Lp (a) is a major inherited risk factor associated with premature heart disease and stroke. The mechanism of Lp (a) atherogenicity has not been elucidated, but likely involves both its ability to influence plasminogen activation as well as its atherogenic potential as a lipoprotein particle after receptor- mediated uptake[29,30]. The patients suffering from coronary artery disease has significant hyper Lp (a) lipoproteinemia compared to the control subjects[31,32]. Lp (a) concentration strongly contributed to CHD risk when

LDL-C was concomitantly increased. Lipoprotein (a), was found as an independent risk factor for ischemic stroke, especially in young adults[33]. High lipoprotein (a) levels correlate with a greater degree of atherosclerotic coronary artery disease and carotid wall thickening but not with coronary calcification. Lipoprotein (a) may induce chemo taxis of monocytes and affect plasminogen activator inhibitor[34] and tissue factor expression. High Lp (a) in blood is a risk factor for cardio vascular diseases. Lp-a concentrations may be affected by disease states, but are only moderately affected by diet, exercise, and other environmental factors. Determination of lipoprotein (a) levels should thus be reserved for high-risk subsets of the population such as individuals with premature MI who have otherwise normal risk profiles or are at particularly high risk because of circumstances such as familial hypercholesteremia[34] High Lp (a) predicts risk of early atherosclerosis similar to high LDL, but in advanced atherosclerosis, Lp (a) is an independent risk factor not dependent on LDL[35]. Lp (a) then indicates a coagulant risk of plaque thrombosis. Apo (a) contains domains that are very similar to plasminogen (PLG). Lp (a) accumulates in the vessel wall and inhibits binding of PLG to the cell surface, reducing plasmin generation which increases clotting. This inhibition of PLG by Lp (a) also promotes proliferation of smooth muscle cells. These unique features of Lp (a) suggest Lp (a) causes generation of clots and atherosclerosis[11]. Approximately 30% of individuals with heart disease have elevated Lp (a) levels. The concentration of Lp (a) in plasma is genetically determined. The gene coding for [a] is located on chromosome 6. It is inherited in a Mendelian dominant fashion which means that approximately 50% of children inherits high Lp (a) like their parents with elevated Lp (a). The exact physiologic function of Lp (a) is unclear but elevated plasma levels of Lp (a) have been shown to be an independent risk factor for coronary artery disease. It is one of the best predictors of heart attack in young men, blockage of vein grafts following coronary bypass surgery, and blockages in the carotid arteries of the neck. Lp (a) likely exerts its deleterious effects by virtue of its resemblance to plasminogen. Plasminogen is a substance produced by the body to aid in the breakdown of blood clots. High plasma Lp (a) concentrations may compete with plasminogen and thereby interfere with the bodies normal clot dissolving mechanism. The Lp (a) particle is also known to be highly susceptible to oxidation, one of the early steps in coronary artery disease[36]. Still the average mean of Lipoprotein (a) level is far less than the normal level expected in the Indian scenario.

CONCLUSION

Serum Lipoprotein (a) is significantly increased in young adult with family history of diabetes or hypertension, compared to others without family history of diabetes or hypertension. Mean Lipoprotein (a) level is more than two fold in the target group, compared to normal. This present study indicates the importance of lipoprotein (a) estimation and follow up study to identify the risk of dyslipdemia and development of CHD in our population.

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