Original Research Article

Comparative study of serum lipoprotein (a) levels in diabetic and non-diabetic patients of acute ischemic stroke

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Abstract

Background: Globally, Stroke is the fourth leading cause of disease burden and apart from the well established risk factors for the stroke such as increasing age, hypertension, diabetes, smoking etc, elevated levels of lipoprotein(a)is also considered as a crucial and independent risk factor for ischemic stroke. **Aim and Objectives**: The aim of the study is to study the levels of LP(a)in diabetic and non diabetic population presenting with acute ischemic stroke. The objectives of the study are to determine whether LP(a)is an important associated factor for acute ischemic stroke in diabetes, to identify whether LP(a)is more in younger or elderly age group with ischemic stroke and also to determine whether LP(a)levels are elevated significantly in patients only with abnormal lipid profile. **Materials and Methods**: A prospective study was done in patients presented with acute ischemic stroke, the diagnosis of acute infarct was confirmed by clinical signs, symptoms and by CT/MRI. The patients were investigated for diabetes mellitus and dyslipidemia. Estimation of serum lipoprotein(a)levels were done in all patients. Study was done after dividing patients into two groups, Ischemic stroke with diabetes mellitus and ischemic stroke without diabetes mellitus which included 40 patients of stroke with diabetic and 40 patient of stroke without diabetes, making a total of 80 patients. All the records were collected and the findings were recorded. **Results:** LP (a)levels were much higher in diabetes than non diabetes patients, which was statistically significant ($p < 0.01$), the mean Lp(a)levels was found to be higher among older stroke patients than the younger ones and this difference was found to be non significant($p > 0.05$) probably due to unequal distribution of the patients. The mean LP(a)levels, were higher among those with abnormal LDL levels which was also found to be statistically significant($p < 0.05$)

Key Word: serum lipoprotein (a).

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INTRODUCTION

The World Health Organization (WHO) defines stroke as a "rapidly developing clinical signs of focal disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death, with no other apparent cause other than of vascular origin.[1] The risk factors for stroke are classified into modifiable and non modifiable risk factors.[2,3] The non modifiable ones are age, gender and family background. The modifiable ones are prior stroke, alcohol, tobacco, drug usage, obesity, hypertension, Diabetes, dyslipidemia etc.[4] Diabetes mellitus is a well known risk factor for atherosclerosis, coronary heart disease, stroke and peripheral arterial disease.[5-8] The most common type of lipid abnormalities encountered in a subject with diabetes mellitus are elevated plasma levels of triglycerides, very low density lipoprotein cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C)and lipoprotein(a) and decreased high density

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lipoprotein cholesterol (HDL- C).[9-10] The stabilization of lipid and lipoprotein levels decreases the incidence of atherosclerotic coronary heart disease.[11] Lipoproteins are the particles that transport cholesterol and the triglycerides in the blood stream. Lipoproteins are mostly composed of proteins (apolipoproteins), phospholipids, triglycerides and cholesterol, [Lp(a)] concentrations are associated with myocardial infarction (MI), coronary artery disease (CAD), peripheral atherosclerosis and cerebral ischemia. Lipoprotein(a) is considered as an independent risk factor for atherosclerosis. Due to unique structural homology with plasminogen, it interferes with the function of plasminogen thus increasing thrombotic risk. Lp(a) is an LDL like molecule consisting of an Apo protein (apo) B-100 particle attached by a disulphide bridge to apo(a)[12] Apo(a) is the member of family of "kringle" containing proteins such as plasminogen, tissue platelet activator (tPA), prothrombin factor XII, and macrophage stimulating factor (MSF)[13,14] Lp(a) binding to immobilized fibrinogen and the fibrin results in the inhibition of the plasminogen binding to these substrates [15]. In addition, Lp(a) competes with plasminogen for its receptors on endothelial cells, leading to diminished plasmin formation, thereby delaying the lysis of clot and thus thrombus formation[16].The presence of oxidized phospholipids in Lipoprotein (a), potentially being taken up by the vessel walls, could also accelerate the development of atherosclerosis. The optimal level, should be no greater than (20 mg/ dl), especially in Indian population.

AIM AND OBJECTIVES

The aim of the study is to study the levels of LP (a) in diabetic and non diabetic population presenting with acute ischemic stroke. The objectives of the study are to determine whether LP (a)is an important associated factor for acute ischemic stroke in diabetes and whether it is more in younger or elderly age group with ischemic stroke and to determine whether LP (a) levels are elevated significantly in patient only with abnormal lipid profile.

MATERIALS AND METHODS

The research proposal was cleared by the Scientific Review Board following which clearance from the Institutional Ethics Committee was obtained. A prospective, comparative study was done in patients who presented with acute ischemic stroke to Saveetha Medical College Hospital between May 2017 and December 2017, they were invited to participate in the study after obtaining consent. The diagnosis of acute infarct was confirmed by clinical signs, symptoms and by CT/MRI. Patients diagnosed with haemorrhagic stroke were excluded. The patients were investigated for diabetes mellitus (based on ADA guidelines) and dyslipidemia. (Cholesterol, Triglyceride levels were determined by standard enzymatic methods. High –density lipoprotein (HDL) and low density lipoprotein (LDL) levels were measured by the ultracentrifugation precipitation combined technique. Estimation of serum lipoprotein(a) levels were done in all patients. 4ml of blood from cephalic vein was drawn in each patient for the study which is at least about 8 hours of fasting time and serum was separated immediately for the analysis.LP (a) concentration was measured by enzyme immunoassay (EIA) using a monoclonal antibody against LP (a). Fresh serum was stored at 2 - 8 degree Celsius. The normal levels of LP (a) is 0 – 30 mg/dl. Study was done after dividing into two groups: A. Ischemic stroke with diabetes mellitus B. Ischemic stroke without diabetes mellitus. Study included 40 patients of stroke with diabetic and 40 patient of stroke without diabetes, making a total of 80 patients. All the records were collected and the findings were recorded. Data was entered into Microsoft Excel data sheet and was analyzed using Statistical Package for the Social Sciences software version 22. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation. Student's t test was used as test of significance to identify the mean difference between the groups. P value $\leq$ 0.05 was considered as statistically significant. Both male and female patients aged > 18 years with ischemic stroke with or without diabetes presenting as stroke were included in the study. Haemorrhagic stroke, age less than 18 years and those who are seriously ill and or with chronic liver or kidney disease with serum creatinine > 2mg% Familial hypercholesterolemia's were excluded.

OBSERVATION AND RESULTS

80 patients included in the study 40 of them were diabetic (27 males/13 females) and remaining 40 of them were non-diabetic (26 males/14 females). The youngest age being 27 years and the oldest was 85 years. Majority of them belong to age group 45 to 65 years (46%). The mean HBA1C% were higher in females (8.95±0.96) than in males (8.61±1.30). The plasma LP(a) levels were abnormal in almost half of the (48.8%) total study subjects. The mean LP(a) levels was 28.03±12.28. The high total cholesterol level (>240mg/dl) were seen in 20 patients (25%). The mean total cholesterol level of the study subjects was 215.23±51.42. The triglyceride level of more than 200mg/dl was seen in 9 patients (11%). The mean LDL level of the total subjects was 138.81±30.94 and 27.5% of them found to have high serum LDL levels (>160mg/dl). The mean HDL level was 43.64±10.16 and 75% of the total study subjects have desirable HDL

cholesterol level. The proportion of abnormal LP(a) was significantly higher among diabetics (75%) than non-diabetics (p<0.001). None of the diabetics had plasma LP(a) <10. The mean LP(a) levels was found to higher among older stroke patient than younger ones. The mean total cholesterol levels of non-diabetics were higher than diabetics (219.7 vs 210.75). The mean serum LDL levels of diabetics were higher than non-diabetics (150.60 vs 127.02) which is found to be statistically significant (p<0.001). The mean Lp(a) levels were higher among those with abnormal LDL levels (31.89) than the one with normal LDL levels (23.76). This difference was found to be statistically significant (p<0.001)

DISCUSSION

A prospective comparative study was done among 80 acute ischemic stroke patients in which 40 were diabetics and 40 were non diabetic individuals and their LP(a) level were compared .In this study, mean LP (a) level on comparing diabetic and non diabetic patients of acute ischemic stroke, LP (a) level were much higher in diabetes than non diabetes patients, this was similar to the study done by Morishita *et al.*[17] 75% of diabetic patients have higher levels of LP(a) whereas only 25% of non diabetes patients have higher levels of LP (a) which was statistically significant (p <0.01) which was in contradiction with the study done by Haffner *et al*. While comparing the Lp(a) value among young (17) and older stroke (63) patients ,the mean Lp(a) levels was found to be higher (27.91) among older stroke patients than the younger ones (25.47) and this difference was found to be non significant.(p>0.05) probably due to unequal distribution of the patients. Larger studies are needed for further confirmation. Study done by Nagayama *et al*[18] reports that high serum Lp(a) is also a genetic and critical risk factor, especially for ischemic stroke in young adults. The mean LP(a) levels among study subjects with normal and abnormal LDL levels, were higher among those with abnormal LDL levels (31.89) than the one with normal LDL levels (23.76). This difference was found to be statistically significant(p<0.05).The mean Lp(a) levels among study subjects with normal and abnormal triglycerides level were higher among those with abnormal triglyceride levels (29.66) than the one with normal triglyceride levels (26.75). This difference was found to be statistically not significant,(p>0.05).Our findings were similar with the study of Hernandez *et al*[19] showing LP (a) concentrations were directly correlated with LDL and triglycerides. The mean LP(a) levels were higher among those with normal HDL levels (28.47) than the one with abnormal HDL levels (27.51)and the mean LP(a)levels were higher among those with abnormal total cholesterol levels (28.8) than the one with normal cholesterol levels (27.12). This difference was found to be statistically not significant in both HDL and total cholestrol levels. Jeetendrakumar *et al*[20] study showed that diabetic patients with stroke had a significantly higher triglycerides and significantly lower HDL cholesterol levels, the total cholesterol and LDL cholesterol levels were similar in both groups.

CONCLUSION

The mean LP (a) levels were higher in diabetic patients with ischemic stroke than non diabetics and were statistically significant. The mean LP (a) levels were higher in patients with ischemic stroke among the older age group. The mean LP (a) levels were higher in patients with abnormal LDL levels, abnormal triglycerides levels and abnormal cholesterol level in which statistically significant rise is found only with abnormal LDL level. In conclusion the present study revealed that elevated serum Lipoprotein (a) levels appears to be an associate factor for acute ischemic stroke in patients with diabetes. It is therefore important to measure serum Lipoprotein (a) level along with lipid profile as an important tool to investigate in all the cases, who are at the risk of developing stroke.

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