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A Prevalence Study on Serum Lipoprotein (a) and Serum LDL level in Stroke

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Abstract
Background: *Stroke is the second leading reason for mortality and morbidity in the world. Many studies indicate an elevated Lipoprotein (a) {Lp(a)} level in individuals with acute cerebral ischemia. The role of Lp(a) in acute stroke is unclear. Increased LDL level is found in various atherothrombotic manifestations including stroke. In this study we discuss the mechanisms, by which Lp(a) may cause stroke. We also studied the association between serum LDL level and Lp(a) in acute patients having stroke. Medical interventions to reduce the Lp(a) level are discussed.*
Method: *We analyzed serum LDL level and Lp(a) level in 100 cases of stroke admitted in the medical wards of Rajah Muthaiah Medical College during the period of September 2016 to October 2018. Elevated Lp(a) level is defined as Serum Lp(a) >30 mg/dl. We also the studied the relation between serum Lp(a) and serum LDL level.*
Result: *Serum Lp(a) was increased in 42 patients (42%) of acute cerebral ischemia. LDL level in the serum was increased in 19% of the patients with the mean LDL level of 109.12 mg/dl. The study showed no positive correlation between serum LDL level and Lp(a) level (P value=0.74).*
Conclusions: *We observed from the study that Lp(a) level were elevated in 42% ($\approx \frac{1}{2}$) of the patients with acute ischemic stroke. But no relation exists between serum Lp(a) and LDL levels.*
Keywords: *Acute Ischemic Stroke, Lipoprotein (a).*

Introduction

Stroke is a prime health problem. Stroke is a precursor of morbidity and mortality.[1] Stroke causes four million deaths a year globally.[2] We all know that hyperlipidemia is a major causative factor for artherosclerosis in Coronary arteries.[3-4] The role played by lipids in the prevention of stroke is not clearly defined.[5] Studies show that, increased levels of LDL and Total Cholesterol increases the incidence of non hemorrhagic stroke.[6] Raised serum Lp(a) level is found in many vascular events like myocardial infarction, cerebral ischemia, re-stenosis in the bypass vein graft, etc.[7-8] Many studies find that even in

patients having normal total cholesterol and LDL, elevated Lp(a) causes coronary artherosclerosis at a younger age.[9-10] The structural homogeneity of Lp(a) with plasminogen gives it the prothrombotic potential.[11] Raised Lp(a) level was found to be associated with acute ischemic stroke patients in various studies. Few studies have contradicted the role of Lp(a) in ischemic stroke. Hence we did this study to measure serum Lp(a) levels in 100 stroke cases and to find any association between serum Lp(a) and LDL.

Method

This descriptive study included 100 consecutively admitted acute ischemic stroke patients in Rajah Muthaiah Medical College Hospital. Clearance from ethical committee was obtained. All patients were subjected to history taking and neurological examination.

Inclusion criteria

Patients diagnosed as having acute ischemic stroke confirmed by CT scan.

Exclusion criteria

a. Patients having cardiovascular causes of stroke, eg (Atrial fibrillation).
b. Patients with hemorrhagic stroke.
c. Patients who are already on drugs that alter the serum lipid parameters. (e.g. Statins, Sex steroids, etc).

Methods of collection of data

Serum lipid parameters and Lipoprotein (a) were analyzed in every patient. Blood investigations like hemoglobin, Leukocyte count, ESR, platelets, and serum creatinine, blood urea were done in stroke patients. Inferential statistics such as Chi-square tests of association and independence and Pearsons correlation efficiencies was prepared for the selected study variables. The correlation of lipoprotein (a) with LDL was also performed. The entire statistical analysis is done using statical percentage of social science (SPSS-21).

Result

This descriptive study included 100 cases of acute ischemic stroke.

Distribution

Gender

Gender	Percentage
Male	56
Female	44
Total	100

Gender distribution showed that males constitute 56% and females constitute 44%.

Lp(a) levels in cases:

Lp(a)	Percentage	Mean	Sd
Normal	58	28.45	13.06
Increased	42		

42% of our study group had elevated Lp(a) levels. The mean Lp(a) levels were 28.45 ± 13.06
Among those 42 cases with raised Lp(a) level, 20 were females and 22 were males.

LDL levels

Lp(a)	Percentage	Mean	Sd
Normal	81	107.12	28.19
Increased	19		

In our study, LDL was increased in 19% of the patients. The mean LDL value was 107.12±28.19.

Correlation of Lp(a) with LDL

	Pearson's correlation	
Serum LDL	Value	'p'
	-0.034	0.74

No positive correlation between LDL levels and Lp(a) (p=0.74) was observed from our study.

Discussion

Our study aim was to find the prevalence of raised Lp(a) levels in ischemic stroke and to find any correlation between Lp(a) and LDL levels. Our study showed that 42% patients of the study group had raised Lp(a) levels. No positive correlation was seen between LDL levels and Lp(a) levels. This shows that even in patients having normal LDL levels there is a risk of ischemic stroke if their Lp(a) levels are raised. This confirms several other hospital and population based cross sectional studies.[12-18] Our study reflects the study conducted by Nagayama et al in which serum lipoprotein(a) was elevated in patients with atherothrombotic stroke with a mean and SD

values of 28.0±19.6. The Lp(a) values of the control population in their study was 16.4±13.5.[19]

Lp(a) and Artherosclerosis

After entering into the arterial lamina from plasma, Lp(a) might be retained more avidly than LDL because of its binding with the extracellular matrix through both Apolipoprotein A and Apolipoprotein B moiety, thereby causing cholesterol deposition in the growing atherosclerotic plaque.[20] Invitro Lp(a) can bind to various extracellular matrix proteins like fibrin and defensin, a group of 29-35 amino acid peptides. Neutrophils release these peptides in severe infection.[21] Defensins form a bridge between Lp(a) and the extracellular matrix. In addition Lp(a) may be retained at the site of mechanical injury. Deposition of fibrin occurs mainly at such sites.[22] Through it Apo lipoprotein moiety, Lp(a) also interacts with B2-integrin Mac-1, thereby promoting carrier of oxidized phospholipid in the human plasma.[23] Lipoprotein (a), a structural analogue pro-enzyme plasminogen may impair fibrinolysis.[24]

In summary increased Lp(a) levels may accelerate atherosclerosis through Lp(a) derived intimal cholesterol entrapment ,recruitment of inflammatory cells and binding of the pro inflammatory oxidized phospholipids.

Determinants of Lp(a) level in serum

In contratst to the other lipid parameters, Lp(a) levels are heritable and genetically determined.

Apolipoprotein A gene present on the chromosome 6q 26-27 determines the Lp(a) levels in serum.[25] Apo (a) protein differ in their size because of size polymorphism (KIV-2 UNTR). That size polymorphism is caused by kringle IV repeats. These variable Apo (a) size are said to be the Apo(a) isoforms.[26]

Studies favoring Lp(a) as a risk factor for stroke

A meta analysis by smoulder et al found that Lp(a) in ischemic stroke patients having elevated Lp(a) levels.[27] Studies done by Bostom et al, Nagayama et al, Vavernova et al also show an elevated level of Lp(a) in acute stroke. They also indicated that Lp(a) level are genetically determined.[28-30] Vankooten and colleagues found an raised Lp(a) levels in ischemic stroke patients.[31] Peng et al found that the serum Lp (a) as a strong determinant factor in acute ischemic stroke.[32] Watts et al demonstrated a significant raise in Lp(a) level in individuals with carotid artherosclerosis.[33]

Medical interventions of the reduction of Lp(a)

Dietary medications like omega-3 polyunsaturated fatty acids and palm oil may reduce Lp(a) levels.[34] Lp(a) level are reduced upto 30-40% in a dose dependent manner by Niacin.[35] Statins cause a minimal raise in the Lp(a) levels despite reducing the incidence of stroke and acute coronary events.[36] Fibrates decrease fibrinogen and also Lp(a) and oxidized LDL values.[37] Tight glycemic control may positively influence Lp(a) values.[38] Lp(a) after reaching the arterial wall ,undergoes further modifications like oxidation and proteolysis. These post translation events could be the targets for medical interventions in the future.[39]

Conclusion

Among these 100 cases of stroke patients studied, 42 patients had increased Lp(a) levels. No gender predilection for raised Lp(a) levels (M=22, F20) was found from our study. Serum Lp(a) levels are determined genetically and heritable. Our study demonstrated that there is no positive correlation between Lp(a) and LDL levels. So it is possible for a person with normal LDL level to have ischemic stroke if he has raised serum Lp(a) levels.

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