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COMPARATIVE STUDY OF LIPOPROTEIN (a)-A MAJOR RISK FACTOR FOR ISCHEMIC STROKE

General Medicine

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ABSTRACT

Aim of the Study: Measurement of serum Lp(a) as a screening tool for the risk of vascular events. **Material & Methods:** A total of 60 cases and 60 controls were admitted in Department of General Medicine, from August 2017 to July 2019 in Mamata Medical College, Khammam, Telangana State. **Results:** 60 cases and 60 controls were included in the study after taking written consent from the patients. Majority of patients in both cases and controls group were in 51-60 years age group. On performing chi square test, it was found that there was no statistically significant difference in age group distribution between cases and controls (P value >0.05). **Conclusion:** It included 60 ischemic stroke patients who were compared with age and sex matched controls during a period of two years. Reducing the circulating values of Lp(a) might prove difficult. It is imperative to control additional risk factors in individuals with elevated lipoprotein(a).

KEYWORDS

Ischemic heart disease; Lipoprotein; Cerebrovascular diseases.

INTRODUCTION

A stroke, or cerebrovascular accident, is defined by abrupt onset of a neurologic deficit that is attributable to a focal vascular cause.[1] The World Health Organization (WHO) definition of stroke is: "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin"[2].

Strokes (cerebrovascular accidents) are one of the most common causes of life-threatening neurological disease, causing mortality and long-term severe disability in people often females have greater disability than males[3]Stroke remains among the five leading causes of death across every income group in most countries in the last comprehensive review by World Health Organisation (WHO)

In 2016, there were 5.5 million (95% CI 5.3 to 5.7) deaths and 116.4 million (111.4 to 121.4) DALYs(Disability Adjusted Life Years) due to stroke. There were 13.7 million (12.7 to 14.7) new stroke cases in 2016. There were 80.1 million (74.1 to 86.3) prevalent cases of stroke globally in 2016; 41.1 million (38.0 to 44.3) in women and 39.0 million (36.1 to 42.1) in men.[4] In 2016, the global lifetime risk of stroke from the age of 25 years onward was approximately 25% among both men and women. There was geographic variation in the lifetime risk of stroke, with the highest risks in East Asia, Central and Eastern Europe.[5]

Studies in subjects with average lipid profiles indicate that raised lipoprotein(a) Lp(a) concentrations are associated with myocardial infarction, coronary artery disease, coronary stenosis, re-occlusion of coronary artery bypass grafts, 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.

Several studies have evaluated the association between Lp(a) and ischemic stroke. Several cross-sectional studies and a few prospective studies provide contradictory findings regarding Lp(a) as a predictor of ischemic stroke. Hence this study was undertaken to estimate lipoprotein (a) as a risk factor in ischemic stroke patients.

Aims Of The Study

1) To determine the role of lipoprotein (a) as a risk factor for ischemic stroke.
2) Measurement of serum Lp(a) as a screening tool for the risk of vascular events.

MATERIALAND METHODS

A total of 60 cases and 60 controls cases, patients who are survivors of ischemic non-cardioembolic stroke with history of sudden onset focal neurological deficit persisting beyond 24 hours admitted

Inclusion criteria

- Clinical evidence of ischemic stroke
- Computed Tomography (CT) scan of brain or magnetic resonance imaging (MRI) of brain consistent with ischemic stroke
- Absence of major predisposing factors causing cardiogenic stroke including atrial fibrillation, valvular heart disease, prosthetic heart values, endocarditis, acute myocardial infarction, dilated cardiomyopathy or ventricular aneurysm.

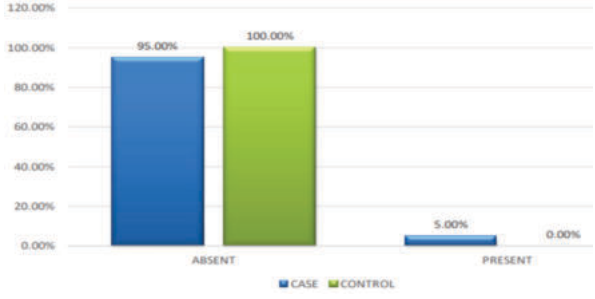
Exclusion criteria:

- Patients with CT / MRI scan showing intracerebral hemorrhage, tumor, or other mass lesion
- History of head injury
- Patients with coronary artery disease (including asymptomatic patients with electrocardiographic evidence of previous myocardial infarction).
- Patients with vasculitis.
- Patients with liver, renal, or thyroid disease.
- Patients taking drugs which may alter lipid and lipoprotein profiles
- Women on contraceptive pills.
- Sepsis.
- Malignancy.
- Active collagen vascular disease.

RESULTS

Table 1: Sex Distribution in Cases and Controls

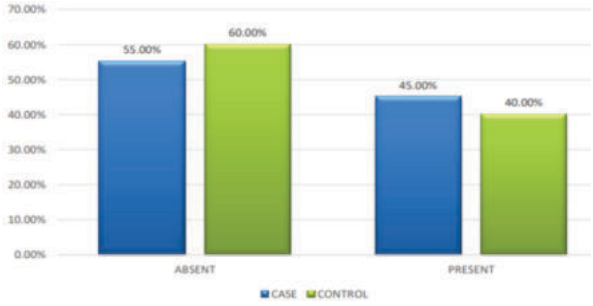
			GROUP		Total
			Case	Control	
SEX		Count	30	22	52
	Female	%	50.03%	36.73%	43.33%
		Count	30	38	68
	Male	%	503%	63.33%	56.73%
Total		Count	60	60	120
		%	100.0%	100.0%	100.0%



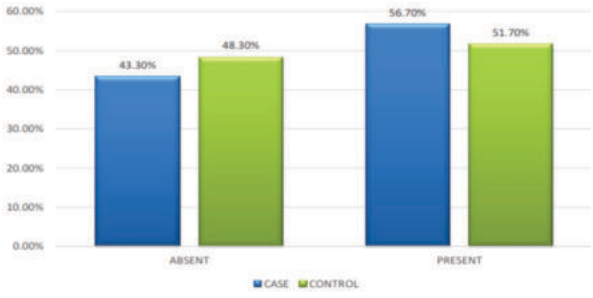
Graph 1:Comparison of Family History between cases and controls

Table 2: Comparison of total cholesterol between cases and controls

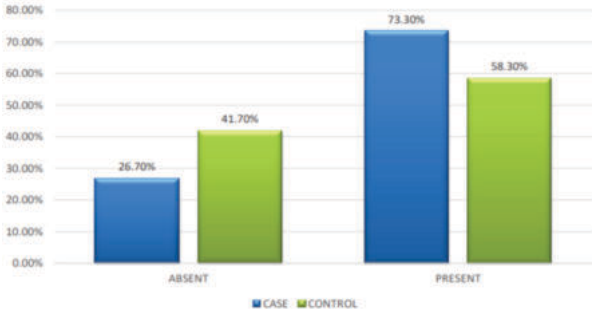
Group	Mean	Std. Deviation	P Value
CASE	193.000	37.9612	0.560 (NS)
CONTROL	188.867	39.4700	



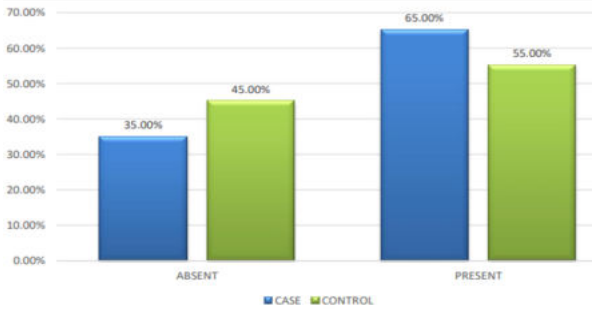
Graph 2 : Comparison of smoking between cases and controls



Graph 3 : Comparison of alcohol between cases and controls



Graph 4: Comparison of Hypertension between cases and controls



Graph 5 : Comparison of Diabetes between cases and controls

Table 3 : Comparison of elevated triglycerides between cases and controls

			GROUP		Total
			Case	Control	
SEX	NO	Count	29	41	70
		%	48.3%	68.3%	58.3%
	YES	Count	31	19	50
		%	51.7%	31.7%	41.7%
Total		Count	60	60	120
		%	100.0%	100.0	100.0%

Table 4: Comparison of HDL between cases and controls

Group	Mean	Std. Deviation	P Value
CASE	52.233	13.2708	0.271 (NS)
CONTROL	49.867	9.9430	

Table 5: Comparison of abnormal lipoprotein between cases and controls

			GROUP		Total
			Case	Control	
Lipoprotein (a)	<30mg/dl	Count	25	49	74
		%	41.7%	81.7%	61.7%
	> 30mg/dl	Count	35	11	46
		%	58.3%	18.3%	38.3%
Total		Count	60	60	120
		%	100.0%	100.0	100.0%

DISCUSSION

Stroke is a major cause of mortality and morbidity in developed as well as developing countries. In spite of advances made in the diagnosis and management of stroke patients, it remains the most common life-threatening neurological disease. Hence other relevant factors are to be identified.

In the present study there are 44 (73.3%) hypertensives and 16 (26.7%) normotensives among cases. Among controls 35 (58.3%) were hypertensives and 25 (41.7%) were normotensives. Analysis revealed P value of 0.083. Therefore, there is no significant relation between systemic hypertension and stroke. These results are consistent with studies of Zenker et al[6] and Van Kooten et al[7].

In the present study there were 39 (65%) diabetic patients among cases whereas 21 (35%) were non-diabetics. Among controls 33 (55%) were diabetics and 27 (45%) were non-diabetics. Analysis showed P value of 0.264 (Not significant). Therefore, there is no significant relation between diabetes and stroke.

The mean Lp(a) levels in a study done by Holanda MM et al in 2004[8] in 26 type 2 Diabetes Mellitus and 34 non-diabetics with ischemic stroke were found to be statistically in significant. Similar results were seen in our study.

In the present study, 56.7% among cases and 51.7% among controls were alcoholics, 45% among cases and 40% among controls were smokers. On performing chi square test this difference in distribution was not found to be statistically significant (P value >0.05).

In the present study, 51.7% among cases and 31.7% among controls had elevated triglyceride levels (TG>150). Mean value of triglycerides was more in cases 57 as compared to controls. On performing unpaired t test this difference was found to be statistically significant (P value <0.05)

In the present study, 18.3% among cases and 11.7% among controls had abnormal HDL levels (HDL). Mean value of HDL was more in cases as compared to controls. On performing unpaired t test this difference was not found to be statistically significant (P value >0.05).

The above findings show that family history of stroke, alcoholism, smoking, elevated cholesterol levels and abnormal HDL levels were not significant risk factors for stroke in our study. However elevated triglyceride levels were found to be a significant risk factor for stroke.

In the present case control study, 60 cases of ischemic stroke had a mean plasma lipoprotein (a) value of 34.140 mg/dl with a S.D of 12.39. This was statistically significantly higher than mean lipoprotein (a) concentration (27.607 mg/dl with S.D of 10.07) in 60 healthy controls.

Shintani et al[9] evaluated 54 patients with cerebral infarction to evaluate the role of lipoprotein(a) in ischemic stroke. When patients with atrial fibrillation were excluded to omit cardiac embolic strokes from analysis, the group consisted of 45 patients. The mean lipoprotein(a) levels in the study were 25 mg/dl with a S.D of 21 and p value of <0.025.

Nagayama et al[10] evaluated 101 serum lipoprotein(a) levels in 101 patients with ischemic stroke and 37 normal control subjects, taking the clinical profiles into consideration. The mean lipoprotein (a) levels were 40.2 mg/dl with a S.D of 20.1 and p value of <0.01. Jurgens et al[11] analyzed serum lipoprotein (a) levels and other lipid parameters in 265

patients with ischemic cerebrovascular disease. The mean lipoprotein(a) level was 41.1 mg/dl with a S.D of 31.8. The p value was found to be statistically significant (p=<0.001).

Our study also indicates the role of elevated LDL cholesterol levels (p = 0.021) as independent risk factors for ischemic stroke.

Our study showed the role of obesity as an independent risk factor in ischemic stroke. There is some controversy about the effect of obesity on Lp(a). In a study conducted by James Corsetti et al[12], lipoprotein(a) concentrations were not influenced by obesity, visceral fat content, or weight loss after a very low energy diet. However, there is also some evidence that obese individuals have higher Lp(a) values and that weight loss (by diet or surgical intervention) is associated with a significant reduction in these values.

Our study did not reveal significant relation between total cholesterol and ischemic stroke. This is consistent with the studies conducted by Lindgren et al[13], which showed no correlation between total cholesterol and stroke.

Jones et al[14] conducted a study in which they evaluated the Lp(a) risk association for 4 different types of vascular disease (CAD, CVD, PVD, abdominal aortic aneurysm) within a predominantly white population. This study indicated that lipoprotein (a) is an independent risk factor for ischemic stroke. The results of our study are in agreement with this study.

The Emerging Risk Factors Collaboration reports an adjusted risk ratio of 1.10 (95% CI 1.02–1.18) for Ischemic stroke, concluding that Lp(a), continues to have an 'independent and modest association with risk of CAD and stroke that appear exclusive to vascular outcomes.

Hoque MM et al[15] conducted a case control study to evaluate the lipoprotein(a) as a risk factor for CVD (cerebrovascular disease). Subjects were grouped as group-I (30, healthy control), Group-II (60, Hemorrhagic CVD) and group-III (60, Ischemic CVD). Fasting (12 hr) blood samples were collected from all subjects and in CVD cases samples were collected after 24 hr of attack. Lipid profile 61 and Lp(a) concentrations were measured in all samples. Mean serum Lp(a) concentration in Group-I, Group-II and Group-III were found to be 17.6 +/- 7.4 mg/dl, 31.9 +/- 15.6 mg/dl and 44.8 +/- 24.0 mg/dl respectively. Both the groups of CVD cases showed significantly higher level of serum Lp(a) concentration compared to healthy control. CVD cases did not differ statistically in respect of their lipid profile when compared with control. Moreover, the serum Lp(a) concentration of CVD cases found to show no correlation with their lipid profile, suggesting the serum Lp(a) concentration a possible independent risk factor for CVD.

Findings of the present study run in parallel with the above authors. The results of our study indicate that high lipoprotein (a) levels are an independent risk factor for ischemic stroke and thus the need to find methods for its prevention and management.

In our study 11/60 (18.3%) cases had elevated LDL and normal Lipoprotein (a). 13/60 (21.6%) cases had normal LDL and elevated Lipoprotein (a).

Pedro Botet et al[16] observed in their study that Lp(a) can be a major risk factor for ischemic CVD even in normocholesterolemic and normotriglyceridemic subjects.

CONCLUSION

1) Elevated serum Lp (a) is an independent risk factor of ischemic stroke.
2) Reducing the circulating values of Lp(a) might prove difficult. It is imperative to control additional risk factors in individuals with elevated lipoprotein(a).
3) Measurement of serum Lp(a) as a screening tool for the risk of vascular events should be considered.

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