Original Article

To Study Lipoprotein (A) As Risk Factor for Acute Ischaemic Stroke

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ABSTRACT

Background: Traditional cardiovascular risk factors, such as age, male sex, hypertension, diabetes mellitus, atrial fibrillation, and dyslipidemia, are associated with ischemic stroke. However, a significant fraction of strokes is still considered to be cryptogenic. Cryptogenic strokes make up roughly 40% of all ischemic stroke cases among stroke patients under the age of 55, highlighting the potential significance of additional, probably unidentified risk factors.
Objectives: To study the significance of lipoprotein (a) as a risk factor for acute ischaemic stroke with its levels in patients of different ages and sex.
Design: single center, cross-sectional, open hospital-based, observational study
Material Methods: 100 patients with acute ischaemic stroke taken who were >18 years of age and s. lipoprotein(a) levels were done. These levels were correlated with age, gender, and conventional risk factors like hypertension, smoking, and diabetes.
Results: In our study out of 100 81% of patients had abnormal lipoprotein(a) levels. The mean lp(a) levels were more in the younger age group [<55yr is 53.34 + 24.06 mg/dl and in >55yr is 45.93 + 24.19 mg/dl] and male sex but they were statistically insignificant.

Key Words: *Ischaemicstroke, lipoprotein (a), young stroke, independent marker*

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INTRODUCTION

A stroke is a sudden, possibly fatal condition brought on by a reduction in cerebral blood flow, resulting in focal cerebral ischemia and ultimately in the death of central nervous system cells.According to the global burden of illness registry, stroke was the third most prevalent cause of death and disability after newborn diseases and ischemic heart disease, but it was the second most common cause of mortality (11.6%) after ischaemic heart disease (16.2%) [1]. In low-income and middle-income nations like India, stroke is causing early deaths and disability with a greater socioeconomic cost due to demographic changes and the rising prevalence of modifiable risk factors [2]. The prevalence of ischaemic strokes is more as compared to the haemorrhagic event, almost 80% of the timeit's ischaemic while the rest 15-20% are haemorrhagic in origin [3]. Traditional cardiovascular risk factors, such as age, male sex, the presence of hypertension, diabetes mellitus, atrial fibrillation, and dyslipidemia, are associated with ischemic stroke. However, a significant fraction of strokes is still considered to be cryptogenic. Cryptogenic strokes make up roughly 40% of all ischemic stroke cases among stroke patients under the age of 55, highlighting the potential significance of additional, probably unidentified risk factors, particularly but not only in this stroke subtype [4]. Because of its putative pro-atherogenic, prothrombotic, and antifibrinolytic qualities, lipoprotein (a) [Lp(a)] may be linked to coronary heart disease and stroke. Until recently only myocardial ischemia and CAD were associated with dyslipidemia. However, it has recently come to light that lipids may also be crucial in the development of cerebrovascular accidents. Aorto-coronary bypass vein graft re-occlusion, cerebral ischemia, myocardial infarction, and coronary stenosis have all been associated with a lipid fraction known as lipoprotein (a) [5, 6 & 7]. Although lipoprotein (a) [Lp(a)] has atherogenic potential, its association with ischemic stroke risk is debatable. Increased lipoprotein (a) levels and the risk of thrombotic stroke are positively correlated, according to numerous research. However, cross-sectional studies produce conflicting findings regarding the significance of Lp (a) as a risk factor for ischemic stroke. To better understand the importance of lipoprotein (a) as a risk factor for acute ischemic stroke in patients of various ages and genders, the present study was conducted.

MATERIAL METHODS

This observational study was conducted at the Department of Medicine Jawaharlal Nehru Medical College A.M.U. Aligarh, Uttar Pradesh, is a tertiary care center in North India. It is a single-center, cross-sectional, open hospital-based, observational study. *Inclusion criteria*-All patients >18 years of age having a diagnosis of Ischemic CVA (as defined by WHO). *Exclusion criteria*-Hemorrhagic CVA patients, patients already onstatins therapy, with chronic diseases e.g. –

Chronic liver disease, chronic kidney disease, or malignancy, pregnant females, and patients denying consent for the study. 100 patients were taken for the study. Patients with a clinical diagnosis of an acute stroke underwent a thorough clinical evaluationand brain imaging. Information about the medical histories, clinical characteristics, and results of diagnostic tests of patients: blood sugar levels, lipid profiles, HbA1c, ECGs, and brain CT/MRIs were noted.

Patients were divided into two groups i.e., $\leq$55 years &>55 years. Patients with age $\leq$ 55 years were termed as young stroke patients [8, 9 & 4].

Smokers- As per National Centre for Health Statistics (NHS) as currently smoking or smoked 100 cigarettes in their lifetime.

Diabetic – known diabetic on therapy or newly diagnosed with FPG$\geq$126 mg/dl, PPG $\geq$ 200 mg/dl, and HbA1c $\geq$ 6.5

Hypertension- if already on antihypertensive drugs or SBP $\geq$130 mm Hg, DBP $\geq$ 80 mm Hg on two or more different occasions.

Dyslipidemia -LDL >100mg/dl,TGL$\geq$150mg/dl orHDL<40mg/dl in men and <50mg/dl in women (adapted by ATP IIIguidelines), Serum Cholesterol >200mg/dl (WHO Asian /pacific guidelines). According to LAI lipoprotein(a) > 20mg/dl is considered raised or abnormal [10].

In the present study, all the qualitative data were analyzed using the Pearson Chi-square test and all the quantitative data was analyzed using the independent sample t-test. Results were expressed as mean ± standard deviation and percentage in the case of continuous variables. The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0. For statistical significance, the p-value of less than 0.05 was considered statistically significant

OBSERVATION& RESULTS-

This is an observationalstudy with 100 acute ischaemic stroke cases. it was undertaken to investigate lipoprotein(a) association with age, sex and various conventional risk factors.

Table 1: Distribution of Age

S.NO	AGE	NO. OF CASES	(%)
1.	<55 YEARS	34	34
2.	> 55 YEARS	66	66
	TOTAL	100	100

Out of total number of patients (n=100) maximum number of cases were of the age >55yrs [(n= 66) 66%] whereas age <55yr [(n=34)34%]. It was statistically significant (p<0.05).

Table 2: Distribution of Sex

S.NO	SEX	NO. OF CASES	(%)
1.	MALE	64	64
2.	FEMALE	36	36
	TOTAL	100	100

Out of total number of patients n=100 males were more [n=64; 64%] compared to females [n=36; 36%]. It was statistically significant (p<0.05).
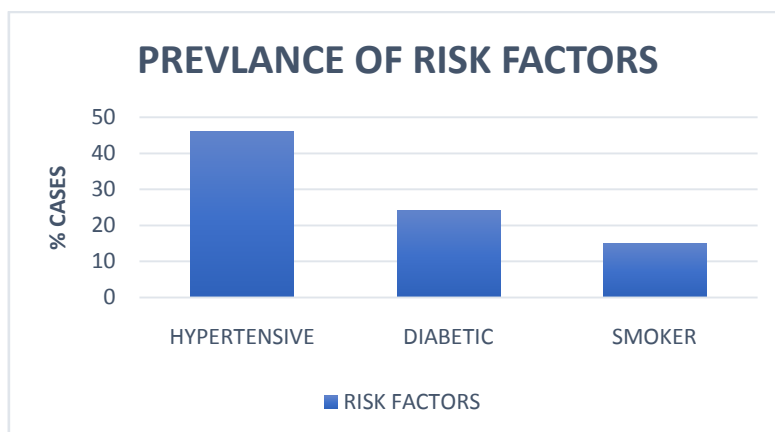

Figure 1: Distribution of Conventional Risk Factors

Out of total number of patients n = 100, 46% (n= 46) were hypertensive,24% (n= 24) were diabetic,15% (n= 15) were smokers.

Table 3: Distribution of Lipoprotein (A)

S.NO	LIPOPROTEIN(a)	NO. OF CASES	% CASES
1.	NORMAL	19	19
2.	ABNORMAL	81	81
	TOTAL	100	100

Out of the total no of patients (n=100) most of the patients had raised lipoprotein (a) in the range of >20mg/dl [n=81; 81%] compared to patients having normal lipoprotein (a) levels i.e., <20mg/dl [n=19; 19%].

Table 4: Distribution LP (A) Along The Age Groups

S.NO	AGE	LIPOPROTEIN(a)					
		NORMAL LP(a)		ABNORMAL LP(a)		TOTAL	
		CASES	%	CASES	%	CASES	%
1.	<55 YEARS	5	26.3	29	35.8	34	34
2.	>55 YEARS	14	73.7	52	64.2	66	66
	TOTAL	19	100	81	100	100	100

Out of total no patients (n=100) patients with normal lipoprotein (a) level 26.3% were <55 years of age (n=5) and 73.7% were >55years of age (n=14). Patients with abnormal lipoprotein (a) 35.8% (n=29) were <55yrs of age and 64.2% (n=52) were >55yrs of age. It was statistically insignificant (X^2= 0.617 p<0.05).
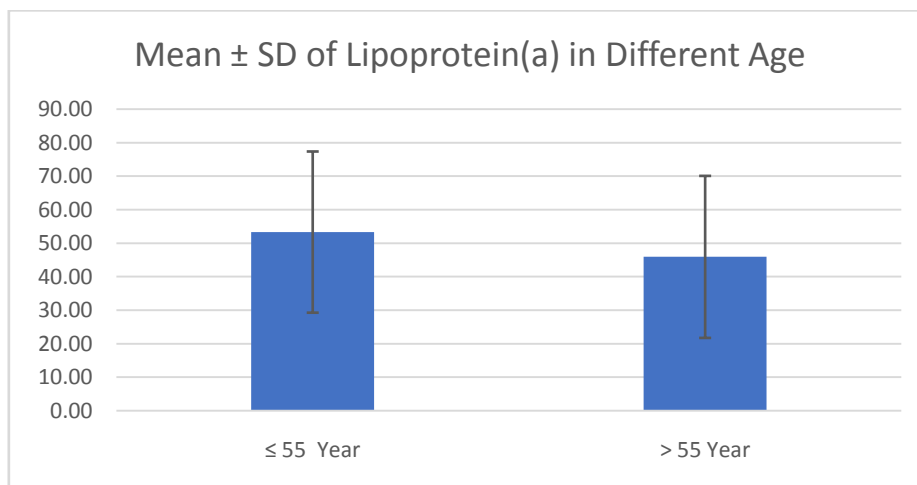

Figure 2: Association of LP (A) with Age

The mean value of lipoprotein (a) $\leq$55yr is 53.34 $\pm$ 24.06 mg/dl and in >55yr is 45.93 $\pm$ 24.19 mg/dl. It is statistically insignificant.

Table 5: Distribution of LP (A) Along Gender

S.NO	AGE	LIPOPROTEIN(a)					
		NORMAL LP(a)		ABNORMAL LP(a)		TOTAL	
		CASES	%	CASES	%	CASES	%
1.	MALE	11	57.9	53	65.4	64	64

2.	FEMALE	8	42.1	28	34.6	36	36
	TOTAL	19	100	81	100	100	100

Out of total no. Patients (n=100) among persons with normal lipoprotein (a) 57.9% (n=11) were males and 42.1% (n=8) were females while in abnormal lipoprotein(a) group 65.4% (n=53) were males and 34.6% (n=28) were females. It was statistically insignificant.
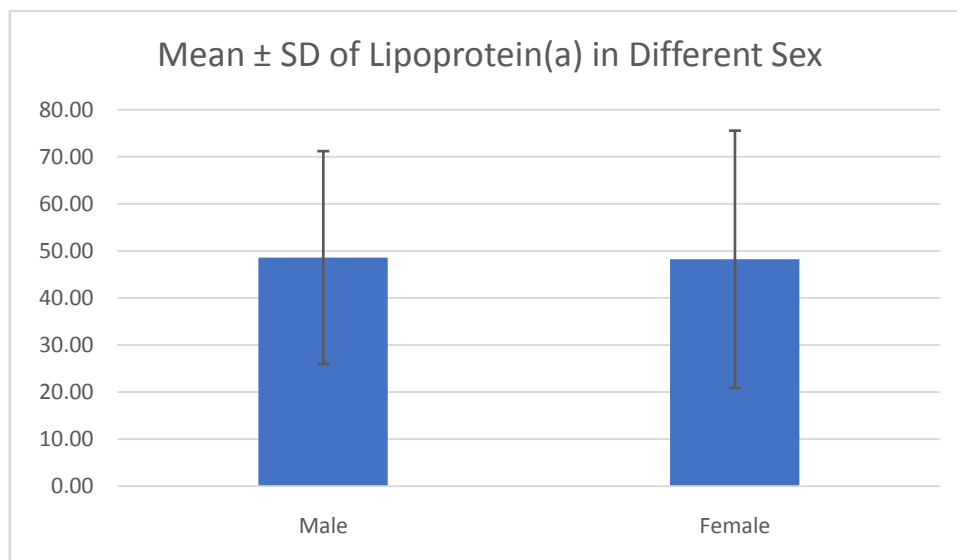

Figure 3: Association of Gender with LP (A)

Mean lipoprotein (a) in males is 48.58 $\pm$ 22.62 mg/dl and in case of females is 48.22 $\pm$ 27.34 mg/dl. Mean lipoprotein (a) were more in males in males but it was statistically insignificant.

Table 6: Association of LDL with LP (A)

S.NO	LDL	LIPOPROTEIN(a)	
		MEAN	STANDARD DEVIATION
1.	NORMAL	49.45	25.81
2.	ABNORMAL	47.98	23.72
	TOTAL	48.45	24.28

In the present study mean lipoprotein(a) levels in normal LDL levels were 49.45 $\pm$ 25.81 mg/dl and in increased lipoprotein(a) is 47.98 $\pm$ 23.72 mg/dl. The correlation between them is statistically insignificant.

Table 7: Association of Diabetes with LP(A)

S.NO	T2DM	LIPOPROTEIN(a)	
		MEAN	STANDARD DEVIATION
1.	YES	50.87	26.20
2.	NO	47.69	23.78
	TOTAL	48.45	24.28

In the present study the mean lipoprotein(a) levels in diabetics were 50.87 $\pm$ 26.20 mg/dl while in case of non-diabetic is 47.69 $\pm$ 23.78 mg/dl. It did not correlate statistically.

Table 8: Association of Hypertension with LP (A)

S.NO	HYPERTENSIVE	LIPOPROTEIN(a)	
		MEAN	STANDARD DEVIATION
1.	YES	47.91	23.42
2.	NO	48.91	25.20
	TOTAL	48.45	24.28

In the present study mean lipoprotein(a) levels in hypertensives were 47.91 $\pm$ 23.42 mg/dl while in case of non-hypertensives were 48.91 $\pm$ 25.20mg/dl. The result was statistically insignificant.

Table 9: Association of Smoking with LP (A)

S.NO	SMOKER	LIPOPROTEIN(a)	
		MEAN	**STANDARD DEVIATION**
1.	**YES**	53.03	26.67
2.	**NO**	47.64	23.92
	TOTAL	48.45	24.28

The mean lipoprotein(a) levels in smokers were 53.03 $\pm$ 26.67 mg/dl while in case of non-smokers were 47.64 $\pm$ 23.92 mg/dl. The results were statistically insignificant

Table 10: Association of Type of Stroke with LP (A)

S.NO	CIRCULATION	LIPOPROTEIN(a)	
		MEAN	**STANDARD DEVIATION**
1.	**ANTERIOR**	48.40	24.70
2.	**POSTERIOR**	49.12	19.39
	TOTAL	48.45	24.28

In the present study mean lipoprotein(a) levels in anterior circulation strokes is 48.4 $\pm$24.70 mg/dl and in posterior circulation stroke is 49.12 $\pm$ 19.39 mg/dl. It is statistically insignificant.

DISCUSSION

The number of males in the study was 64(64%) while the rest 36(36%) were females [11]. state men have a higher probability of having a stroke compared to their female counterparts. This skewed behaviour may be secondary to the more risk factors pertaining to lifestyle i.e. alcoholism, smoking etc is much more commonly practised by the masculine gender [12]. It was correlating with the study done by [13] in which 62% were male and 38% female [14], in which 60% were males and the rest 40% females.

34% of cases were ≤55 years while the maximum number of cases 66% lie in the category of >55 years. It is similar to [15] which had 62.9% cases in the older age group with a maximum of that with age >55 years.

The age of the patient affects sex differences in ischemic stroke epidemiology because sex has varying effects on stroke risk and prognosis throughout life. Males have a greater risk than females to develop an ischemic stroke in their early years of adulthood. In middle age, ischemic stroke rates in women start to rise along with menopause and the lack of female sex hormones. Women's stroke rates continue to rise beyond middle age [16, 17 & 18]. Similar is seen in our study as <55 years of age 29.4% (n = 10; total case =34) cases were female while in >55 years 39.4% (n= 26; total case =66) were females.

Among all the conventional risk factors taken hypertension was the most commonly seen with 46% prevalence among the sample size followed by diabetics (24%) and least common being smoking (15%). The similar pattern was also seen with [19] reporting 44.1% hypertensive, 25.4% diabetics and 19% smoker in there sample population.

In the study mean lipoprotein(a) levels in both age groups were 53.34mg/dl $\pm$ 24.06(<55yr) & 45.93 $\pm$ 24.19 mg/dl. Also, the frequency of abnormal lipoprotein(a) in both groups was not significantly different (35.8% in <55 years and 64.2% in >55 years.). It was concluded lipoprotein(a) was not significantly associated with age [20]. also showed no significantly different levels for age [21], had similar findings and so [22] and [23].

Mean lipoprotein(a) levels in males & females were 48.58$\pm$22.62 mg/dl and 48.22 $\pm$ 27.34 mg/dl respectively. There was no significant difference between the two. Even the distribution of abnormal levels of lipoprotein(a) among both sex is not statistically significant. Our findings regarding lipoprotein(a) distribution across gender are not significant and are in line with [23], [21], [24] and [25].

Lipoprotein(a) levels did not increase statistically with the increase in LDL from normal to abnormal. Hence emboldens the idea of lipoprotein(a) being an independent marker and not being dependent on lipid profile parameters. It was also seen in [25] and [26].

It was earlier thought lipoprotein(a) levels are more in diabetics. But in our study no significant change in lp(a) levels is seen with diabetic, hypertensive status or the patients being smoker.This result was similar to the study conducted by [25], [27] and [28].

The mean lipoprotein(a) levels were almost similar between the two types of strokes (48.40 $\pm$ 24.70 mg/dl in anterior v/s 49.12 $\pm$ 19.39 mg/dl in posterior). The relation between the two entities is statistically insignificant [25] and [29]

reported similar findings. Hence lipoprotein(a) increases the risk of stroke as evident by 81% cases having abnormal lp(a) levels but its effect on the subtypes is controversial.

CONCLUSION

Incidence of acute ischaemic strokes is more in males. The lp(a) levels are raised in acute ischaemic stroke cases but does not correlate with conventional risk factors like diabetes, smoking, hypertension or dyslipidemia. Lp(a) levels did not correlate significantly with age and gender. The study further proves the hypothesis of lp(a) being independent risk factor.

LIMITATIONS

As this was a hospital-based single-centre study, hence the results of the study may not be a true representative of the general population. The number of participants taken for this study was small.

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