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# Assessment of Lipoprotein (A) value in cerebrovascular accident cases of Tripura, Northeast India.

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## ABSTRACT

*Background*: Atherosclerotic cardiovascular disorders, such as stroke, have been linked to the formation of lipoprotein (A) [Lp(a)], a genetically determined lipoprotein variation. Elevated Lp(a) is a crucial component in the pathogenesis of stroke since it is linked to an increased risk of ischaemic stroke. The study assessed Lp(a) levels in acute stroke patients.

*Methods*: 49 stroke individuals and 49 age- and sex-matched healthy participants participated in the study. Lipid profiles, serum Lp(a) levels, and several biochemical markers were assessed. SPSS software was utilised for statistical analyses, with a significance threshold of $p < 0.05$.

*Results*: The mean age of stroke patients was 61 years, with 46.94% being female. Elevated Lp(a) levels were observed in stroke patients (57.01 ± 15.99 mg/dL) compared to controls (17.75 ± 11.61 mg/dL), with a significant difference ($p < 0.0001$). Elevated Lp(a) levels were found in 85.71% of cases and in only one control subject. Females had higher mean Lp(a) levels (61.76 ± 15.93 mg/dL) than males (52.26 ± 12.05 mg/dL) among stroke patients ($p < 0.05$).

*Conclusion*: Raised Lp(a) levels are significantly correlated with acute stroke in this cohort, particularly among females. Dyslipidemia is also prevalent among stroke patients. These findings highlight the importance of Lp(a) as an independent risk factor for stroke.

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*Recommendations*: Routine screening for Lp(a) levels in individuals at risk of cardiovascular diseases, especially those with a family history or existing comorbidities, is recommended. Further research into targeted therapies to lower Lp(a) levels is essential.

*Keywords: Lipoprotein (A), Stroke, Dyslipidemia, Cardiovascular Risk*

## INTRODUCTION

The lipoprotein variant known as lipoprotein (A) [Lp(a)] has drawn a lot of attention because of its strong correlation with cardiovascular illnesses, such as stroke. Low-density lipoprotein (LDL) particles bound to a distinct protein recognized as apolipoprotein(a) make up Lp(a). Genetically determined, elevated levels of Lp(a) are regarded as an independent risk factor for atherosclerotic cardiovascular disease (ASCVD), encompassing cerebrovascular events such as stroke and coronary artery disease. The processes by which Lp(a) contributes to vascular disease and the possible treatment targets to lessen its effects have been clarified by recent developments.

According to recent research, Lp(a) plays a multifaceted function in causing atherosclerosis by increasing cholesterol deposition, enhancing inflammation, and boosting the formation of blood clots. An increased risk of ischaemic stroke has been linked to greater Lp(a) levels, according to a substantial body of research. For example, a 2018 meta-analysis with over 90,000 participants found that people with high Lp(a) levels were 1.41 times more likely to have an ischaemic stroke than people with lower levels [1].

Notwithstanding these results, Lp(a) levels are mostly unaffected by conventional lipid-lowering medications like statins, underscoring the need for innovative treatment approaches. The invention of small interfering RNA (siRNA) therapeutics and antisense oligonucleotides, which precisely target the hepatic production of apolipoprotein(a), are examples of recent advancements. In early clinical trials, these treatments shown encouraging outcomes, lowering Lp(a) levels by 80–98% [2]. Muvalaplin is one such medication option that has shown promise in decreasing Lp(a) levels by obstructing the connection between apolipoprotein(a) and apolipoprotein B100, which stops Lp(a) particles from forming [3].

Lp(a) has more clinical importance than just its involvement in atherosclerosis. Increased risk of peripheral artery disease and aortic valve stenosis has also been linked to elevated Lp(a) levels. Because Lp(a) elevation has a genetic foundation, people who have a family history of

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cardiovascular disease should exercise extra caution. International medical societies' current guidelines are increasingly calling for Lp(a) screening, particularly in those with a history of early-onset cardiovascular events or high LDL-C levels even after receiving the best care possible [4].

Therefore, this study aimed at evaluating Lipoprotein (A) levels in patients with acute stroke.

## METHODOLOGY

*Study Design*

A case-control study.

*Study Setting*

The study took place in the Department of Medicine and the Department of Biochemistry at Tripura Medical College and Dr. BRAM Teaching Hospital, Agartala. The study period spanned from April 2018 to March 2020.

*Participants*

A total of 49 individuals with acute stroke were selected from those admitted to the medicine ward. Additionally, 49 age- and sex-matched controls were selected from the healthy relatives of patients and willing medical and paramedical staff of the hospital.

*Inclusion Criteria*

- Patients with acute stroke

- Age over 35 years

- Absence of a history of smoking and previous cerebrovascular disease

*Exclusion Criteria*

- Patients below 35 years of age

- Patients with subarachnoid hemorrhage

- Patients with transient ischemic attacks

- Patients on statin drugs or any medication known to modify lipoproteins

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*Bias*

To minimize bias, cases and controls were matched for age and sex. Controls were selected from healthy relatives and hospital staff to ensure a comparable baseline.

*Data Collection*

Complete histories, including disease course, family history, laboratory findings, and clinical data, were collected from all participants after obtaining informed consent.

*Procedure*

All patients had fasting venous blood drawn for routine investigations, lipid profile analysis, and Lp(a) assessment. Serum from blood samples was kept at -20°C until analysis after they were centrifuged for 10 minutes at 3000 rpm.

*Lipoprotein (A) Estimation*

Lipoprotein (A) levels were estimated using a turbidimetric immunoassay with the Quantia-Lp(a) kit provided by Coral Clinical Systems (Goa, India). This method is based on the principle of agglutination reaction. The normal reference range for Lipoprotein (A) was taken as ≤ 30 mg/dl.

*Lipid Profile*

Beckman Coulter analysers were utilised to determine serum total cholesterol, TGRs, and HDL-cholesterol by enzymatic techniques. Using the Friedewald formula, LDL-cholesterol was determined.

*Statistical Analysis*

SPSS statistical software was used for all statistical analyses. The format for values is Mean ± Standard Deviation. To evaluate variations in the gender distribution between the two groups, the Chi-square test was employed. P-values < 0.05 were supposed statistically significant.

*Ethical Considerations*

The study was approved by the Institutional Ethics Committee (vide no. F.3 (P0-75)/IEC/SFTMC/2010 – 11/16805 - 16822).

**RESULT**

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The demographic details of the control subjects and stroke individuals are shown in Table 1. The stroke patients ranged in age from 40 to 70 years old, with a mean age of 61. In the case group, there were 44.99% female participants, compared to 46.94% female cases. Between the two groups, there was no discernible change in the distribution of age or gender ($p > 0.05$). Twenty percent of the stroke patients had type 2 diabetes, and fourteen and a half had hypertension.

**Table 1: Demographic Data of Stroke Patients and Controls**

| Parameter | Stroke Patients | Controls | P-value |
|---|---|---|---|
| Age (Mean) | 61 | 59 | > 0.05 |
| Gender | | | |
| - Male | 26 | 27 | > 0.05 |
| - Female | 23 | 22 | |
| T2DM (%) | 20 | - | - |
| Hypertension (%) | 17.28 | - | - |

Serum [Lp(a) levels were found to be substantially higher in stroke patients compared to the control group. The mean Lp(a) level in stroke patients was 57.01 ± 15.99 mg/dL, while in controls it was 17.75 ± 11.61 mg/dL ($p < 0.0001$). Elevated Lp(a) levels were present in 85.71% of the stroke cases and in only one control subject. Additionally, among stroke patients, females had significantly higher mean Lp(a) levels (61.76 ± 15.93 mg/dL) compared to males (52.26 ± 12.05 mg/dL) ($p < 0.05$).

**Table 2: Lipoprotein (A) and Lipid Profile in Stroke Patients and Controls**

| Parameter | Stroke Patients | Controls | P-value |
|---|---|---|---|
| Lp(a) (mg/dL) | 57.01 ± 15.99 | 17.75 ± 11.61 | < 0.0001 |
| Total Cholesterol (mg/dL) | 214.7 ± 50.02 | 165 ± 35.29 | < 0.0001 |
| LDL-Cholesterol (mg/dL) | 141.77 ± 39.96 | 103.9 ± 31.59 | < 0.0001 |
| HDL-Cholesterol (mg/dL) | 41.82 ± 6.76 | 52.92 ± 7.72 | < 0.0001 |
| Triglycerides (mg/dL) | 222.67 ± 125 | 114.45 ± 17.6 | < 0.0001 |

There were notable distinctions between stroke individuals and the control group based on the lipid profile study. In comparison to controls, stroke patients exhibited lower levels of HDL

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cholesterol and greater levels of triglycerides, LDL cholesterol, and total cholesterol. There was a statistically substantial difference ($p < 0.0001$). In the stroke cases, there was no discernible relationship between high LDL or total cholesterol levels and Lp(a) levels.

The BMI, fasting blood glucose, and CRP levels of stroke patients and healthy controls were compared. According to the findings, stroke patients' fasting blood glucose, CRP, and BMI were all much higher than those of the control group. Increased CRP levels indicate inflammation, which is frequently linked to stroke, and higher BMI and raised blood glucose levels are risk factors for stroke.

**Table 3: Additional Biochemical Parameters in Stroke Patients and Controls**

| Parameter | Stroke Patients | Controls | P-value |
|---|---|---|---|
| BMI (kg/m²) | 28.5 ± 4.2 | 25.3 ± 3.1 | < 0.05 |
| Fasting Blood Glucose (mg/dL) | 130 ± 25 | 95 ± 10 | < 0.01 |
| CRP (mg/L) | 10.2 ± 3.5 | 2.1 ± 0.8 | < 0.0001 |

Ischaemic stroke and hemorrhagic stroke were the two categories of stroke patients that were identified. Hemorrhagic strokes made up 28.57% of the instances of stroke, whereas ischaemic strokes accounted for the majority (71.43%).

**Table 4: Distribution of Stroke Types in Stroke Patients**

| Stroke Type | Stroke Patients | Percentage (%) |
|---|---|---|
| Ischemic Stroke | 35 | 71.43 |
| Hemorrhagic Stroke | 14 | 28.57 |

The mean levels of [Lp(a) in male and female stroke patients. The data indicate that female stroke patients had significantly higher Lp(a) levels (61.76 ± 15.93 mg/dL) compared to male stroke patients (52.26 ± 12.05 mg/dL).

**Table 5: Comparison of Lp (a) Levels by Gender in Stroke Patients**

| Gender | Lp(a) Levels (mg/dL) | P-value |
|---|---|---|
| Male | 52.26 ± 12.05 | < 0.05 |
| Female | 61.76 ± 15.93 | < 0.05 |

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## DISCUSSION

The study examined differences in lipid profiles, biochemical profiles, and demographic characteristics between stroke individuals and healthy controls. Comparability was ensured by the demographic study, which showed no discernible variation in the age or gender distribution between the two groups. Nonetheless, a sizable fraction of stroke patients also had co-occurring diseases, such as hypertension (14.28%) and type 2 diabetes mellitus (20%), indicating the frequency of these risk factors in stroke patients.

Serum Lp(a) levels were analysed, and the results showed that stroke patients had much higher levels than controls. The mean Lp(a) level in individuals with stroke was 57.01 mg/dL, significantly more than the control group's 17.75 mg/dL ($p < 0.0001$). Furthermore, although they were uncommon in the control group, higher Lp(a) levels were seen in 85.71% of stroke patients. The study found that there may be a gender difference in Lp(a) levels and their correlation with stroke risk, as female stroke patients had considerably higher mean Lp(a) levels than male stroke patients.

According to the evaluation of their lipid profiles, stroke patients showed much greater levels of triglycerides, LDL cholesterol, and total cholesterol as well as lower levels of HDL cholesterol when compared to controls. These results highlight the dyslipidaemia that is frequently seen in stroke victims and its possible involvement in the aetiology of stroke. Interestingly, no significant link was detected between raised Lp(a) levels and high LDL cholesterol or total cholesterol levels in stroke patients, despite the large changes in lipid profiles. This finding suggests that Lp(a) may act as a stand-alone risk factor for stroke.

Additional biochemical parameter analysis revealed that stroke patients had higher levels of CRP, fasting blood glucose, and BMI in comparison to controls. These results support the notion that stroke patients have anomalies related to inflammation and metabolism, which may raise their risk of stroke.

Overall, the study highlights substantial differences in Lp(a) levels, lipid profiles, and other biochemical parameters between stroke patients and healthy controls. Elevated Lp(a) levels, particularly in females, and dyslipidemia were prominent features among stroke patients. These results suggest that Lp(a) and lipid abnormalities may play critical roles in stroke pathogenesis and could be valuable targets for early identification and management of stroke risk.

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The risk of cardiovascular and cerebrovascular events has been reported to be greatly increased by elevated levels of Lp(a). A 5-fold increased risk for myocardial infarction, stroke, and limb amputation was seen in individuals with Lp(a) levels between 30 and 50 mg/dL in a trial including stable outpatients with symptomatic artery disease. Levels beyond 50 mg/dL were associated with a risk that was more than ten times higher [5]. According to a different study, Lp(a) values have a direct correlation with both non-alcoholic hepatic steatosis and cardiovascular risk variables [6]. This suggests that Lp(a) should be included in routine evaluations of cardiovascular risk.

Significant lipid abnormalities were observed in non-diabetic stroke patients, with reduced HDL being the most prevalent anomaly in both the ischaemic and hemorrhagic stroke groups. As an example, it was found that whilst 46.1% of patients with hemorrhagic stroke had the same anomaly, 54.1% of patients with ischaemic stroke had lower HDL levels [7]. Furthermore, there was a strong correlation found between increased levels of serum lipoprotein-associated phospholipase A2 (Lp-PLA2) and the severity of acute ischaemic stroke as well as plaque instability. Particularly, there was a higher risk of severe neurological damage and cerebrovascular stenosis in patients with increased Lp-PLA2 levels [8].

Elevated Lp(a) levels were found to be strongly correlated with the risk of both hemorrhagic and ischaemic stroke in the Chinese Han population. Stronger correlations were seen in men and younger patients, with higher odds ratios (OR) for stroke across different quartiles resulting from greater Lp(a) levels [9]. High levels of lipoprotein(a) have been associated with worse short-term outcomes in older patients with acute ischaemic stroke and type 2 diabetes mellitus. With an OR of 2.899 for the third quartile and 3.334 for the fourth quartile relative to the lowest quartile, the study found Lp(a) to be an independent risk factor for unfavourable outcomes [10].

Regular clinical evaluations of Lp(a) levels have also revealed strong correlations with unfavourable cardiovascular consequences. A large cohort research found that compared to those with levels ≤50th decile, those with Lp(a) levels in the >90th decile had increased hazard ratios (HR) for severe adverse cardiovascular events (HR: 1.25), atherosclerotic cardiovascular disease (HR: 1.37), and coronary artery disease (HR: 1.62).

## CONCLUSION

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The important role that raised Lp(a) levels play in the pathophysiology of stroke is highlighted by this study. Compared to healthy controls, stroke patients showed significantly greater levels of Lp(a), indicating that Lp(a) is a separate risk factor for stroke. The results also point to gender disparities among stroke patients, with women exhibiting higher Lp(a) levels than men. Furthermore, the lipid profile analysis identified dyslipidaemia, which is typified by decreased HDL cholesterol and increased levels of total, LDL, and triglycerides in stroke patients. In order to reduce the risk of stroke, these data highlight the necessity of focused screening as well as possible treatment approaches meant to lower Lp(a) levels.

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