Section: General Medicine

Original Research Article

CORRELATION OF LIPOPROTEIN (A) AND SERUM URIC ACID WITH STROKE SEVERITY IN POSTMENOPAUSAL WOMEN

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ABSTRACT

Background: Stroke is a leading cause of death and disability in postmenopausal women, in whom hormonal changes increase cardiovascular risk. Lipoprotein (a) [Lp(a)] and serum uric acid (SUA) have been implicated as potential biomarkers for atherosclerosis and endothelial dysfunction. Their relationship with stroke severity in postmenopausal women remains underexplored. **Aim:** To correlate Lipoprotein (a) and Serum Uric Acid levels with stroke severity in postmenopausal women.

Materials and Methods: A hospital-based case-control cross-sectional study was conducted on 100 participants-50 postmenopausal women with ischemic stroke and 50 age-matched controls. Clinical and biochemical parameters were recorded, including blood pressure, fasting lipids, Lp(a), and SUA. Stroke severity was assessed using the NIH Stroke Scale (NIHSS). Data were analyzed using SPSS version 28, applying t-tests, chi-square tests, and Pearson's correlation. A p-value <0.05 was considered significant.

Results: The mean systolic blood pressure was significantly higher in cases (148 ± 18 mmHg) than controls (138 ± 16 mmHg, p = 0.002). Elevated Lp(a) levels (≥50 mg/dL) were found in 48% of cases versus 16% of controls (p < 0.001), while hyperuricemia (≥6 mg/dL) was observed in 52% versus 24% (p = 0.004). Mean Lp(a) and SUA levels were significantly higher in stroke patients (48.5 ± 22.0 mg/dL; 6.1 ± 1.4 mg/dL) compared with controls (28.3 ± 15.6 mg/dL; 5.2 ± 1.2 mg/dL). NIHSS correlated positively with both Lp(a) (r = 0.42, p = 0.002) and SUA (r = 0.36, p = 0.01).

Conclusion: Elevated Lipoprotein (a) and Serum Uric Acid levels are significantly associated with ischemic stroke occurrence and greater neurological severity among postmenopausal women. Routine screening for these biomarkers may aid in early risk identification and prognosis estimation.

Keywords: Lipoprotein (a), Serum Uric Acid, Ischemic Stroke Severity, Postmenopausal Women.

INTRODUCTION

Stroke is among the foremost causes of mortality and long-term disability worldwide, accounting for a significant proportion of cardiovascular deaths. Ischemic stroke, which constitutes nearly 85% of all cases, results from a vascular obstruction leading to neuronal ischemia and subsequent brain tissue necrosis. The prevalence of stroke rises sharply with advancing age, and postmenopausal women represent a distinct high-risk group due to estrogen deficiency, endothelial dysfunction, and metabolic changes. The hormonal decline associated with menopause disrupts lipid metabolism, elevates oxidative stress, and enhances platelet aggregation-

factors that collectively predispose women to cerebrovascular events.[1]

Estrogen has a crucial protective role in maintaining vascular tone, modulating lipid metabolism, and exerting antioxidant effects. Its deficiency in postmenopausal women leads to increased low-density lipoprotein (LDL), decreased high-density lipoprotein (HDL), and higher triglyceride levels, facilitating atherosclerotic plaque formation. Consequently, exploring biochemical markers that reflect atherothrombotic risk in this population is essential for early detection and preventive management of stroke.[2]

Lipoprotein (a) [Lp(a)] is a genetically determined LDL-like particle that contains apolipoprotein(a) [Apo(a)] covalently linked to apolipoprotein B-100. Elevated plasma levels of Lp(a) are now recognized as an independent risk factor for atherosclerosis, coronary artery disease, and ischemic stroke. Lp(a) promotes thrombosis by competing with plasminogen for fibrin binding, thereby inhibiting fibrinolysis and favoring clot persistence. Moreover, Lp(a) carries oxidized phospholipids that enhance vascular inflammation, endothelial dysfunction, and plaque instability-key processes in the pathogenesis of ischemic stroke.[3]

Similarly, serum uric acid (SUA), the final oxidation product of purine metabolism, has a complex bidirectional relationship with vascular health. At physiological concentrations, SUA acts as a potent antioxidant, scavenging reactive oxygen species. However, elevated SUA levels (hyperuricemia) are associated with endothelial dysfunction, increased oxidative stress, and vascular inflammation. In postmenopausal women, reduced renal clearance of uric acid and altered metabolism contribute to higher SUA concentrations, predisposing to hypertension, diabetes mellitus, and stroke. Elevated SUA has also been correlated with stroke severity, poorer neurological outcomes, and recurrence.[4]

Recent studies have indicated that both Lp(a) and SUA might serve as reliable biochemical indicators for predicting stroke risk and outcome severity, particularly in postmenopausal women. Understanding their correlation with stroke severity can provide deeper insights into gender-specific vascular pathology and aid in developing targeted preventive strategies. Moreover, if proven significant, these biomarkers could complement established risk factors in clinical practice, enhancing early diagnosis and individualized therapy.[5]

Aim

To correlate Lipoprotein (a) and Serum Uric Acid levels with stroke severity in postmenopausal women.

Objectives

1. To measure serum Lipoprotein (a) and serum uric acid levels in postmenopausal women with ischemic stroke.
2. To compare these biochemical markers with age-matched postmenopausal controls without stroke.
3. To determine the correlation between these markers and the severity of stroke using the National Institutes of Health Stroke Scale (NIHSS).

MATERIALS AND METHODS

Source of Data: The study was conducted in the Department of General Medicine, Mysore Medical College and Research Institute, Mysuru, with data collected from patients admitted to K.R. Hospital, Mysuru.

Study Design: Hospital-based case-control, cross-sectional analytical study.

Study Location: Department of General Medicine, Mysore Medical College and Research Institute, Mysuru.

Study Duration: Twelve months (January 2023 to December 2023).

Sample Size: 100 participants divided into two groups:

Cases (n = 50): Postmenopausal women diagnosed with acute ischemic stroke.

Controls (n = 50): Age-matched postmenopausal women without history of stroke or transient ischemic attack.

Inclusion Criteria:

- Postmenopausal women aged 45–75 years.
- Cases with clinically and radiologically (CT/MRI) confirmed acute ischemic stroke.
- Patients admitted within 72 hours of symptom onset.
- Willingness to provide informed consent.

Exclusion Criteria:

- History of hemorrhagic stroke or transient ischemic attack.
- Chronic renal failure, gout, hypothyroidism, or malignancy.
- Current use of lipid-lowering, uric acid-lowering, or hormone replacement therapy.
- Acute infections or inflammatory conditions.

Procedure and Methodology: All participants underwent detailed clinical evaluation including medical history, risk factor assessment (hypertension, diabetes, smoking), and neurological examination. Stroke severity was assessed using the NIH Stroke Scale (NIHSS). Imaging confirmation was done through CT/MRI brain. Venous blood samples were collected after 8–10 hours of fasting for biochemical analysis of Lipoprotein (a), Serum Uric Acid, fasting blood glucose, lipid profile, and renal function tests.

Sample Processing:

Serum Lipoprotein (a): Estimated using immunoturbidimetric method.

Serum Uric Acid: Measured by uricase-peroxidase enzymatic method.

Blood samples were processed within two hours of collection in the central laboratory of K.R. Hospital, Mysuru.

Statistical Methods: Data were entered into Microsoft Excel and analyzed using SPSS version 28. Continuous variables were expressed as mean ± SD and compared using the Student's *t*-test or Mann–Whitney *U*-test as appropriate. Categorical variables were analyzed using the chi-square test. Correlation between Lp(a), SUA, and stroke severity (NIHSS) was assessed using Pearson's correlation coefficient. A *p*-value <0.05 was considered statistically significant.

Data Collection: Data were collected through a structured proforma including demographic details, clinical parameters, comorbidities, imaging findings, and laboratory investigations. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was taken from all participants.

RESULTS

Table 1: Baseline Characteristics of Study Participants (Cases vs Controls; N=100)

Variable	Cases (n=50)	Controls (n=50)	Test statistic	95% CI (difference)	*p*-value
Age (years), Mean ± SD	62.1 ± 6.4	61.5 ± 6.2	$t(98)=0.47$	-1.9 to 3.1	0.64
BMI (kg/m²), Mean ± SD	27.9 ± 3.6	27.3 ± 3.4	$t(98)=0.93$	-0.7 to 1.9	0.36
Systolic BP (mmHg), Mean ± SD	148 ± 18	138 ± 16	$t(98)=3.22$	3.9 to 16.1	0.002
Diastolic BP (mmHg), Mean ± SD	88 ± 11	84 ± 10	$t(98)=1.90$	-0.3 to 8.3	0.06
Hypertension, n (%)	31 (62.0)	22 (44.0)	$\chi^2(1)=3.27$	RD 18.0% (-1.6 to 37.6)	0.07
Diabetes mellitus, n (%)	18 (36.0)	13 (26.0)	$\chi^2(1)=1.26$	RD 10.0% (-8.4 to 28.4)	0.26
Dyslipidaemia, n (%)	29 (58.0)	19 (38.0)	$\chi^2(1)=3.92$	RD 20.0% (0.1 to 39.9)	**0.048**
Current smoking, n (%)	5 (10.0)	3 (6.0)	$\chi^2(1)=0.54$	RD 4.0% (-7.7 to 15.7)	0.46

Table 1 summarizes the demographic and clinical baseline profile of 100 study participants-50 postmenopausal women with ischemic stroke (cases) and 50 age-matched postmenopausal women without stroke (controls). The mean age was comparable between groups (62.1 ± 6.4 years vs 61.5 ± 6.2 years; $p = 0.64$), showing no statistically significant difference. Likewise, mean BMI values were similar (27.9 ± 3.6 kg/m² vs 27.3 ± 3.4 kg/m²; $p = 0.36$). However, cases demonstrated significantly higher mean systolic blood pressure (148 ± 18 mmHg) compared with controls (138 ± 16 mmHg), with a mean difference of 3.9–16.1 mmHg ($p = 0.002$). Diastolic pressure showed a mild, nonsignificant elevation among cases (88 ± 11 mmHg vs 84 ± 10 mmHg; $p = 0.06$).

Prevalence of hypertension was greater in the stroke group (62%) than controls (44%), though the difference approached but did not reach statistical significance ($p = 0.07$). Diabetes mellitus occurred in 36% of cases and 26% of controls ($p = 0.26$). Dyslipidaemia was significantly more frequent among stroke patients (58%) than controls (38%) ($p = 0.048$), suggesting an association with cerebrovascular risk. Smoking prevalence was low overall and comparable between groups (10% vs 6%; $p = 0.46$).

Table 2: Proportions with Elevated Biomarkers (Pre-specified Clinical Cut-offs)

Biomarker (cut-off)	Cases (n=50) n (%)	Controls (n=50) n (%)	Test statistic	Risk difference, 95% CI	p-value
Lipoprotein(a) ≥ 50 mg/dL	24 (48.0)	8 (16.0)	$\chi^2(1)=11.76$	32.0% (14.8 to 49.2)	**<0.001**
Serum uric acid ≥ 6.0 mg/dL	26 (52.0)	12 (24.0)	$\chi^2(1)=8.32$	28.0% (9.8 to 46.2)	**0.004**

Table 2 highlights the distribution of elevated Lipoprotein (a) [Lp(a)] and Serum Uric Acid (SUA) based on established clinical thresholds. Nearly half of the stroke patients (48%) had raised Lp(a) levels (≥ 50 mg/dL) compared with only 16% of controls, and this difference was highly significant ($\chi^2 = 11.76$, $p < 0.001$). Similarly, hyperuricemia (SUA ≥ 6 mg/dL) was observed in 52% of cases versus 24% of controls ($\chi^2 = 8.32$, $p = 0.004$). The risk difference was 32% for Lp(a) and 28% for SUA, both with narrow 95% confidence intervals excluding zero, demonstrating that elevated biomarker prevalence was substantially higher in the stroke group.

Table 3: Mean Levels of Lp(a) and Serum Uric Acid (Cases vs Controls)

Analyte	Cases (n=50) Mean ± SD	Controls (n=50) Mean ± SD	Mean difference	95% CI (difference)	Test statistic	p-value
Lipoprotein(a), mg/dL	48.5 ± 22.0	28.3 ± 15.6	20.2	12.6 to 27.8	$t(98)=5.30$	**<0.001**
Serum uric acid, mg/dL	6.1 ± 1.4	5.2 ± 1.2	0.90	0.38 to 1.42	$t(98)=3.45$	**0.001**

Table 3 compares quantitative biomarker concentrations between cases and controls. Mean Lp(a) levels were markedly elevated in stroke patients (48.5 ± 22.0 mg/dL) compared with controls (28.3 ± 15.6 mg/dL), yielding a mean difference of 20.2 mg/dL (95% CI 12.6–27.8; $t(98)=5.30$; $p <$

0.001). Serum uric acid levels were also significantly higher in cases (6.1 ± 1.4 mg/dL) than controls (5.2 ± 1.2 mg/dL), with a mean difference of 0.9 mg/dL (95% CI 0.38–1.42; $p = 0.001$).

Table 4: Correlation of Biomarkers with Stroke Severity (NIHSS at Admission; Cases Only, n=50)

Relationship	Pearson r	95% CI for r	Test statistic	p-value
NIHSS ↔ Lp(a) (mg/dL)	0.42	0.16 to 0.63	$t(48)=3.21$	**0.002**
NIHSS ↔ Serum uric acid (mg/dL)	0.36	0.09 to 0.58	$t(48)=2.67$	**0.01**

Table 4 demonstrates the relationship between biomarker levels and stroke severity, measured by the National Institutes of Health Stroke Scale (NIHSS) among stroke patients. A moderate positive correlation was observed between NIHSS scores and Lp(a) ($r = 0.42$, 95% CI 0.16–0.63; $p = 0.002$), indicating that higher Lp(a) levels were associated with greater neurological deficit severity. Serum uric acid also showed a significant positive correlation with NIHSS ($r = 0.36$, 95% CI 0.09–0.58; $p = 0.01$), suggesting that patients with elevated SUA tended to experience more severe strokes. Multiple regression analysis further supported that both Lp(a) and SUA independently predicted stroke severity (*adjusted* $R^2 = 0.24$; $p = 0.001$).

DISCUSSION

Table 1 (Baseline profile): Age and BMI were well matched, minimizing confounding from adiposity and age-related risk. The stroke group's higher systolic BP (mean difference 10 mmHg, p=0.002) and greater dyslipidaemia prevalence (58% vs 38%, p=0.048) mirror the vascular risk clustering repeatedly described in ischemic stroke cohorts, where hypertension and atherogenic dyslipidaemia remain dominant drivers of first-ever stroke-particularly in postmenopausal women, in whom loss of estrogen augments endothelial dysfunction and lipid atherogenicity Zhu T et al.(2025).[6] Large case–control series examining SUA alongside traditional risks also report higher rates of hypertension and dyslipidaemia in stroke cases versus controls, consistent with pattern (non-significant trends for HT and diabetes, but significant elevation in SBP and dyslipidaemia) Yang Y et al.(2024).[7]

Table 2 (Proportions above clinical cut-offs): Nearly half of cases had Lp(a) ≥50 mg/dL versus 16% of controls (RD 32%, p<0.001). This three-fold enrichment aligns with the well-established, largely genetic, and independent association between elevated Lp(a) and atherothrombotic events, including ischemic stroke; population and mechanistic work attribute risk to impaired fibrinolysis and oxidized phospholipid cargo on Lp(a) Yang Y et al.(2023).[8] Likewise, hyperuricemia (SUA ≥6.0 mg/dL) was twice as common in cases (52% vs 24%, RD 28%, p=0.004), congruent with South Asian hospital studies where elevated SUA clusters with hypertension/diabetes and is overrepresented in AIS patients compared with controls Fang Z et al.(2025),[9] cut-off based contrasts therefore echo prior prevalence gradients reported for both biomarkers across stroke vs non-stroke groups.

Table 3 (Group mean differences): The case–control gap in Lp(a) (20 mg/dL; p<0.001) is sizeable and clinically meaningful, reinforcing Lp(a)'s role beyond standard lipids in women after menopause, when levels tend to rise and interact with prothrombotic states Lin GJ et al (2025).[10] The SUA difference (0.9 mg/dL; p=0.001) is directionally consistent with Indian and regional datasets showing higher mean SUA in AIS, particularly in patients with co-existing hypertension/diabetes. While some cohorts have suggested a U-shaped or context-dependent relationship between SUA and outcomes, the between-group elevation at presentation-what table captures-has been repeatedly observed in first-ever AIS Wan H et al (2020).[11]

Table 4 (Correlation with stroke severity): Moderate positive correlations between NIHSS and Lp(a) (r=0.42) and NIHSS and SUA (r=0.36) indicate that higher levels of each biomarker track with greater neurological deficit at admission. This aligns with pathophysiology: Lp(a) promotes atherothrombosis and plaque vulnerability, plausibly linking to larger or more disabling infarcts Mastroiacovo D et al.(2023),[12] SUA, when elevated, is tied to endothelial dysfunction, oxidative stress, and platelet activation, and has been associated with worse in-hospital course in several South Asian cohorts Lin J et al.(2025)[13]. Notably, some studies report mixed findings for SUA vis-à-vis outcomes-neuroprotective antioxidant effects at physiologic ranges versus deleterious vascular effects at higher levels Zhang S et al (2020),[14] but data situate SUA in the latter, risk-concordant range.

CONCLUSION

This study demonstrated a significant association between elevated levels of Lipoprotein (a) and Serum Uric Acid with ischemic stroke occurrence and severity in postmenopausal women. Mean values of both biomarkers were considerably higher in stroke patients than in age-matched controls, suggesting their potential role as independent biochemical risk factors. Moreover, the positive correlation of Lp(a) and uric acid with NIHSS scores indicates that elevated levels not only predict susceptibility to stroke but also relate to greater neurological deficit severity at presentation. These findings underscore the importance of integrating Lp(a) and uric acid estimation in the routine risk

assessment and prognostic evaluation of postmenopausal women prone to cerebrovascular events. Early detection and management of elevated biomarker levels could contribute to improved prevention strategies and better clinical outcomes.

Limitations of the Study

1. The sample size was relatively small (n = 100), which may limit the generalizability of the findings to the wider population.
2. The study design was cross-sectional, restricting causal inference between elevated biomarkers and stroke severity.
3. Single-center hospital-based data may introduce selection bias and may not represent community-level variations.
4. Other potential confounders such as dietary habits, renal function variations, estrogen levels, and genetic predisposition influencing Lp(a) were not analyzed.
5. Long-term follow-up for assessing functional recovery or recurrence risk was not included.
6. Biomarker levels were measured once during acute presentation and not dynamically over the course of recovery, which may affect temporal interpretation.

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