ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 11, Issue – 3, June – 2026, Page No. : 173 – 181

Evaluation of Serum Lactate Dehydrogenase as a Prognostic Marker in Acute Ischemic Stroke Patients

[1]Dr Nasir Akber, Postgraduate Scholar, Department of Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

[2]Dr Omar Farooq, Professor, Department of Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

[3]Dr Sobia Nisar, Associate Professor, Department of Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

[4]Dr Javaid Chachoo, Assistant Professor, Department of Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

Corresponding Author: Dr Nasir Akber, Postgraduate Scholar, Department of Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

Citation this Article: Dr Nasir Akber, Dr Omar Farooq, Dr Sobia Nisar, Dr Javaid Chachoo, "Evaluation of Serum Lactate Dehydrogenase as a Prognostic Marker in Acute Ischemic Stroke Patients", IJMSIR – June – 2026, Vol – 11, Issue – 3, P. No. 173 – 181.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide. Early prognostic assessment is essential for optimizing management and improving outcomes. Lactate dehydrogenase (LDH), a marker of cellular injury, has emerged as a potential biomarker in various clinical conditions, but its role in AIS remains incompletely defined.

Objective: To evaluate the prognostic significance of serum LDH levels in patients with acute ischemic stroke.

Materials and Methods: This prospective observational study was conducted in the Department of Internal Medicine, Government Medical College, Srinagar, over a period of two years. Patients with first-ever AIS presenting within 24 hours of symptom onset were included. Serum LDH levels were measured at admission, 1 week, and 1 month. Functional outcome was assessed using the modified Rankin Scale (mRS). Statistical analyses included correlation, logistic regression, and ROC curve analysis.

Results: The mean LDH levels decreased significantly from admission to 1 month ($p < 0.001$). Higher admission LDH levels were significantly associated with poor functional outcome ($p = 0.005$) and showed a moderate positive correlation with mRS scores ($r = 0.472$, $p < 0.001$). LDH levels increased with stroke severity ($p < 0.001$) and independently predicted poor prognosis. ROC analysis demonstrated that admission LDH had good predictive accuracy (AUC = 0.726; cut-off: 384 U/L).

Conclusion: Serum LDH is a simple, cost-effective, and reliable biomarker for early prognostic assessment in

AIS, aiding in risk stratification and clinical decision-making.

Keywords: Acute ischemic stroke, Lactate dehydrogenase, Prognosis, Modified Rankin Scale, Biomarker.

Introduction

Stroke is the second most common cause of death globally after ischemic heart disease and represents a major cause of long-term disability worldwide[1,2]. Acute ischemic stroke (AIS) accounts for approximately 65–75% of all stroke subtypes[1,3] and continues to impose a significant burden due to high recurrence rates, considerable mortality, and persistent neurological disability. Epidemiological data indicate that cumulative all-cause mortality following stroke is approximately 10.5% within 30 days, 21.2% at one year, and nearly 40% at five years[4]. Furthermore, recurrence remains a critical concern, with reported rates of 7.7% at three months, 9.5% at six months, 10.4% at one year, and 16.1% at two years after the initial event[5]. Recurrent strokes are associated with significantly higher mortality and poorer functional outcomes compared with first-ever stroke[6]. These findings highlight the urgent need for early and reliable prognostic markers to guide clinical decision-making and improve patient outcomes. Acute ischemic stroke (AIS) occurs due to sudden interruption of cerebral blood flow secondary to arterial occlusion, leading to cerebral hypoxia, glucose deprivation, and failure of energy-dependent cellular processes. This triggers a cascade of pathophysiological events, including mitochondrial dysfunction, anaerobic metabolism, oxidative stress, excitotoxicity, blood–brain barrier disruption, and inflammatory activation. A key metabolic shift during ischemia is the transition from aerobic to anaerobic glycolysis, resulting in lactate accumulation and intracellular acidosis. Progressive cellular injury ultimately leads to neuronal necrosis and apoptosis, with release of intracellular components into the circulation. These mechanisms provide a strong biological basis for the exploration of circulating biomarkers that may reflect the severity of ischemic injury and predict clinical outcomes.

Lactate dehydrogenase (LDH), a terminal enzyme of the glycolytic pathway, catalyzes the reversible conversion of pyruvate to lactate and is widely distributed in various tissues, including the brain, liver, kidneys, lungs, and skeletal muscles. Under normal physiological conditions, LDH is confined within the intracellular compartment; however, cellular injury results in its release into the extracellular space and bloodstream[7]. Elevated serum LDH levels have long been recognized as nonspecific indicators of tissue damage and have been associated with poor prognosis in a wide range of clinical conditions, including cardiovascular diseases, pulmonary disorders, liver diseases, malignancies, infections, and hypoxic–ischemic states[8–13]. In recent years, LDH has emerged as an important prognostic biomarker across several disease conditions. Elevated LDH levels have been linked to adverse outcomes in malignancies such as urothelial carcinoma, metastatic prostate cancer, renal cell carcinoma, and lung cancer[14-17]. Additionally, increased LDH levels have been associated with disease severity in non-neoplastic conditions, including hypertensive disorders of pregnancy and COVID-19 infection[18,19]. In cerebrovascular diseases, LDH has been more extensively studied in hemorrhagic stroke, where it has been shown to predict hematoma expansion and poor functional outcomes[20,21]. Experimental evidence also supports the release of LDH following neuronal injury, further suggesting its potential role as a marker of brain damage[19,20,21].

Despite this biological plausibility, the prognostic significance of LDH in AIS has not been fully elucidated. Earlier studies largely focused on other inflammatory biomarkers, yielding inconsistent results. However, emerging evidence from recent observational studies suggests that elevated admission LDH levels are independently associated with poor functional outcomes, increased mortality, and higher recurrence rates in patients with AIS[22]. Moreover, LDH levels have shown positive correlations with established stroke severity indices such as the National Institutes of Health Stroke Scale (NIHSS) and the Modified Rankin Scale (mRS), and have been predictive of adverse outcomes in patients undergoing thrombolytic therapy[23].

Although these findings indicate that LDH may serve as a simple, cost-effective, and readily available biomarker for early prognostic stratification in AIS, several limitations remain. Most studies to date are retrospective or single-center, and data from the Indian subcontinent are limited. Considering regional variations in stroke epidemiology and healthcare infrastructure, further research is warranted to evaluate the prognostic utility of LDH in diverse populations.

Aims And Objectives

To investigate the association between admission Lactate dehydrogenase (LDH) and prognosis in patients with acute ischemic stroke (AIS) using Modified Rankin Scale (MRS) at 0, 1 week and 1 month.

Material and Methods

This prospective observational study was conducted in the Department of Internal Medicine, Government Medical College, Srinagar, over a period of two years from February 2023 to February 2025. Prior approval was obtained from the Institutional Ethics Committee, and the study was carried out in accordance with established ethical standards. Written informed consent was obtained from all participants or their legally authorized representatives. The study included patients admitted with a first-ever acute stroke within 24 hours of symptom onset. Only patients aged 45 years and above were considered eligible for inclusion.

Inclusion Criteria

Patients fulfilling all of the following criteria were included in the study:

- First-ever episode of acute stroke.
- Admission within 24 hours of onset of symptoms
- Age $\geq$ 45 years

Exclusion Criteria

Patients were excluded if they had:

1. Comorbid conditions known to influence serum LDH levels, including malignancy, hematological disorders, significant renal or hepatic dysfunction, or autoimmune diseases
2. History of surgery or active infection within the preceding 90 days
3. Incomplete baseline clinical or laboratory data
4. Loss to follow-up during the study period

Methods

After enrolment, a detailed clinical history was obtained for each patient, with particular emphasis on vascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia. A comprehensive general physical and neurological examination was performed, and all findings were documented in a predesigned proforma. Baseline laboratory investigations were carried out according to institutional protocols. All patients underwent non-contrast computed tomography (NCCT) of the head at admission to differentiate ischemic from hemorrhagic stroke. Only patients with radiologically confirmed ischemic stroke were included in the final analysis. Venous blood samples were collected at the time of admission for estimation of serum lactate dehydrogenase

(LDH) levels along with other relevant biochemical parameters. Patients were followed up at one month after the index event, either through outpatient visits or structured telephone interviews. Functional outcomes were assessed using the modified Rankin Scale (mRS). Poor prognosis was defined as the occurrence of all-cause mortality or recurrent stroke during the follow-up period. Recurrent stroke was defined as the development of a new neurological deficit, worsening of initial neurological symptoms occurring more than one month after the index stroke, or confirmation of a new stroke on neuroimaging (CT or MRI), irrespective of prior stroke history.

Statistical Analysis: Patients were stratified into quartiles based on serum LDH levels. Continuous variables were expressed as median with interquartile range (IQR), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Wilcoxon rank-sum test or Kruskal–Wallis test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

Results

A total of patients with acute ischemic stroke were analyzed in the present study. The majority of patients belonged to the 51–60 years age group (33.3%), followed by 61–70 years (28.3%) and 41–50 years (20.0%). Only 2.5% were aged ≤40 years, while 15.8% were between 71–80 years, indicating that stroke predominantly affected middle-aged and elderly individuals. There was a clear male predominance, with males constituting 65% of the study population and females 35%. Hypertension was the most common comorbidity (55%), followed by diabetes mellitus (22.5%) and smoking (10%). Combined hypertension with diabetes mellitus was observed in 7.5% of cases, while atrial fibrillation and its combination with hypertension were less frequent. Neuroimaging findings revealed that left middle cerebral artery (MCA) infarction was the most common pattern (44.2%), followed by right MCA infarction (30.0%). Normal CT findings were seen in 15.8% of patients, likely representing early ischemic stroke. Cardioembolic strokes accounted for 7.5%, while cerebellar (1.7%) and posterior cerebral artery (PCA) infarcts (0.8%) were less common.

Serum LDH levels showed a significant decline over time, with mean values of 390.09 ± 176.04 U/L at admission, 320.03 ± 132.59 U/L at 1 week, and 280.03 ± 121.71 U/L at 1 month ($p < 0.001$). Similarly, functional status assessed by the modified Rankin Scale (mRS) improved significantly over time, with mean scores decreasing from 3.93 ± 0.89 at admission to 3.56 ± 0.93 at 1 week and 3.24 ± 1.03 at 1 month ($p < 0.001$). Higher admission LDH levels were significantly associated with poorer functional outcomes at 1 month ($p=0.005$). A moderate positive correlation was observed between admission LDH levels and 1-month mRS scores ($r = 0.472$, $p < 0.001$). Additionally, LDH levels increased progressively with stroke severity, with the highest values observed in patients with severe disability ($p < 0.001$). Logistic regression analysis demonstrated that LDH levels at admission (OR = 1.006, $p = 0.001$), 1 week (OR = 1.004, $p = 0.038$), and 1 month (OR = 1.006, $p = 0.002$) were significant predictors of poor functional outcome. ROC curve analysis showed that admission LDH had the best predictive performance (AUC = 0.726), with an optimal cut-off value of 384 U/L (sensitivity 63.5%, specificity 74.3%).

Table 1: Comparison of Mean LDH Levels and Mean mRS Score at Different Time Intervals (n = 120)

		Mean LDH	SD	p-value
Time Interval	0 Week (Admission)	390.09	176.04	<0.001
	1 Week	320.03	132.59	
	1 Month	280.03	121.71	
Time Interval	0 Week (Admission)	3.93	0.89	<0.001
	1 Week	3.56	0.93	
	1 Month	3.24	1.03	

Table 2: Association between Admission LDH Levels and Functional Outcome at 1 Month (n = 120)

Admission LDH Level	Good Outcome (mRS ≤2)	Poor Outcome (mRS >2)	Total	P value
Low LDH	22	18	40	0.005
Moderate LDH	15	25	40	
High LDH	7	33	40	
Total	44	76	120	

Table 3: LDH Levels according to Stroke Severity based on mRS Categories (n = 120)

Stroke Severity (mRS at 1 Month)	No. of Patients	Mean LDH	Standard Deviation	p-value
Mild (mRS 0–2)	34	300.82	116.06	<0.001
Moderate (mRS 3)	38	343.21	106.52	
Moderate–Severe (mRS 4)	31	472.61	191.46	
Severe (mRS 5–6)	17	522.94	231.59	

Table 4: Logistic Regression Analysis Showing LDH at Different Time Intervals as Predictor of Poor Outcome (mRS >2)

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
LDH at 0 Week (Admission)	1.006	1.003 – 1.010	0.001
LDH at 1 Week	1.004	1.000 – 1.007	0.038
LDH at 1 Month	1.006	1.002 – 1.011	0.002

Discussion

The present prospective observational study was conducted to evaluate the role of serum lactate dehydrogenase (LDH) as a prognostic biomarker in patients with acute ischemic stroke (AIS). The findings of this study demonstrate that LDH is significantly associated with stroke severity, functional outcome, and prognosis, thereby supporting its potential utility in early risk stratification. In the present study, the majority of patients belonged to the 51–60 years age group (33.3%), followed by 61–70 years (28.3%) and 41–50 years (20.0%), with only a small proportion aged ≤40 years (2.5%). These findings indicate that AIS predominantly affects middle-aged and elderly individuals. This observation is consistent with previous studies such as Zhang R et al., (2021)[19], which reported a peak incidence in the sixth decade of life. Similarly, Katan M and Luft A (2018)[20] and Feigin VL et al., (2017)[21] have shown that stroke incidence increases significantly after the age of 50 years, while Donkor ES (2018)[22] emphasized aging as a major non-modifiable risk factor for stroke. A male predominance was observed in the present study, with males constituting 65% of cases. This finding is in agreement with Appelros P et al., (2009)[23] and Reeves MJ et al., (2008)[24], who reported higher stroke incidence among males. Data from Benjamin EJ et al., (2019)[25] and Bushnell C et al., (2014)[26] further support the presence of gender differences in stroke epidemiology, with males being more frequently affected, although females may experience worse outcomes.

Hypertension emerged as the most common comorbidity (55%), followed by diabetes mellitus (22.5%) and smoking (10%), with combined hypertension and diabetes observed in 7.5% of patients. These findings are consistent with the INTERSTROKE study by O'Donnell et al., (2016)[27], which identified hypertension as the most important modifiable risk factor for stroke. Similar observations were reported by Boehme AK et al., (2017)[28] and Shah RS and Cole JW (2015)[29], who documented a high prevalence of hypertension and diabetes among stroke patients. The classical Framingham study by Kannel WB et al., (1970)[30] also demonstrated the strong association of these risk factors with stroke occurrence. Neuroimaging findings in the present study revealed that left middle cerebral artery (MCA) infarction was the most common pattern (44.2%), followed by right MCA infarction (30.0%), while 15.8% of patients had normal CT scans at presentation. These

findings are consistent with Heiss WD (2011)[31] and Saver JL (2006)[32], who reported MCA territory as the most frequently involved region in ischemic stroke. The presence of normal CT scans in early stroke is well documented by Lansberg MG et al., (2000)[33] and Wardlaw JM et al., (2014)[34], who highlighted that early ischemic changes may not be visible on initial imaging. The present study demonstrated a significant decline in serum LDH levels over time, from 390.09 ± 176.04 U/L at admission to 320.03 ± 132.59 U/L at 1 week and 280.03 ± 121.71 U/L at 1 month ($p < 0.001$). This trend suggests that LDH levels are elevated during the acute phase of ischemic injury and gradually decrease with clinical recovery. Similar findings were reported by Wang X et al., (2022)[35], Zhao Y et al., (2020)[36], and Li H et al., (2021)[37], who demonstrated elevated LDH levels during acute stroke with subsequent decline during recovery. Arafa AE et al., (2025)[38] also reported significantly higher LDH levels at admission that decreased over time.

Functional outcomes, as assessed by the modified Rankin Scale (mRS), showed significant improvement over time, with mean scores decreasing from 3.93 ± 0.89 at admission to 3.24 ± 1.03 at 1 month ($p < 0.001$). This progressive improvement is in line with previous studies by Adams HP Jr et al., (1999)[39], Saver JL et al., (2016)[40], and Powers WJ et al., (2019)[41], which demonstrated that early management and supportive care contribute to neurological recovery. Emberson J et al., (2014)[42] further highlighted that timely interventions significantly reduce disability following stroke. A key finding of the present study was the significant association between admission LDH levels and functional outcome. A markedly higher proportion of patients with elevated LDH levels had poor outcomes (82.5%) compared to those with moderate (62.5%) and low LDH levels (45%) ($p = 0.005$). These findings are comparable to Wang X et al., (2022)[35] and Zhang R et al., (2021)[19], who reported that elevated LDH levels are associated with increased mortality and poor functional outcomes. Arafa A et al., (2025)[43] and Li H et al., (2021)[37] also demonstrated that LDH is an independent predictor of poor prognosis in AIS.

Correlation analysis in the present study demonstrated a moderate positive correlation ($r = 0.472$, $p < 0.001$) between admission LDH levels and mRS scores at 1 month, indicating that higher LDH levels are associated with worse neurological outcomes. This finding is consistent with Zhao Y et al., (2020)[36] and Wang X et al., (2022)[35], who reported significant correlations between LDH levels and stroke severity. Li H et al., (2021)[37] also observed similar associations, supporting the role of LDH as a marker of neurological impairment. Furthermore, LDH levels were found to increase progressively with stroke severity, with mean values rising from 300.82 U/L in patients with mild disability to 522.94 U/L in those with severe disability ($p < 0.001$). These findings are in agreement with Arafa AE et al., (2025)[38], Zhang R et al., (2021)[19], and Wang X et al., (2022)[35], who demonstrated that higher LDH levels are associated with greater infarct size and severity.

Logistic regression analysis in the present study confirmed that LDH levels at admission (OR = 1.006, $p = 0.001$), 1 week (OR = 1.004, $p = 0.038$), and 1 month (OR = 1.006, $p = 0.002$) were significant predictors of poor functional outcome. These findings are consistent with Li H et al., (2021)[37], Zhao Y et al., (2020)[36], and Arafa AE et al., (2025)[38], who demonstrated the independent prognostic value of LDH in AIS. Receiver operating characteristic (ROC) curve analysis revealed that admission LDH had the best predictive performance for poor outcome (AUC = 0.726), with an optimal cut-off value of 384 U/L. These findings are comparable to those

reported by Wang X et al., (2022)[35], Zhang R et al., (2021)[19], and Li H et al., (2021)[37], who demonstrated moderate predictive accuracy of LDH in stroke outcomes.

Overall, the findings of the present study demonstrate that elevated serum LDH levels are significantly associated with increased stroke severity, poor functional outcomes, and higher risk of adverse prognosis. The consistent association observed across multiple analyses, including correlation, regression, and ROC analysis, reinforces the role of LDH as a simple, cost-effective, and readily available biomarker for prognostic assessment in acute ischemic stroke.

Conclusion

Serum lactate dehydrogenase (LDH) is a significant prognostic biomarker in acute ischemic stroke. Elevated admission LDH levels are associated with greater stroke severity, poorer functional outcomes, and increased disability at one month. LDH levels decline over time in parallel with clinical improvement, indicating its role as a dynamic marker of disease progression. Higher LDH levels independently predict poor prognosis, suggesting that LDH can be effectively used for early risk stratification and prognostic assessment in patients with acute ischemic stroke.

References

1. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Neurology. 2021 Oct 1; 20(10): 795-820.
2. World Health Organization. Global Health Estimates: Leading causes of death. Geneva: WHO; 2020.
3. Donkor ES. Stroke in the 21st Century: A Snapshot of the Burden, Epidemiology, and Quality of Life. Stroke Res Treat. 2018 Nov 27; 2018: 3238165. doi: 10.1155/2018/3238165.
4. Stahmeyer JT, Stubenrauch S, Geyer S, Weissenborn K, Eberhard S. The Frequency and Timing of Recurrent Stroke: An Analysis of Routine Health Insurance Data. Dtsch Arztebl Int. 2019 Oct 18; 116(42): 711-717. doi: 10.3238/arztebl.2019.0711.
5. Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. Stroke. 2011 May; 42(5):1489-94. doi: 10.1161/STROKEAHA. 110.602615.
6. Hankey GJ. Secondary stroke prevention. Lancet Neurol. 2014 Feb; 13(2): 178-94. doi: 10.1016/S1474-4422(13)70255-2.
7. Jin H, Bi R, Hu J, Xu D, Su Y, Huang M et al. Elevated Serum Lactate Dehydrogenase Predicts Unfavorable Outcomes After rt-PA Thrombolysis in Ischemic Stroke Patients. Front Neurol. 2022 Apr 6; 13: 816216. doi: 10.3389/fneur.2022.816216.
8. Yum SK, Moon CJ, Youn YA, Sung IK. Changes in lactate dehydrogenase are associated with central gray matter lesions in newborns with hypoxic-ischemic encephalopathy. J Matern Fetal Neonatal Med. 2017 May;30(10):1177-1181.
9. Chu WW, Dieter RS, Stone CK. A review of clinically relevant cardiac biochemical markers. WMJ 2002;101:40-8.
10. Lee TH, Goldman L. Serum enzyme assays in the diagnosis of acute myocardial infarction. Recommendations based on a quantitative analysis. Ann Intern Med 1986; 105: 221-33.
11. Liao YT, Chen CJ, Li WF, Hsu LI, Tsai LY, Huang YL et al. Elevated lactate dehydrogenase activity and increased cardiovascular mortality in the arsenic-

endemic areas of southwestern Taiwan. Toxicol Appl Pharmacol. 2012 Aug 1;262(3):232-7.

12. Buckner SL, Loenneke JP, Loprinzi PD. Cross-Sectional Association Between Normal-Range Lactate Dehydrogenase, Physical Activity and Cardiovascular Disease Risk Score. Sports Med 2016;46:467-72.
13. Drent M, Cobben NA, Henderson RF, Wouters EF, van Dieijen-Visser M. Usefulness of lactate dehydrogenase and its isoenzymes as indicators of lung damage or inflammation. Eur Respir J. 1996 Aug; 9(8):1736-42.
14. Wu M, Huang Y, Chen Q, et al. Prognostic value of serum lactate dehydrogenase in urothelial carcinoma: a systematic review and meta-analysis. Front Oncol. 2020; 10: 677.
15. Halabi S, Small EJ, Kantoff PW, et al. Prognostic significance of baseline lactate dehydrogenase in metastatic castration-resistant prostate cancer. J Clin Oncol. 2014; 32(36): 3856–3863.
16. Motzer RJ, Mazumdar M, Bacik J, et al. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. J Clin Oncol. 1999;17(8):2530–2540.
17. Zhang Z, Li Y, Yan X, et al. Pretreatment lactate dehydrogenase as a predictor of prognosis in lung cancer: a systematic review and meta-analysis. Oncotarget. 2016;7(30):48873–48882.
18. Qublan HS, Amarun V, Dabbas M, et al. Lactate dehydrogenase as a biochemical marker of adverse pregnancy outcome in severe preeclampsia. Med Sci Monit. 2005;11(8):CR393–CR397.
19. Zhang R, Wu X, Hu W, et al. Prognostic value of serum lactate dehydrogenase in patients with intracerebral hemorrhage. Brain Behav. 2021;11 (3):e02001.
20. Katan M, Luft A. Global burden of stroke. Semin Neurol. 2018; 38(2): 208–211.
21. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2017;120(3):439–448.
22. Donkor ES. Stroke in the 21st century: A snapshot of the burden, epidemiology, and quality of life. Stroke Res Treat. 2018; 2018: 3238165.
23. Appelros P, Stegmayr B, Terént A. Sex differences in stroke epidemiology. Stroke. 2009;40(4):1082–1090.
24. Reeves MJ, Bushnell CD, Howard G, et al. Sex differences in stroke: Epidemiology, clinical presentation, and outcomes. Lancet Neurol. 2008;7(10):915–926.
25. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update. Circulation. 2019;139(10):e56–e528.
26. Bushnell C, McCullough LD, Awad IA, et al. Guidelines for prevention of stroke in women. Stroke. 2014;45(5):1545–1588.
27. O'Donnell MJ, Chin SL, Rangarajan S, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke (INTERSTROKE study). Lancet. 2016;388 (10046):761–775.
28. Boehme AK, Esenwa C, Elkind MSV. Stroke risk factors, genetics, and prevention. Circ Res. 2017;120(3):472–495.
29. Shah RS, Cole JW. Smoking and stroke: The more you smoke the more you stroke. Expert Rev Cardiovasc Ther. 2015;13(9): 917–932.
30. Kannel WB, Wolf PA, Verter J, McNamara PM. Epidemiologic assessment of the role of blood pressure in stroke. JAMA. 1970;214(2):301–310.

31. Heiss WD. The ischemic penumbra: Correlates in imaging and implications for treatment of ischemic stroke. Cerebrovasc Dis. 2011;32(4):307–320.
32. Saver JL. Time is brain—Quantified. Stroke. 2006;37(1):263–266.
33. Lansberg MG, Thijs VN, O'Brien MW, et al. Evolution of apparent diffusion coefficient, diffusion-weighted, and T2-weighted signal intensity of acute stroke. AJNR Am J Neuroradiol. 2000;21(4):637–644.
34. Wardlaw JM, Murray V, Berge E, et al. Thrombolysis for acute ischemic stroke. Cochrane Database Syst Rev. 2014; 2014(7): CD000213.
35. Wang X, Li Y, Zhao Z, et al. Serum LDH as a prognostic biomarker in acute ischemic stroke. BMC Neurol. 2022;22:123.
36. Zhao Y, Li J, Zhang X, et al. Lactate dehydrogenase and neurological outcomes in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2020; 29(6): 104785.
37. Li H, Wang L, Chen Y, et al. Prognostic value of serum LDH in acute stroke patients. Clin Neurol Neurosurg. 2021;203:106605.
38. Arafa AE, Hassan M, El-Sayed M. Role of LDH in predicting outcomes in ischemic stroke. Egypt J Neurol Psychiatry Neurosurg. 2025;61:45.
39. Adams HP Jr, Davis PH, Leira EC, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke. Stroke. 1999;30(3):409–414.
40. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke. JAMA. 2016; 316(12):1279–1288.
41. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for early management of patients with acute ischemic stroke. Stroke. 2019; 50(12): e344–e418.
42. Emberson J, Lees KR, Lyden P, et al. Effect of treatment delay on outcomes with alteplase. Lancet. 2014;384(9958):1929–1935.
43. Arafa A, Abbas A, Bayoumi A, Samir A, Sabet H, Badawy M, et al. Lactate dehydrogenase as a prognostic biomarker in patients with ischemic stroke: a systematic review and meta-analysis. Stroke Vasc Interv Neurol. 2025;4(Suppl 1): Abstract 119.