

Serum Ferritin at Admission as a Prognostic Marker of Stroke Severity and Mortality in Acute Ischemic Stroke: A Cross-Sectional Study

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Abstract

Background: Acute ischemic stroke (AIS) is a major cause of neurological disability and mortality. Besides its conventional role as an indicator of body iron stores, serum ferritin is an acute-phase reactant and may participate in ischemic neuronal injury through iron-mediated oxidative stress. Elevated serum ferritin has therefore been investigated as a potential prognostic biomarker in acute ischemic stroke.

Aim: To evaluate serum ferritin levels at admission as a prognostic marker of neurological severity and mortality in patients with acute ischemic stroke.

Materials and Methods: This hospital-based cross-sectional study included 115 patients with symptomatic acute ischemic stroke admitted to the Department of General Medicine, McGann District Hospital, Shivamogga, between June 2023 and June 2024. Adult consenting patients with acute ischemic stroke were included. Patients with hemorrhagic stroke, anemia, pregnancy or lactation, and inflammatory or neoplastic conditions capable of altering serum ferritin were excluded. Serum ferritin was measured at admission using a Beckman Coulter Chemistry Analyzer based on spectrophotometry. Stroke severity was assessed at discharge using the National Institutes of Health Stroke Scale (NIHSS). Data were analyzed using SPSS version 26.

Results: Of 115 patients, 73 (63.48%) were male and 42 (36.52%) were female. The mean age was 49.39 ± 14.10 years. At discharge, 78 (67.83%) patients had moderate stroke, 25 (21.74%) had moderate-to-severe stroke, and six (5.22%) each had mild and severe stroke. Mean admission ferritin increased progressively across NIHSS categories: 163.20 ± 117.36 ng/mL in minor stroke, 219.68 ± 82.21 ng/mL in moderate stroke, 358.11 ± 85.48 ng/mL in moderate-to-severe stroke, and 416.39 ± 90.33 ng/mL in severe stroke ($p < 0.0001$). Ferritin demonstrated a strong positive correlation with NIHSS ($r = 0.97$, $p = 0.03$). All six patients in the severe/highest-ferritin group died.

Conclusion: Increasing serum ferritin levels at admission were associated with increasing neurological severity and mortality. Serum ferritin may be useful as an adjunctive prognostic biomarker in acute ischemic stroke.

Keywords: Acute Ischemic Stroke, Serum Ferritin, NIHSS, Prognosis, Mortality, Oxidative Stress.

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Introduction

Stroke is one of the most important causes of mortality and long-term disability worldwide. It is characterized clinically by the abrupt onset of neurological dysfunction attributable to a vascular cause.[1,2] Acute ischemic stroke results from interruption of cerebral blood flow and initiates a complex cascade of energy failure, excitotoxicity, oxidative stress, inflammation, blood-brain barrier disruption, and neuronal death. These mechanisms determine the extent of neurological impairment and subsequent functional outcome.

Although clinical examination and neuroimaging remain central to the assessment of acute ischemic

stroke, considerable interest has focused on circulating biomarkers that may provide additional information regarding neurological severity and prognosis. The National Institutes of Health Stroke Scale (NIHSS) provides standardized quantification of neurological deficits and is widely used for assessing stroke severity and monitoring clinical progression.[3]

Iron metabolism may have an important role in cerebral ischemic injury. Iron is physiologically essential for cellular metabolism, oxygen transport, mitochondrial function, and several enzymatic reactions. However, excessive free iron can

promote generation of reactive oxygen species and lipid peroxidation, potentially aggravating ischemic tissue injury.[4] Ferritin is the principal intracellular iron-storage protein and is routinely used clinically as an indicator of body iron stores. However, ferritin also behaves as an acute-phase reactant, and serum concentrations may rise during inflammatory conditions.[5] Following cerebral ischemia, disturbances in iron homeostasis and inflammatory activation may therefore contribute to elevated serum ferritin.

Iron may exacerbate ischemic tissue damage through several mechanisms. Reperfusion following cerebral ischemia generates reactive oxygen species, while free iron can facilitate oxidative reactions and enhance membrane lipid peroxidation. These mechanisms may intensify neuronal injury.[6] Elevated body iron stores have additionally been proposed to enhance atherogenesis and thrombosis. Previous clinical investigations have reported associations between serum ferritin and stroke severity. Garg et al. observed significantly greater ferritin concentrations among patients with more severe acute ischemic stroke and among patients who subsequently deteriorated.[7] A recent study likewise found higher serum ferritin among AIS patients with greater neurological deficits, although the relationship may be nonlinear. (PubMed)

The thesis underlying the present analysis identified a paucity of regional South Indian evidence regarding admission ferritin and CRP as prognostic markers in acute ischemic stroke.

Accordingly, the present study evaluated whether serum ferritin measured at admission was associated with NIHSS-defined stroke severity and mortality.

The objective was to determine the relationship between admission serum ferritin concentration and neurological severity at discharge and to assess its potential usefulness as a prognostic marker in patients with acute ischemic stroke.

Materials and Methods

This hospital-based cross-sectional study was conducted in the Department of General Medicine, McGann District Hospital, and Shivamogga. The study was performed over one year, from June 2023 to June 2024. The minimum calculated sample size was 115, based on parameters derived from previous studies, including a standard deviation of 2.8, relative precision of 0.40, and

alpha error of 5%. A total of 115 patients with symptomatic acute ischemic stroke fulfilling the predefined eligibility criteria were enrolled. Written informed consent was obtained. Patients younger than 18 years, pregnant and lactating women, and patients with hemorrhagic stroke were excluded. Patients with inflammatory or neoplastic conditions capable of independently increasing CRP or serum ferritin were excluded. Patients with anemia, defined as hemoglobin <13 g/dL in males and <12 g/dL in females, were also excluded.

Demographic and clinical information was collected using a semi-structured questionnaire and standardized proforma. Detailed medical history and neurological examination were performed. Particular attention was given to vascular risk factors including hypertension, diabetes mellitus, ischemic heart disease, smoking, and alcohol consumption. Routine laboratory investigations included complete blood count, renal and liver function tests, fasting lipid profile and random blood glucose. Electrocardiography and two-dimensional echocardiography were undertaken. Neuroimaging included non-contrast computed tomography of the brain, with MRI/MRA and carotid Doppler performed when clinically indicated. Venous blood samples were collected at admission. Serum ferritin concentrations were determined using a Beckman Coulter Chemistry Analyzer based on spectrophotometry.

Stroke severity was evaluated using the NIHSS at discharge. Scores were classified as minor (1–4), moderate (5–15), moderate-to-severe (16–20), and severe (21–42). The primary analysis examined the relationship between serum ferritin at admission and NIHSS-defined severity at discharge. The relationship between ferritin and mortality was additionally evaluated. Data were entered into Microsoft Excel and analyzed using SPSS version 26. The thesis reports percentages, proportions and inferential statistical testing, including Chi-square testing. A p-value <0.05 was considered statistically significant. The study was initiated after approval from the Institutional Ethics Committee, and written informed consent was obtained from participants.

Results

A total of 115 acute ischemic stroke patients were evaluated. The mean age was 49.39 ± 14.10 years. Patients aged >60 years formed the largest group (27.83%), followed by those aged 51–60 years (26.96%).

Table 1: Demographic and clinical characteristics

Characteristic	No. of patients	Percentage
Age 18–30 years	18	15.65%
Age 31–40 years	10	8.70%
Age 41–50 years	24	20.87%
Age 51–60 years	31	26.96%
Age >60 years	32	27.83%
Male	73	63.48%
Female	42	36.52%
Diabetes mellitus	34	29.57%
Hypertension	52	45.22%
Ischemic heart disease	25	21.74%
Smoking	40	34.78%
Alcohol addiction	12	10.43%

Males constituted 63.48% of participants. Hypertension was the most frequently recorded comorbidity/risk factor (45.22%), followed by smoking (34.78%) and diabetes mellitus (29.57%).

Table 2: Distribution according to NIHSS score at discharge

NIHSS category	No. of patients	Percentage
Mild (<5)	6	5.22%
Moderate (5–15)	78	67.83%
Moderate-to-severe (16–20)	25	21.74%
Severe (21–42)	6	5.22%
Mean $\pm$ SD	11.87 $\pm$ 2.13	—

The majority (67.83%) had moderate neurological impairment. Moderate-to-severe stroke accounted for 21.74%, while mild and severe strokes each accounted for 5.22%.

Table 3: Relationship between admission serum ferritin and NIHSS severity

NIHSS severity	Serum ferritin at admission (ng/mL), Mean $\pm$ SD
Minor (1–4)	163.20 $\pm$ 117.36
Moderate (5–15)	219.68 $\pm$ 82.21
Moderate-to-severe (16–20)	358.11 $\pm$ 85.48
Severe (21–42)	416.39 $\pm$ 90.33
p-value	<0.0001

Serum ferritin showed a progressive increase with increasing NIHSS severity. The lowest mean concentration occurred among minor strokes, whereas the highest concentration was observed in severe strokes. The difference was statistically significant ($p < 0.0001$).

Table 4: Serum ferritin level and mortality

Ferritin level (ng/mL), Mean $\pm$ SD	Survived n (%)	Death n (%)
163.20 $\pm$ 117.36	6 (100%)	0 (0%)
219.68 $\pm$ 82.21	78 (100%)	0 (0%)
358.11 $\pm$ 85.48	25 (100%)	0 (0%)
416.39 $\pm$ 90.33	0 (0%)	6 (100%)

All patients represented in the first three ferritin/severity categories survived, whereas all six patients represented in the highest ferritin/severe category died.

Table 5: Correlation between NIHSS score and serum ferritin

Parameter	Result
Correlation coefficient (r)	0.97
p-value	0.03

A strong positive correlation was reported between serum ferritin and NIHSS score ($r=0.97$, $p=0.03$), indicating that increasing neurological severity was associated with increasing serum ferritin concentration.

Overall, 109 of 115 patients (94.78%) survived, while six patients (5.22%) died.

Discussion

The principal finding of the present study was a progressive increase in serum ferritin with

increasing severity of acute ischemic stroke. Mean admission ferritin increased from 163.20 ± 117.36 ng/mL among patients with minor stroke to 416.39 ± 90.33 ng/mL among those with severe neurological deficits. This gradient was statistically significant ($p < 0.0001$), while the reported correlation between ferritin and NIHSS was strongly positive ($r = 0.97$, $p = 0.03$).

These findings support the hypothesis that disturbances of iron metabolism and inflammatory activation may accompany more extensive cerebral ischemic injury. Ferritin is both an iron-storage protein and an acute-phase reactant. Excess iron can participate in reactions generating reactive oxygen species, potentially increasing oxidative stress, lipid peroxidation, cellular membrane damage, and neuronal death.[4,5]

The results are consistent with Garg et al., who reported a significant positive association between serum ferritin and acute ischemic stroke severity. In their prospective observational study, admission ferritin was higher among patients with more severe stroke and markedly higher among patients who subsequently deteriorated. They concluded that elevated admission ferritin was associated with disease progression and poorer outcome.[7] (PubMed)

Erdemoglu and Ozbakir similarly reported that increased serum ferritin was associated with more severe stroke and unfavorable early prognosis.[8] Other Indian investigations have also reported increased ferritin concentrations in patients with greater stroke severity.[9,10]

The association with mortality observed in the present study is particularly noteworthy. All six deaths occurred among patients represented in the highest ferritin/severe-stroke category. The thesis consequently concluded that higher admission ferritin could be associated with increased mortality. Xia et al. subsequently reported an association between higher ferritin and increased 30-day mortality among stroke patients; after adjustment, high ferritin (≥ 373) was associated with greater mortality risk.[11] (PubMed)

Recent evidence nevertheless indicates that the relationship between iron status and stroke outcomes may be more complex than a simple linear relationship. A 2025 study of 288 first-ever anterior-circulation AIS patients found significantly higher ferritin in patients with NIHSS > 5 and an independently increased likelihood of greater neurological deficit with increasing ferritin, but also identified a U-shaped relationship.[12] (PubMed) Moreover, a multicenter cohort has reported that iron deficiency itself may be associated with unfavorable 90-day functional outcomes.[13] (PubMed) These observations

suggest that both excessive and inadequate iron availability may potentially influence recovery after cerebral ischemia. The present study has several limitations. It was conducted at a single center and included 115 patients. The cross-sectional design limits causal inference, and ferritin is a nonspecific acute-phase reactant affected by inflammation and other physiological factors. Furthermore, the thesis reports ferritin according to NIHSS severity groups; therefore, the mortality association should not be interpreted as demonstrating an independently validated ferritin mortality threshold. Multivariable modeling and long-term functional outcomes were not reported.

Despite these limitations, the marked stepwise rise in serum ferritin across NIHSS categories supports its potential role as an adjunct to clinical neurological assessment.

Conclusion

Serum ferritin measured at admission was significantly associated with neurological severity in patients with acute ischemic stroke. Mean ferritin increased progressively from minor through severe stroke, and a strong positive correlation was observed between ferritin and NIHSS score. Higher ferritin was also associated with the mortality pattern observed in the study, with all six deaths occurring in the severe/highest-ferritin category. Serum ferritin may therefore represent a readily measurable adjunctive biomarker for risk stratification in acute ischemic stroke. Larger prospective multicenter studies using multivariable analysis, serial ferritin measurements, and long-term functional outcomes are required to determine its independent prognostic value.

References

1. Donkor ES. Stroke in the 21st century: a snapshot of the burden, epidemiology, and quality of life. *Stroke Res Treat.* 2018;2018: 3238165. doi:10.1155/2018/3238165.
2. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century. *Stroke.* 2013;44(7):2064-89. doi:10.1161/STR.0b013e318296aeca.
3. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack. *Stroke.* 2021;52:e364-e467.
4. Theil EC. Ferritin: the protein nanocage and iron biomineral in health and in disease. *Inorg Chem.* 2013;52:12223-33. doi:10.1021/ic400484n.
5. Van der A DL, Grobbee DE, Roest M, Marx JJM, Voorbij HA, van der Schouw YT. Serum ferritin is a risk factor for stroke in postmenopausal women. *Stroke.* 2005;36:1637-41.

6. Narayan M, Singh SK. Study of association between serum ferritin and prognosis of patients in acute ischemic and haemorrhagic stroke.
7. Garg R, Aravind S, Kaur S, Chawla SPS, Aggarwal S, Goyal G. Role of serum ferritin as a prognostic marker in acute ischemic stroke: a preliminary observation. *Ann Afr Med.* 2020; 19(2):95-102. doi:10.4103/aam.aam_35_19.
8. Erdemoglu AK, Ozbakir S. Serum ferritin levels and early prognosis of stroke. *Eur J Neurol.* 2002;9(6):633-7. doi:10.1046/j.1468-1331.2002.00472.x.
9. Egovindarajulu K, Maaran AT, Prathiba P, Saiprashanth PR. A study on the prognostic significance of serum ferritin in patients with acute ischemic stroke. *IOSR J Dent Med Sci.* 2016;15:31-9.
10. Koul RK, Yaseen Y, Amreen S, Shah PA, Hakeem MM. Role of serum ferritin in determining the severity and prognosis of stroke: a hospital-based study. *Int J Sci Stud.* 2017;6:142-5.
11. Xia X, Liu J, Fang W, Chen Z, Wang J, Xu H. The association between ferritin levels and all-cause mortality in stroke patients. *Front Neurol.* 2024;15:1386408. doi:10.3389/fneur.2024.1386408.
12. Serum ferritin and admission stroke severity in first-ever acute ischemic stroke: a cross-sectional study. *Front Neurol.* 2025. doi:10.3389/fneur.2025.1683774.
13. The prognostic role of iron deficiency in acute ischemic stroke patients: a prospective multicentric cohort study. *J Neurol Sci.* 2025. (PubMed)