DOI: 10.7860/JCDR/2025/81350.22051

Original Article

Internal Medicine Section

Ferritin Levels in Acute Ischaemic Stroke: Insights and Association with Stroke Severity by National Institutes of Health Stroke Scale and Functional Outcomes on the Modified Rankin Scale

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ABSTRACT

Introduction: Acute Ischaemic Stroke (AIS) is a leading contributor to both mortality and long-term disability globally. Serum ferritin, an acute-phase reactant involved in iron metabolism, has been implicated in oxidative stress and neuronal damage in stroke patients. Exploring the relationship between serum ferritin levels, stroke severity, and functional outcomes can help improve risk assessment and optimise treatment strategies.

Aim: The present study aimed to evaluate the association between serum ferritin levels and stroke severity as assessed by the National Institutes of Health Stroke Scale (NIHSS) and functional outcomes measured by the Modified Rankin Scale (mRS). Additionally, the study sought to identify clinical and demographic factors associated with serum ferritin levels in AIS patients.

Materials and Methods: The present prospective cross-sectional study was conducted at the Critical Care Unit of Smt BK Shah Medical Institute and Research Hospital,Sumandeep Vidyapeeth Deemed to be University, Vadodara Gujarat, India, from January 2025 to February 2025. Ethical approval was obtained from the Institutional Ethics Committee. A total of 42 AIS patients meeting the inclusion criteria were enrolled. Serum ferritin levels were measured upon admission in all patients. Stroke severity was assessed using NIHSS at admission, and functional outcomes were evaluated using mRS on the seventh day. Statistical analyses, including Chi-square tests, were performed to determine associations, with a p-value <0.05 considered significant.

Results: The study included 42 patients with AIS with mean age of 56.10±7.19 years, with 24 (57.1%) patients being male and 25 (59.5%) patients residing in rural areas. Elevated serum ferritin levels was observed in 29 (69.1%) patients which was significantly associated with severe stroke (p=0.002) and worse functional outcomes (p<0.001). Severe stroke (higher NIHSS) was more common in female patients, smokers, urban residents, and cardiac disease and Transient Ischaemic Attack (TIA). Similarly, severe disability (higher mRS) was linked to female sex, smoking, and dyslipidaemia. Abnormal ferritin levels were significantly associated with female sex (p=0.01), smoking (p=0.004), cardiac disease (p=0.02), and TIA (p=0.03).

Conclusion: Serum ferritin levels were significantly associated with stroke severity and poor functional outcomes, indicating their potential role as a prognostic marker in AIS. Additionally, smoking, cardiac disease, and TIA history were linked to altered ferritin levels. These findings highlight the importance of ferritin as an inflammatory marker and its relevance in stroke management and risk stratification.

Keywords: Dyslipidaemia, Oxidative stress, Transient Ischaemic attack

INTRODUCTION

The AIS is a sudden neurological impairment that persists for over 24 hours, resulting from a blockage in blood flow to a specific brain region, which can be thrombotic or embolic event in cerebral artery causing ischaemia and potential neuronal injury [1]. AIS accounts for approximately 85% of all stroke cases, making it the most common type of stroke worldwide. Over the past decade, the cumulative incidence of stroke has varied between 105 and 152 per 100,000 people annually, while the crude prevalence has ranged from 44.29 to 559 per 100,000 individuals across different regions of our country [2].

Ischaemic stroke may be caused by large vessel disease, small vessel disease, cardioembolism, or other unidentified causes [3]. Advanced age, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, history of Transient Ischaemic Attack (TIA), dyslipidaemia, and addictions such as alcohol consumption and cigarette smoking are considered as key risk factors for acute stroke [4,5].

The clinical outcomes of stroke range from mild neurological impairment to severe disability or death, depending on the extent of brain injury and the timeliness of medical intervention. As the second leading cause of mortality worldwide, stroke also imposes a substantial economic burden due to hospitalisation and long-term care costs [6].

Markers of AIS are C-reactive protein, Interleukin (IL)-6, d-dimer, S100B protein, Neuron Specific Enolase (NSE), Matric Metalloproteinase (MMP), and ferritin. Ferritin is an acute-phase reactant and iron storage protein that rises in response to inflammation and oxidative stress- key components of AIS. Elevated ferritin levels reflect iron-induced neuronal injury and have been shown to correlate with stroke severity (NIHSS) and poor functional outcomes (mRS) [7]. Ferritin is widely available, cost-effective, and easy to measure. Unlike other markers (e.g., CRP, IL-6, NSE), ferritin uniquely reflects both inflammation and oxidative damage related to iron overload. This dual role makes it a more comprehensive and practical prognostic marker in AIS.

The NIHSS assesses the severity of neurological impairment in acute stroke patients. It helps in triaging patients for reperfusion therapy and predicting clinical outcomes [8]. The mRS evaluates functional disability ranging from no symptoms to severe disability and death [9].

The cross-sectional study by Sultana J and Sharma DJ analysed 100 AIS patients. Serum ferritin was measured on admission with stroke severity assessed using NIHSS and outcomes by mRS after four weeks. High ferritin levels were found in 61% of patients, primarily associated with severe strokes and poor recovery. A strong positive correlation was observed between ferritin levels and both NIHSS and mRS scores (p=0.00001) [7].

Ferritin is widely recognised as an inflammatory marker; however, its direct correlation with stroke severity and disability outcomes remains insufficiently explored in clinical practice. The novelty of this study and the gap it addresses lies in evaluating ferritin as a potential early prognostic biomarker in AIS, aiding in both risk stratification and treatment planning. This study connects ferritin levels with validated stroke assessment tools such as the NIHSS and mRS in a well-defined patient population. Furthermore, it uncovers significant associations between elevated ferritin and key clinical variables including sex, smoking, hypertension, diabetes, dyslipidaemia, cardiac disease, and TIA history- providing new insight into vulnerable subgroups within the AIS population.

Thus, the aim of the present study was to evaluate the association between serum ferritin levels and stroke severity as assessed by the NIHSS and functional outcomes measured by the mRS and also to identify clinical and demographic factors associated with serum ferritin levels in AIS patients.

MATERIALS AND METHODS

The present prospective cross-sectional study was carried out at the Critical Care Unit of Shri Bhikhibai Kanjibhai Shah Medical Institute and Research Hospital, Piparia, Waghodia, Gujarat, India, over one month duration January 2025 to February 2025. The ethical approval was obtained from the Sumandeep Vidhyapeeth Institutional Ethics Committee (SVIEC/ON/Medi/RP/JAN/25/47). The study followed the ethical standards outlined in the Declaration of Helsinki and the Indian Council of Medical Research. Informed consent of all patients were taken as per protocol.

Sample size calculation: $n=Z^2 \times p \times q / e^2$ {Z=1.96 at 95% Confidence Interval (CI) ,p=prevalence of AIS in critical care department taken as 11% =0.11 [10], q=1-p=0.89, e=margin of error=10%}. The sample size calculated is 38, and by adding a 10% non-response rate, the total sample size is 42.

Inclusion criteria: Patients with AIS, with an onset within 24 hours, admitted to the critical care unit, and aged between 18 and 80 years were included in the study. Only patients who were not candidates for thrombolysis were considered. Eligibility criteria for Thrombolysis were as per American Heart Association/American Stroke Association guidelines [10].

Exclusion criteria: Patient with sepsis, hemorrhagic stroke, CNS malignancy. A total of 42 patients were included and 8 patients were excluded as per criteria.

Study Procedure

The study included 42 patients with acute stroke admitted to the Critical Care Unit between January 2025 and February 2025. Participants were selected based on inclusion and exclusion criteria, and written informed consent was obtained. A standardised protocol for history-taking and clinical examination was followed. Acute stroke was confirmed through clinical assessment and Computed Tomography (CT) brain/Magnetic Resonance Imaging (MRI) imaging. Thrombolysis patients were excluded to reduce confounding, allow clearer interpretation of ferritin as a prognostic biomarker, and ensure that changes in NIHSS and mRS scores were due to stroke severity and inflammatory status- not altered by intervention. Blood samples for CBC, renal function, liver function and coagulation profile, and serum ferritin (measured by ELISA) were collected at time of admission. Stroke severity was assessed using the NIHSS at the time of admission, while functional outcomes were evaluated using the mRS on the seventh day of hospitalisation by independent evaluators who were blinded to patients clinical details to minimise assessment bias [Table/Fig-1,2] [9,11].

Grade	NIHSS	Stroke severity
0	0	No stroke
1	0-4	Minor stroke
2	5-15	Moderate stroke
3	16-20	Moderate to severe stroke
4	21-42	Severe stroke

[Table/Fig-1]: NIHSS [11].

mRS Score	Clinical Description
0	No symptoms.
1	No significant disability. Able to carry out all usual activities despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance. Unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

[Table/Fig-2]: Modified Rankin Scale (mRS) [9].

Parameters analysed were: 1) Demographic profile: age, sex, residence, clinical parameters such as: 2) History of addiction: smoking and alcohol; 3) History of comorbid illness: Diabetes Mellitus (DM)/Hypertension (HTN)/Cardiac disease/TIA/dyslipidaemia; 4) NIHSS grade distribution in population; 5) mRS grade distribution in population; 6) Distribution of ferritin in study population; 7) Association of NIHSS, mRS and serum ferritin with demographic parameters and clinical parameters were assessed.

STATISTICAL ANALYSIS

Appropriate statistical tests were applied for prevalence and associations within the data. Chi-square test with p-value less than 0.05 was considered statistically significant. Multivariate logistic regression analyses to identify independent predictors of three key outcomes: (1) stroke severity; (2) poor functional outcome; and (3) abnormal serum ferritin levels also done.

RESULTS

The study included 42 participants with a mean age of 56.10±7.19 years. Males comprised 57.1% of the subjects, and 59.5% were from rural areas. Smoking was reported in 29 (69.0%) patients and alcohol abuse in 21 (50.0%) patients. Hypertension and diabetes were present in 21 (50.0%) and 12 (28.6%) patients, respectively. Cardiovascular disease was reported in 9 (21.4%) patients, TIA in 8 (19.0%) patients, and dyslipidaemia in 20 (47.6%) patients [Table/Fig-3].

The NIHSS grade distribution among study patients showed that the majority 21 (50.0%) patients had moderate stroke. Minor stroke was observed in 9 (21.4%) patients, while 8 patients (19.0%) had a moderate to severe stroke. The least common was severe stroke, found in 4 (9.5%) of the patients [Table/Fig-1,4].

The mRS grade distribution among study participants showed that the most common grades were 3 and 4, each observed in 14 (33.3%) patients. Grade 2 was noted in 8 (19.0%) patients, while Grade 1

Parameters	Mean±SD
Age	56.10±7.19
Gender	**Frequency (%)**
Female	18 (42.9%)
Male	24 (57.1%)
Residence profile	**Frequency (%)**
Rural	25 (59.5%)
Urban	17 (40.5%)
Smoking	
No	13 (30.9%)
Yes	29 (69.0%)
Alcohol	
No	21 (50.0%)
Yes	21 (50.0%)
Diabetes	
No	30 (71.4%)
Yes	12 (28.6%)
Hypertension (HTN)	
No	21 (50.0%)
Yes	21 (50.0%)
Cardiac Disease	
No	33 (78.6%)
Yes	9 (21.4%)
Transient Ischaemic Attack (TIA)	
No	34 (81.0%)
Yes	8 (19.0%)
Dyslipidaemia	
No	22 (52.4%)
Yes	20 (47.6%)

[Table/Fig-3]: Distribution of demographic profile and clinical profile of study participants. (n=42).

NIHSS grade	NIHSS	Frequency (%)
1	Minor stroke	9 (21.4%)
2	Moderate stroke	21 (50.0%)
3	Moderate to severe stroke	8 (19.0%)
4	Severe stroke	4 (9.5%)

[Table/Fig-4]: NIHSS gradedistribution in study participants.

was the least common, seen in 2 (4.8%) patients. Additionally, 4 (9.5%) patients had the most severe disability, classified as Grade 5 [Table/Fig-2,5].

mRS grade	Frequency (%)
1	2 (4.8%)
2	8 (19.0%)
3	14 (33.3%)
4	14 (33.3%)
5	4 (9.5%)

[Table/Fig-5]: Modified Rankin Scale (mRS) grade distribution in study participants.

The distribution of serum ferritin levels among study participants showed that 29 (69.1%) patients had high ferritin levels, while only 13 (30.9%) had normal levels. This indicates a higher prevalence of altered ferritin levels in the study population [Table/Fig-6].

Serum ferritin	Frequency (%)
Normal (25-200 ng/dL)	13 (30.9)
Abnormal (>200 ng/dL)	29 (69.1)

[Table/Fig-6]: Distribution of serum ferritin in study participants.

The association between NIHSS grades and various clinical and demographic parameters revealed several significant findings [Table/Fig-7]. Female patients had a higher prevalence of severe stroke (NIHSS Grades 3 and 4) than males, with a statistically significant association (p=0.001). Rural residents had a higher proportion of patients in lower NIHSS grades, whereas urban residents experienced more severe strokes (p=0.017). Smoking was significantly associated with worse NIHSS grades, with a higher proportion of smokers in Grades 2, 3, and 4 (p=0.03). Similarly, cardiac disease (p=0.008) and a history of TIA (p=0.004) were linked to more severe strokes.

Parameters		NIHSS Grade 1	NIHSS Grade 2	NIHSS Grade 3	NIHSS Grade 4	Chi-square (p-value)
Sex	Female	2	8	8	0	15.42 (0.001)
	Male	7	13	0	4	
Residence	Rural	6	16	3	0	10.10 (0.017)
	Urban	3	5	5	4	
Smoking	No	6	4	3	0	8.71 (0.03)
	Yes	3	17	5	4	
Alcohol	No	6	12	3	0	5.92 (0.11)
	Yes	3	9	5	4	
Diabetes	Absent	6	15	5	4	2.01 (0.56)
	Present	3	6	3	0	
Hypertension	Absent	3	9	5	4	5.9 (0.11)
	Present	6	12	3	0	
Cardiac disease	Absent	9	17	3	4	11.63 (0.008)
	Present	0	4	5	0	
Transient Ischaemic Attack (TIA)	Absent	9	18	3	4	13.16 (0.004)
	Present	0	3	5	0	
Dyslipidaemia	Absent	6	11	5	0	5.46 (0.14)
	Present	3	10	3	4	
mRS Grades	Grade 1	2	0	0	0	77.21 (<0.001)
	Grade 2	5	3	0	0	
	Grade 3	2	12	0	0	
	Grade 4	0	6	8	0	
	Grade 5	0	0	0	4	
S. Ferritin	Normal	7	6	0	0	14.66 (0.002)
	Abnormal	2	15	8	4	

[Table/Fig-7]: Association of NIHSS grades with various clinical and demographic parameters (Chi-square test (χ^2 test) for association).

NIHSS grades also showed a strong correlation with mRS grades (p<0.001), as patients with higher NIHSS scores exhibited greater disability. Serum ferritin levels were significantly associated with stroke severity, with patients having high ferritin levels more likely to have higher NIHSS grades (p=0.002). However, no significant associations were found with alcohol consumption (p=0.11), diabetes (p=0.56), hypertension (p=0.11), or dyslipidaemia (p=0.14). These findings highlight the influence of smoking, cardiac disease, TIA history, and elevated serum ferritin on stroke severity.

The association between mRS grades and various clinical and demographic parameters revealed several significant findings [Table/Fig-8]. Female patients had a higher prevalence of severe disability (mRS Grades 3 and 4) than males, with a statistically significant association (p=0.01). Smoking was strongly correlated with worse functional outcomes, as smokers had a higher proportion of patients in mRS Grades 3, 4, and 5 (p=0.02). Similarly, dyslipidaemia was significantly associated with poor functional outcomes (p=0.02), suggesting a potential link between lipid abnormalities and post-stroke disability.

Serum ferritin levels also showed a strong correlation with mRS grades, as patients with high ferritin levels had a significantly higher

Parameters		mRS Grades					Chi-square (p-value)
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	
Sex	Female	1	0	8	9	0	12.83 (0.01)
	Male	1	8	6	5	4	
Residence	Rural	1	6	9	9	0	7.01 (0.13)
	Urban	1	2	5	5	4	
Smoking	No	1	6	2	4	0	11.25 (0.02)
	Yes	1	2	12	10	4	
Alcohol	No	1	6	8	6	0	6.57 (0.16)
	Yes	1	2	6	8	4	
Diabetes	Absent	1	6	9	10	4	2.45 (0.65)
	Present	1	2	5	4	0	
Hypertension	Absent	1	2	6	8	4	6.57 (0.16)
	Present	1	6	8	6	0	
Cardiac Disease	Absent	2	8	10	9	4	5.93 (0.20)
	Present	0	0	4	5	0	
Transient Ischaemic Attack (TIA)	Absent	2	8	12	8	4	8.64 (0.07)
	Present	0	0	2	6	0	
Dyslipidaemia	Absent	2	4	11	5	0	11.64 (0.02)
	Present	0	4	3	9	4	
S. Ferritin	Normal	1	8	4	0	0	26.29 (<0.001)
	Abnormal	1	0	10	14	4	

[Table/Fig-8]: Association of mRS grades with various clinical and demographic parameters (Chi-square test (χ^2 test) for association).

prevalence of severe disability (mRS Grades 4 and 5) (p<0.001). However, no significant associations were found with residence (p=0.13), alcohol consumption (p=0.16), diabetes (p=0.65), hypertension (p=0.16), cardiac disease (p=0.20), or TIA (p=0.07). These findings suggest that while factors such as sex, smoking, dyslipidaemia, and serum ferritin levels influence functional outcomes in stroke patients, other factors may have a lesser impact.

The association of serum ferritin levels with various clinical and demographic parameters revealed several significant findings [Table/Fig-9]. Females had a significantly higher prevalence of abnormal ferritin levels than males (p=0.01), suggesting a possible sex-related variation in iron metabolism. Smoking showed a strong association with abnormal ferritin levels (p=0.004), indicating that smokers may have an increased risk of altered iron storage or inflammation-related changes in ferritin levels. Additionally, patients with cardiac disease had a significantly higher prevalence of abnormal ferritin levels (p=0.02), which may reflect the role of ferritin as an inflammatory marker in cardiovascular pathology. A similar trend was observed in patients with a history of TIA, where abnormal ferritin levels were more common (p=0.03).

In contrast, no significant association was found between serum ferritin levels and residence (rural vs. urban, p=0.39), alcohol consumption (p=0.31), diabetes (p=0.83), hypertension (p=0.31), or dyslipidaemia (p=0.42). These findings suggest that while certain lifestyle factors and comorbidities influence ferritin levels, others do not have a statistically significant impact.

Independent predictors of severe stroke (NIHSS Grades 3-4) using logistic regression analysis. Female sex (AOR=4.52), smoking (AOR=5.14), cardiac disease (AOR=6.71), TIA history (AOR=7.92), and elevated serum ferritin (AOR=8.63) were significantly associated with increased odds of severe stroke (p<0.05). Urban residence showed a trend toward significance (p=0.063) [Table/Fig-10].

Factors independently associated with poor functional outcome on the mRS Grades 4-5. Female sex, smoking, dyslipidaemia, and abnormal serum ferritin were independently associated with higher disability levels. Ferritin had the strongest association (AOR=10.13, p=0.007), reinforcing its potential as a prognostic biomarker in AIS recovery [Table/Fig-11].

Parameters		S. Ferritin		Chi-square (p-value)
		Normal	Abnormal	
Sex	Female	2	16	5.80 (0.01)
	Male	11	13	
Residence	Rural	9	16	0.73 (0.39)
	Urban	4	13	
Smoking	No	8	5	8.24 (0.004)
	Yes	5	24	
Alcohol	No	8	13	1.00 (0.31)
	Yes	5	16	
Diabetes	Absent	9	21	0.045 (0.83)
	Present	4	8	
Hypertension	Absent	5	16	1.00 (0.31)
	Present	8	13	
Cardiac disease	Absent	13	20	5.13 (0.02)
	Present	0	9	
TIA	Absent	13	21	4.43 (0.03)
	Present	0	8	
Dyslipidaemia	Absent	8	14	0.63 (0.42)
	Present	5	15	

[Table/Fig-9]: Association of serum ferritin with various clinical and demographic parameters (Chi-square test (χ^2 test) for association).

Variables	Adjusted Odds Ratio (AOR)	95% CI	p-value
Female sex	4.52	1.02-19.89	0.047
Urban residence	3.87	0.93-16.17	0.063
Smoking	5.14	1.03-25.65	0.045
Cardiac disease	6.71	1.13-39.82	0.036
TIA	7.92	1.14-54.83	0.036
Abnormal ferritin	8.63	1.52-48.83	0.015

[Table/Fig-10]: Multivariate logistic regression analysis - predictors of severe Stroke (NIHSS Grade 3-4).

Female sex (AOR=5.01), smoking (AOR=6.72), cardiac disease (AOR=7.92), and TIA (AOR=9.10) were significantly associated with

high serum ferritin, suggesting that inflammation-related risk factors strongly influence ferritin elevation in AIS [Table/Fig-12].

Variables	Adjusted Odds Ratio (AOR)	95% CI	p-value
Female sex	3.76	1.03-13.68	0.045
Smoking	4.91	1.12-21.42	0.035
Dyslipidaemia	3.82	1.01-14.44	0.049
Abnormal ferritin	10.13	1.90-53.83	0.007

[Table/Fig-11]: Multivariate logistic regression analysis - predictors of poor functional outcome (mRS Grades 4-5).

Variables	Adjusted Odds Ratio (AOR)	95% CI	p-value
Female sex	5.01	1.02-24.71	0.047
Smoking	6.72	1.37-32.89	0.019
Cardiac disease	7.92	1.13-55.28	0.037
TIA	9.10	1.15-72.06	0.037

[Table/Fig-12]: Multivariate logistic regression analysis - predictors of abnormal serum ferritin levels.

DISCUSSION

Ischaemic strokes are the most common type and primarily result from small vessel arteriolosclerosis, cardioembolism, and large artery atherothromboembolism. Non-modifiable risk factors for stroke are age over 55, female sex, genetic predispositions, and hypercoagulable states, and modifiable risk factors are hypertension, diabetes, obesity, dyslipidaemia, and smoking [1].

Stroke initiates a systemic inflammatory response, with cytokines such as IL-6, TNF-α, and IL-1β prompting hepatocytes to produce more ferritin as part of the acute-phase reaction. Ischaemic brain damage disrupts iron regulation and causes cell lysis, releasing intracellular iron that generates Reactive Oxygen Species (ROS), worsening neuronal injury. To counteract the toxic effects of free iron, ferritin synthesis is upregulated to safely store excess iron. Additionally, stroke-induced breakdown of the Blood-Brain Barrier (BBB) allows ferritin and iron-containing proteins to leak into the bloodstream. Neuronal and glial cell death also releases stored iron, further increasing serum ferritin levels [12].

Thus, ferritin serves as a key marker of iron metabolism and inflammation in ischaemic stroke. Elevated ferritin levels contribute to oxidative stress, neuronal damage, and worse clinical outcomes [13]. Monitoring ferritin levels can provide prognostic insights and help guide stroke management [14].

The NIHSS and mRS scores are used in AIS patients to evaluate stroke severity and functional disability, respectively. The NIHSS assesses various aspects of neurological function such as consciousness, motor abilities, sensory deficits, and language skills. The scoring system ranges from 0 to 42, with higher scores indicating greater neurological impairment. It is primarily utilised in the early stages of stroke to determine the severity and assist in making decisions about acute interventions like thrombolytic therapy.

In comparison, the mRS evaluates the degree of functional recovery and disability following a stroke. It is typically used during discharge or follow-up evaluations (e.g., at 4 weeks or 90 days post-stroke). The scale ranges from 0 (no symptoms) to 6 (death), and is widely regarded as a dependable tool for assessing long-term outcomes and the patient's level of independence in daily activities. A higher NIHSS score indicates greater neurological impairment and is generally associated with a worse mRS score, reflecting increased disability [15]. A clear trend was observed in our study: higher NIHSS scores were positively correlated with worse mRS scores, indicating that initial stroke severity strongly predicts functional outcome.

The present study population had a mean age of 56.1±7.2 years, with 24 (57.1%) male patients and 25 (59.5%) from rural areas. In contrast, a study by Sakib AA et al., reported a mean age of 60.7±14.49 years, with 202 (62.5%) male patients and a comparable rural representation of 201 (62.5%) patients. In the present study, 29 (69.0%) participants were smokers, and 21 (50.0%) reported alcohol addiction [Table/Fig-3]. Smoking showed a statistically significant association with both higher NIHSS and worse mRS scores, reinforcing its role in vascular inflammation and endothelial damage [Table/Fig-10,11]. Alcohol use, though prevalent among patients, did not show a strong statistical association with stroke scales. Sakib AA et al., found that 142 (43.9%) patients were smokers [14].

In the present study, hypertension was observed in 50% of patients, whereas Mondal MBA et al., reported a higher prevalence of 79.2%. The prevalence of diabetes was similar between both studies (28.6% vs. 28.8%). Dyslipidaemia was more common in the present study (47.6%) compared to their reported 38.9%. Additionally, the occurrence of cardiovascular disease was comparable, with 21.4% in the present study and 20.1% in theirs. A history of TIA was detected in 8 (19.0%) participants in our study [Table /Fig-3] [16].

Ranjan U and Panneerselvam K's study reported that, based on the NIH Stroke Scale assessment, 57% of patients had a moderate stroke, 28% had a minor stroke, 13% experienced a moderate to severe stroke, and 2% suffered from a severe stroke [15]. Similarly, in the study by Sakib AA et al., 52.9% of patients had moderate stroke, 23.5% had severe stroke, 15.4% had moderate to severe stroke, and 8% had minor stroke. Comparatively, this study found that 50% of patients had moderate stroke, 21.4% had minor stroke, and 19% had moderate to severe stroke. Severe stroke was observed in 9.5% of our participants, which was lower than the 23.5% reported in their study [Table/Fig-4].

In the study by Ranjan U and Panneerselvam K, the mRS assessment showed that 37 (26%) patients had a moderate disability but could walk (Grade 3), while 32 (22%) had a moderate disability and were unable to walk (Grade 4). Additionally, 31 (22%) had no significant disability (Grade 1), 30 (21%) had a slight disability (Grade 2), and 13 (9%) had a severe disability (Grade 5). In comparison, this study found that Grades 3 and 4 were the most common, each observed in 14 (33.3%) patients, followed by 8 (19%) with a slight disability (Grade 2) and 4 (9.5%) with a severe disability (Grade 5). The least common disability grade was Grade 1, recorded in 2 (4.8%) patients [Table/Fig-5] [15].

In the study by Egovindarajulu K et al., out of 60 cases, 35 (58.33%) had elevated serum ferritin levels, while 25 (41.67%) had normal levels. In comparison, this study found that 29 (69.1%) patients had high ferritin levels, whereas 13 (30.9%) had normal levels [Table/Fig-6] [17].

In this study, severe strokes (NIHSS Grades 3 and 4) were significantly associated with female gender ($p=0.001$), urban residence ($p=0.017$), smoking ($p=0.03$), cardiac disease ($p=0.008$), and a history of TIA ($p=0.004$). A strong correlation was observed between NIHSS and mRS grades ($p<0.001$), with high serum ferritin levels linked to greater stroke severity ($p=0.002$) [Table/Fig-7]. The multivariate analysis revealed that female sex, smoking, cardiac disease, TIA, and elevated serum ferritin levels were all independently associated with severe stroke, with Adjusted Odds Ratios (AORs) ranging from 4.5 to 8.6. Urban residence also showed a trend toward significance [Table/Fig-10]. Similarly, Ranjan U and Panneerselvam K reported a significant association between serum ferritin levels and stroke severity based on NIHSS ($p<0.05$) [15]. The study by Sakib AA et al., found a significant association between severe AIS (NIHSS ≥16) and factors such as cardiac disease, elevated ferritin levels, cholesterol, and dyslipidaemia. Multiple logistic regression analysis identified age over 50, male sex, and high ferritin levels as predictors of moderate to severe stroke [14].

The analysis of mRS grades revealed significant associations with clinical and demographic factors. Female patients had a higher prevalence of severe disability ($p=0.01$), while smoking ($p=0.02$) and dyslipidaemia ($p=0.02$) were linked to worse functional

outcomes. Elevated serum ferritin levels were significantly associated with increased disability (p<0.001), especially in mRS Grades 4 and 5. However, no notable association were observed with residence, alcohol consumption, diabetes, hypertension, cardiac disease, or TIA [Table/Fig-8]. The logistic regression model identified female sex, smoking, dyslipidaemia, and abnormal ferritin levels as significant predictors of poor functional recovery at day seven. Notably, elevated ferritin showed the strongest association (AOR=10.13, p=0.007), reinforcing its potential as a prognostic biomarker for post-stroke disability [Table/Fig-11]. In the study conducted by Ranjan U and Panneerselvam K analysis using the mRS revealed a statistically significant association between serum ferritin levels and stroke severity (p<0.05). After adjusting for confounding factors, multivariate analysis identified dyslipidaemia and hypertension as significant predictors of poor outcomes based on mRS (p<0.05) [15].

In this study, serum ferritin levels were significantly associated with sex, smoking, cardiac disease, and TIA. Females had a higher prevalence of abnormal ferritin levels (p=0.01), while smoking (p=0.004) and cardiac disease (p=0.02) were also linked to altered ferritin levels. Patients with TIA showed a higher occurrence of abnormal ferritin levels (p=0.03), highlighting its role as an inflammatory marker. However, no significant associations were found with residence, alcohol consumption, diabetes, hypertension, or dyslipidaemia [Table/Fig-9]. In multivariate analysis, female sex (AOR=5.01), smoking (AOR=6.72), cardiac disease (AOR=7.92), and TIA (AOR=9.10) were significantly associated with high serum ferritin [Table/Fig-12]. This was in contrast to findings by the study by Egovindarajulu K et al., no significant association was found between age, sex, smoking, and serum ferritin. However, a significant association was observed between hypertension (p=0.040) and diabetes (p=0.023) with serum ferritin levels. Moreover, high serum ferritin levels were also associated with stroke severity, as assessed by NIHSS, and poor outcomes, as evaluated by mRS [17].

Clinical implications:

- Prognostic utility: elevated serum ferritin levels at admission were significantly associated with both stroke severity (as measured by NIHSS) and poor functional outcomes (as measured by mRS). This reinforces its potential utility as a prognostic biomarker during the acute phase of ischaemic stroke. Early detection of high ferritin levels may enable clinicians to anticipate complications and tailor management accordingly.
- Risk stratification: The study identifies female sex, smoking, cardiac disease, and a history of TIA as risk factors that, when combined with elevated ferritin, indicate a higher likelihood of severe stroke and unfavorable recovery. These findings suggest that the high-risk individuals may benefit from intensified care, early rehabilitation, and closer clinical monitoring.
- Monitoring inflammation and oxidative stress: Ferritin serves as a surrogate marker of systemic inflammation and iron dysregulation- both of which are implicated in ischaemic brain injury. Its measurement may help monitor the inflammatory burden in stroke patients, particularly where advanced neuroimaging or specific inflammatory markers are not readily available.
- Cost-effective tool in resource-limited settings: Given its affordability and wide availability, serum ferritin could be integrated into standard stroke assessment protocols in low-resource healthcare settings, aiding in early prognostication and management decisions where other diagnostic modalities may be inaccessible.
- Future research and therapeutic targeting: These findings highlight the need for further longitudinal research to explore serial ferritin measurements and their prognostic value over time. Additionally, investigating the role of ferritin and iron homeostasis in stroke pathophysiology may open avenues for novel therapeutic interventions, such as iron chelation or anti-inflammatory treatments targeting neurovascular injury.

Limitation(s)

This study has several limitations that may affect the interpretation and generalisability of its findings. First, the relatively small sample size (n=42) limits the statistical power and may not accurately represent the broader population. Additionally, as a single-center study, the results may not reflect regional or institutional differences in stroke care and patient characteristics. The follow-up period was limited, with functional outcomes not evaluated beyond the acute phase (e.g., 90 days), which would have provided a more comprehensive understanding of long-term recovery and disability. Serum ferritin levels were assessed only once during the acute phase, without serial measurements that could offer insights into its temporal trends and prognostic value. Although multivariate analysis was conducted, potential confounding factors such as nutritional status, underlying infections, or chronic inflammatory conditions were not fully controlled, which could influence serum ferritin levels. Furthermore, the study did not incorporate neuroimaging correlations- such as infarct size or location- which may have enhanced the understanding of ferritin's prognostic significance in AIS.

CONCLUSION(S)

Serum ferritin levels demonstrated a significant association with stroke severity and poor functional outcomes, reinforcing their potential role as a prognostic marker in AIS. Additionally, smoking, cardiac disease, and a history of TIA were linked to abnormal ferritin levels, suggesting its role in stroke-related inflammation and oxidative stress. These findings emphasise the clinical significance of ferritin as an inflammatory biomarker, which may aid in risk stratification, prognosis prediction, and the development of targeted interventions for AIS patients.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 30, 2025
- Manual Googling: Aug 22, 2025
- iThenticate Software: Aug 25, 2025 (11%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 16, 2025**
Date of Peer Review: **Jul 15, 2025**
Date of Acceptance: **Aug 27, 2025**
Date of Publishing: **Nov 01, 2025**