Role of Serum Ferritin as a Prognostic Marker in Acute Ischemic Stroke: A Preliminary Observation

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Abstract

Background: Acute ischemic stroke is an important cause of morbidity and mortality. Search has been on to find out the factors which can help in formulating the prognosis of acute ischemic stroke. One of the prognostic indicators, which has gained great clinical interest in recent times, is serum ferritin. Aims: To assess the serum ferritin levels in patients with acute ischemic stroke and to study the role of serum ferritin as a prognostic marker in these patients. Materials and Methods: This prospective, observational study was conducted on 50 patients of acute ischemic stroke aged ≥18 years who presented within 48 hours of onset of symptoms. Clinical severity of stroke was assessed at admission and on the 6th day using Canadian Stroke Scale (CSS), and serum ferritin levels were measured at admission and on the 6th day in all these subjects. Results: The mean serum ferritin levels at admission in patients with “more severe stroke” (CSS score at admission ≤7) and “less severe stroke” (CSS score at admission >7) were 282.77 ± 120.53 and 205.12 ± 110.96 ng/mL, respectively. The mean serum ferritin levels at admission were 173.71 ± 109.69 ng/mL in subjects who did not deteriorate and 336.86 ± 57.28 ng/mL in those who deteriorated, while the mean serum ferritin levels on the 6th day were 193.29 ± 101.88 and 343.95 ± 52.34 ng/mL in subjects who did not deteriorate and those who deteriorated, respectively. Conclusions: Serum ferritin has a significant positive correlation with the severity of acute ischemic stroke (P < 0.001), and the levels correlate with the outcome of the disease (P < 0.001); the patients with higher serum ferritin at admission tend to deteriorate more as compared to those with lower levels. Thus, serum ferritin can be used as a prognostic marker in acute ischemic stroke.

Keywords: Acute ischemic stroke, prognostic marker, serum ferritin

Résumé

Contexte: L’AVC ischémique aigu est une cause importante de morbidité et de mortalité. Des recherches sont en cours pour découvrir les facteurs qui peuvent aider à formuler le pronostic d’un AVC ischémique aigu. L’un des indicateurs pronostiques, qui a suscité un grand intérêt clinique ces derniers temps, est la ferritine sérique. Objectifs: Évaluer les taux sériques de ferritine chez les patients ayant subi un AVC ischémique aigu et étudier le rôle de la ferritine sérique comme marqueur pronostique chez ces patients. Matériel et méthodes: Cette étude observationnelle prospective a été menée sur 50 patients ayant subi un AVC ischémique aigu âgés de ≥18 ans et qui se sont présentés dans les 48 heures suivant l’apparition des symptômes. La gravité clinique de l’AVC a été évaluée à l’admission et au 6e jour à l’aide de l’échelle canadienne de l’AVC (CSS), et les taux sériques de ferritine ont été mesurés à l’admission et au 6e jour chez tous ces patients. Résultats: Les taux moyens de ferritine sérique à l’admission chez les patients avec “AVC plus severe” (score CSS à l’admission ≤7) et “AVC moins severe” (score CSS à l’admission >7) étaient de 282.77 ± 120.53 et 205.12 ± 110.96 ng/mL, respectivement. Les niveaux moyens de ferritine sérique à l’admission étaient de 173.71 ± 109.69 ng/mL chez les sujets qui ne se sont pas détériorés et de 336.86 ± 57.28 ng/mL chez ceux qui se sont détériorés, tandis que les niveaux moyens de ferritine sérique au 6ème jour étaient de 193.29 ± 101.88 et 343.95 ± 52.34 ng/mL chez les sujets qui ne se sont pas détériorés et ceux qui se sont détériorés, respectivement. Conclusions: La ferritine sérique a une corrélation positive significative avec la gravité de l’AVC ischémique aigu (P <0.001), et les niveaux sont en corrélation avec l’issue de la maladie (P <0.001); les patients avec une ferritine sérique plus élevée à
INTRODUCTION

Stroke or cerebrovascular accident (CVA) is defined as an abrupt-onset neurological deficit attributable to a focal vascular cause. [1] CVA is the third leading cause of death after heart diseases and cancer and is now emerging as the most common preventable life-threatening neurological problem, worldwide. [2, 3]

Global estimates associated with stroke are 400–800 strokes per 100,000 population, [4] 16 million new acute strokes every year, [5] 5.5 million deaths per year, [6] and 28–30 day case fatality due to a stroke ranging from 17% to 35%. [7]

According to a recent report, the estimated global lifetime risk of stroke in 2016 for individuals aged 25 years or more was 24.9%, which was an increase from 22.8% in 1990. The report estimated an almost equal risk of stroke among men and women; the lifetime risk of ischemic stroke was 18.3% and of hemorrhagic stroke was 8.2%. [8]

Worldwide, approximately 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low- and middle-income countries. [9, 10] Over the last few decades, the stroke incidence in low- and middle-income countries has increased manifold, while it has reduced by 42% in high-income countries. [9] Besides, stroke occurs 15 years earlier and causes more deaths in low- and middle-income countries in comparison to those in high-income countries. [11]

Strokes mainly affect individuals at the peak of their productive life. Despite its tremendous impact on countries' socioeconomic development, this growing problem has received very little attention to date. [12]

The effects of a stroke depend on the site and severity of brain injury. Severity and follow-up of neurological deficit in stroke can be done with scales such as Canadian Stroke Scale (CSS), National Institute of Health Stroke Scale (NIHSS), and Glasgow Coma Scale (GCS). [13]

Of all the causes of cerebrovascular disease, atherothrombosis is by far the most important. [14, 15] Thrombotic occlusions causing cerebral infarctions are usually superimposed on atherosclerotic plaques; these occlusions may be accompanied by anterograde extension, as well as thrombus fragmentation and distal embolization. [16]

Ischemic stroke is an important cause of morbidity, mortality, and disability in developed and developing countries. Modification of risk factors, early diagnosis, and institution of proper treatment can reduce the impact of this disease and is of paramount importance. Search has been on to find out the factors which can help in formulating the prognosis of individual stroke cases. One of the prognostic indicators, which has gained great clinical interest in recent times, is the level of serum ferritin. Initially, considered only as a stress response to stroke, serum ferritin is now under research as a prognostic marker of stroke. [1]

Serum ferritin concentrations are normally in the range of 15–300 ng/mL and are lower in children than adults. Mean values are lower in women before the menopause in comparison to men. [17, 18] Serum ferritin concentration decreases with blood donation and increases with alcohol intake. [19-21]

Previous studies have suggested that iron overload contributes to the development of vascular disease by promoting thrombosis after arterial injury. High serum ferritin at admission was reported to predict a poor prognosis in acute stroke patients (within 24–48 h after stroke onset), implicating that increase in the body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Thus, it has been suggested that high serum ferritin influences the prognosis of ischemic stroke and also acts as a risk factor for ischemic episodes by enhancing atherogenesis. [22, 23]

Although thrombolytic therapy has emerged as the gold standard treatment for patients with acute ischemic stroke, it cannot be administered to many of these patients due to multiple factors including time constraints, availability, high cost (especially in developing countries), and presence of contraindications to thrombolysis. Proving the therapeutic potential of iron chelation therapy can be a great advancement in the field of treatment of acute ischemic stroke. [17] Very few national studies have explored the role of serum ferritin in prognostication of acute ischemic stroke; hence, this study was undertaken to assess serum ferritin levels in patients of acute ischemic stroke and to study the role of serum ferritin as a prognostic marker in these patients.

MATERIALS AND METHODS

It was a prospective observational study conducted on 50 patients of acute ischemic stroke admitted in the Medicine department of a tertiary care teaching hospital after getting approval from the institutional ethics committee.

Inclusion criteria

Both males and females, aged ≥18 years, who presented within 48 hours of onset of symptoms of acute ischemic stroke, diagnosed on the basis of clinical examination and neuro-imaging (computed tomography/magnetic resonance imaging brain) were included in the study.
Exclusion criteria
Patients who presented after 48 hours of onset of symptoms of acute ischemic stroke; those with recent infection, malignancy, anemia, or liver failure; those who had received blood/blood component transfusion in the previous 7 days; and those who received thrombolysis were excluded from the study.

Data collection procedure
The study conformed to the Declaration of Helsinki. All the participants were informed of the purpose of the study and were ensured strict confidentiality. Written informed consent was taken from all the patients (wherever possible) or from their attendants before their enrolment for the study. After detailed history and thorough clinical examination, the clinical severity of stroke was assessed using CSS at the time of admission. CSS is an 8-item scale which measures the level of consciousness, orientation, speech, motor function, and facial weakness in a stroke patient. This scale has a minimum score of 1.5 and a maximum score of 11.5; the lower the score, the greater is the neurological deficit [Table 1]. Furthermore, necessary laboratory investigations including serum ferritin (assessed using the instrument “Immulite” based on the principle of “chemiluminescence”) were undertaken in all the enrolled patients at admission. On the 6th day of admission, the severity of stroke was re-assessed clinically using CSS and serum ferritin levels were again measured in all the subjects. The CSS scores at admission and on the 6th day were then compared and the patients were categorized into two groups: “not deteriorated” group (patients in whom, over the course of 6 days, the CSS score increased or remained the same) and “deteriorated” group (patients in whom the CSS score decreased). The mean admission-day and 6th-day serum ferritin levels were determined in each of these groups, and the comparison between the two groups (“not deteriorated” and “deteriorated”) was then made using the Student’s t-test.

On the basis of admission-day CSS score, the patients were further divided into two groups: “less severe stroke” group (patients with admission-day CSS score >7) and “more severe stroke” group (patients with admission-day CSS score ≤7). The mean admission-day serum ferritin level was determined in each of these groups and comparison between the two groups (“less severe stroke” and “more severe stroke”) was then made using the Student’s t-test. Similarly, on the basis of the 6th-day CSS score, the patients were divided into two groups: “good outcome” group (patients with 6th-day CSS score >7) and “poor outcome” group (patients with 6th-day CSS score ≤7). The mean admission-day and 6th-day serum ferritin levels of the two groups were compared using the Student’s t-test.

Results
Of the 50 patients enrolled in this study, 28 (56%) were males and 22 (44%) were females. Nine patients (18%) were

| Variable                      | Number of subjects | Minimum | Maximum | Mean    | SD     |
|-------------------------------|--------------------|---------|---------|---------|--------|
| Serum ferritin at admission   | 50                 | 65      | 462     | 245.50  | 121.365|
| CSS at admission              | 50                 | 3.5     | 10.0    | 7.16    | 1.4792 |
| Serum ferritin on 6th day     | 50                 | 95      | 457     | 259.58  | 112.257|
| CSS on 6th day                | 50                 | 2       | 11      | 7.56    | 2.079  |

CSS=Canadian stroke scale, SD=Standard deviation
Statistically significant negative correlation was found between serum ferritin levels and CSS scores both at admission and on the 6th day in the study population [Table 6].

Of the nine subjects who belonged to the age group of ≤60 years, five (55.6%) subjects did not deteriorate and four subjects deteriorated. In the age group of 61–70 years, of the 27 subjects, 13 did not deteriorate while 14 deteriorated. Among the subjects aged >70 years, 10 out of 14 did not deteriorate while four deteriorated [Table 7]. There was no statistically

| Variable | Pearson correlation | Type of correlation | P |
|----------|-------------------|-------------------|---|
| Admission ferritin versus admission CSS | -0.492 | Negative correlation | <0.001 |
| 6th-day ferritin versus 6th-day CSS | -0.903 | Negative correlation | <0.001 |

CSS=Canadian stroke scale

Table 3: Serum ferritin levels in different age groups at admission and on the 6th day

| Variables | Age group | Number of subjects | Mean serum ferritin | SD | F value (ANOVA) |
|-----------|-----------|--------------------|---------------------|----|-----------------|
| Serum ferritin at admission | ≤60 | 9 | 254.33 | 119.413 | 0.542, P=0.585 |
| | 61-70 | 27 | 257.52 | 115.912 | |
| | >70 | 14 | 216.64 | 136.462 | |
| | Total | 50 | 245.50 | 121.365 | |
| Serum ferritin on 6th day | ≤60 | 9 | 264.33 | 101.741 | 1.185, P=0.315 |
| | 61-70 | 27 | 277.81 | 106.615 | |
| | >70 | 14 | 221.36 | 126.946 | |
| | Total | 50 | 259.58 | 112.257 | |

SD=Standard deviation

Table 4: Canadian stroke scale scores in different age groups at admission and on the 6th day

| Variables | Age group | Number of subjects | Mean CSS | SD | F |
|-----------|-----------|--------------------|----------|----|---|
| CSS at admission | ≤60 | 9 | 7.611 | 0.9930 | 0.638, P=0.533 |
| | 61-70 | 27 | 7.148 | 1.4197 | |
| | >70 | 14 | 6.893 | 1.8416 | |
| | Total | 50 | 7.160 | 1.4792 | |
| CSS on 6th day | ≤60 | 9 | 7.78 | 1.460 | 0.287, P=0.752 |
| | 61-70 | 27 | 7.35 | 2.156 | |
| | >70 | 14 | 7.82 | 2.342 | |
| | Total | 50 | 7.56 | 2.079 | |

CSS=Canadian stroke scale, SD=Standard deviation

Table 5: Serum ferritin and Canadian stroke scale scores at admission and on the 6th day in male and female subjects

| Variables | Sex | Number of subjects | Mean | SD | T value (t-test) | Cohen’s d |
|-----------|-----|--------------------|------|----|----------------|---------|
| Serum ferritin at admission | Male | 28 | 256.32 | 124.188 | 0.708, P=0.483 | 0.20 |
| | Female | 22 | 231.73 | 119.099 | |
| Serum ferritin on 6th day | Male | 28 | 273.00 | 117.777 | 0.953, P=0.345 | 0.27 |
| | Female | 22 | 242.50 | 104.992 | |
| CSS at admission | Male | 28 | 7.125 | 1.6422 | -0.187, P=0.853 | 0.05 |
| | Female | 22 | 7.205 | 1.2786 | |
| CSS on 6th day | Male | 28 | 7.41 | 2.289 | -0.567, P=0.572 | 0.16 |
| | Female | 22 | 7.75 | 1.811 | |

CSS=Canadian stroke scale, SD=Standard deviation

Table 6: Correlation between serum ferritin and Canadian stroke scale at admission and on 6th day

| Variable | Pearson correlation | Type of correlation | P |
|----------|-------------------|-------------------|---|
| Admission ferritin versus admission CSS | -0.492 | Negative correlation | <0.001 |
| 6th-day ferritin versus 6th-day CSS | -0.903 | Negative correlation | <0.001 |

CSS=Canadian stroke scale

aged ≤60 years, 27 patients (54%) were in the age group of 61–70 years, and 14 patients (28%) were aged >70 years. The mean age of subjects in this study was 66.62 ± 5.47 years.

The mean serum ferritin levels and mean CSS scores at admission and on the 6th day are summarized in Table 2. The age-related variations in serum ferritin levels and CSS scores at admission and on the 6th day were not statistically significant [Tables 3 and 4]. The gender-related variations in the serum ferritin levels and CSS scores at admission and on the 6th day were also statistically insignificant [Table 5].
significant difference in the clinical outcomes between the various age groups \( (P = 0.363) \).

Among 28 male subjects, 15 (53.6\%) did not deteriorate while 13 (46.4\%) deteriorated. Of 22 female subjects, 13 (59.1\%) did not deteriorate while nine (40.9\%) deteriorated. There was no gender wise difference in the outcomes of the disease \( (P = 0.696) \).

The mean serum ferritin at admission was 173.71 ± 109.69 ng/mL for subjects who did not deteriorate and 336.86 ± 57.28 ng/mL for subjects who deteriorated. The mean serum ferritin levels on the 6\(^{th}\) day for subjects who did not deteriorate and those who deteriorated were 193.29 ± 101.88 and 343.95 ± 52.34 ng/mL, respectively. There were statistically significant differences in the mean serum ferritin levels at admission \( (P < 0.001) \) and on the 6\(^{th}\) day \( (P < 0.001) \) between the two groups, i.e. deteriorated and not deteriorated [Table 8].

In this study, the mean serum ferritin level at admission in patients with “more severe stroke” (admission-day CSS score \( \leq 7 \)) was 282.77 ± 120.53 ng/mL and that in patients with “less severe stroke” (admission-day CSS score \( > 7 \)) was 205.12 ± 110.96 ng/mL; the difference between these two levels of mean serum ferritin was statistically significant \( (P = 0.022) \) [Table 9].

The mean serum ferritin levels at admission in patients with “poor outcome” (6\(^{th}\)-day CSS score \( \leq 7 \)) and “good outcome” (6\(^{th}\)-day CSS score \( > 7 \)) were 341.64 ± 54.55 ng/ml and 149.36 ± 88.54 ng/mL, respectively; the difference between these two levels of mean serum ferritin was statistically highly significant \( (P < 0.001) \) [Table 10]. Besides, serum ferritin at admission had a strong negative correlation with CSS on the 6\(^{th}\) day [Table 11].

The mean serum ferritin levels on the 6\(^{th}\) day in patients with “poor outcome” and “good outcome” were 349.48 ± 48.72 and 169.68 ± 80.72 ng/mL, respectively; the difference between these two levels was also statistically highly significant \( (P < 0.001) \) [Table 12].

**DISCUSSION**

Stroke is a nontraumatic, focal vascular injury of the nervous system and typically results in permanent damage in the form of cerebral infarction or intracerebral hemorrhage and/or subarachnoid hemorrhage. An ischemic stroke occurs due to cessation of blood flow due to extracranial or intracranial thrombosis, embolism, and hypoperfusion.

Previous studies have suggested that iron overload contributes to the development of vascular disease by promoting thrombosis after arterial injury. In addition, high serum ferritin at admission has been reported to predict a poor prognosis in acute stroke patients, implicating that increase in body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Thus, it has been suggested that high serum ferritin influences the prognosis of ischemic stroke and also acts as a risk factor for ischemic episodes by enhancing atherogenesis.\(^{[22,23]}\) A study by

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**Table 7: Clinical outcomes in the various age groups**

| Age group (years) | CSS changes | Total | \( \chi^2 \) |
|-------------------|-------------|-------|-----------|
| ≤60               | Not deteriorated | 5 (55.6) | 4 (44.4) | 9 (100.0) | 2.029, \( P=0.363 \) |
| 61-70             | Not deteriorated | 13 (48.1) | 14 (51.9) | 27 (100.0) | P=0.022 |
| >70               | Not deteriorated | 10 (71.4) | 4 (28.6) | 14 (100.0) | 2.363, \( P<0.001 \) |
| Total             | Not deteriorated | 28 (56.0) | 5 (44.0) | 50 (100.0) | 109.696, \( P=0.001 \) |

CSS=Canadian stroke scale

**Table 8: Mean serum ferritin levels at admission and on 6\(^{th}\) day in deteriorated and not deteriorated subjects**

| Variables                  | CSS          | Number of subjects | Mean      | SD        | \( T \) value (\( t \)-test) | Cohen’s d |
|----------------------------|--------------|--------------------|-----------|-----------|----------------------------|-----------|
| Serum ferritin at admission| Not deteriorated | 28                 | 173.71    | 109.696   | −6.322, \( P<0.001 \) | 1.86      |
|                           | Deteriorated  | 22                 | 336.86    | 57.287    | −6.304, \( P<0.001 \) | 1.86      |
| Serum ferritin on 6\(^{th}\) day| Not deteriorated | 28                 | 193.29    | 101.884   | −6.304, \( P<0.001 \) | 1.86      |
|                           | Deteriorated  | 22                 | 343.95    | 52.341    | −6.304, \( P<0.001 \) | 1.86      |

CSS=Canadian stroke scale, SD=Standard deviation

**Table 9: Relationship of mean serum ferritin levels at admission with severity of stroke at admission**

| Variables                | CSS at admission | Number of subjects | Mean ferritin | SD        | \( T \) value (\( t \)-test) | Cohen’s d |
|--------------------------|------------------|--------------------|---------------|-----------|----------------------------|-----------|
| Admission serum ferritin | ≤7               | 26                 | 282.77        | 120.536   | 2.363, \( P=0.022 \) | 0.67      |
|                          | >7               | 24                 | 205.12        | 110.981   |                           |           |

CSS=Canadian stroke scale, SD=Standard deviation

**Table 10: Relationship of mean serum ferritin levels at admission with severity of stroke on the 6\(^{th}\) day**

| Variables                  | CSS on 6\(^{th}\) day | Number of subjects | Mean ferritin | SD        | \( T \) value (\( t \)-test) | Cohen’s d |
|----------------------------|------------------------|--------------------|---------------|-----------|----------------------------|-----------|
| Admission serum ferritin   | ≤7 (poor)              | 25                 | 341.64        | 54.553    | 9.244, \( P<0.001 \) | 2.61      |
|                           | >7 (good)              | 25                 | 149.36        | 88.547    |                           |           |
Van der DL et al. on 11,471 postmenopausal women between 49 and 70 years of age observed that higher serum ferritin concentrations in the postmenopausal women were associated with an increased risk of ischemic stroke.[24]

The present study was carried out on 50 patients (28 males and 22 females) with acute ischemic stroke admitted within 48 hours of onset of symptoms. The mean serum ferritin levels at admission and on the 6th day were 245.50 ± 121.36 and 259.58 ± 112.25 ng/mL, respectively. In similar studies conducted by Egovindarajulu et al.[25] and Koul et al.,[26] the mean serum ferritin levels at admission were 241.39 ± 120.16 and 278.20 ± 141.90 ng/mL, respectively.

The age- and gender-related variations in the serum ferritin levels and CSS scores at admission and on the 6th day were statistically insignificant. Egovindarajulu et al. in their study also noted that there was no significant difference in the serum ferritin levels between the two age groups (≤50 years and >50 years) taken in their study (P = 0.918).[25]

This study found statistically significant negative correlation between serum ferritin levels and CSS scores both at admission and on the 6th day in the study population. The mean serum ferritin in the group with “more severe stroke” on admission (CSS score ≤7) was significantly higher than in the group with “less severe stroke” on admission (CSS score >7) (P = 0.022). In a similar study carried out on 60 patients with acute ischemic stroke, serum ferritin was measured at admission, and the stroke severity was measured by the NIHSS. Of 60 patients, 35 had high serum ferritin and 25 had normal serum ferritin at admission. Of these 35 patients with high serum ferritin, 22 had severe stroke (according to NIHSS) and 13 had moderate stroke. Of 25 patients with low serum ferritin at admission, none had severe stroke. This study observed positive correlation between serum ferritin and NIHSS scores (P = 0.000).[25] Another study noted that serum ferritin levels were higher in patients with large lesion size (P < 0.01) and deceased patients (P < 0.01).[18] Koul et al. in their study also revealed that there was a significant correlation between the values of serum ferritin and NIHSS (P < 0.001) and modified Rankin score (P < 0.001), both of which are used to evaluate the severity of stroke.[26] Therefore, it is suggested that the admission-day serum ferritin correlates with the severity of stroke on admission.

Of the 50 subjects recruited in this study, 22 deteriorated while 28 did not deteriorate. The mean admission-day serum ferritin in deteriorated patients was significantly higher than in patients who did not deteriorate (P < 0.001). The mean serum ferritin level on the 6th day was also significantly higher in deteriorated patients as compared to those who did not deteriorate (P < 0.001). In a similar study conducted by Pankaj et al. on patients with acute ischemic stroke, the mean admission-day serum ferritin in the clinically deteriorated group (458.7 ng/mL) was significantly higher than in the clinically improved group (87.01 ng/mL).[26] Narayanan and Singh observed that mean serum ferritin in deteriorated patients was 463.91 ng/mL, which was significantly higher than in those who improved (where it was only 96.44 ng/mL).[17] In another study which enrolled 51 patients with acute stroke, the serum ferritin levels were significantly higher in patients with large lesion size (P < 0.01) and deteriorated neurologic status during clinical follow-up (P = 0.03).[18] Demerdash et al. also observed significantly greater values of serum ferritin in patients with larger-sized lesions (P < 0.01) and deteriorated neurologic condition during follow-up. Cerebrospinal fluid (CSF) and serum ferritin levels were correlated with neurologic deficit (r = 0.50, P < 0.001). The authors concluded that elevated levels of CSF and serum ferritin correlate with the severity of stroke and may indicate a poor prognosis in terms of neurologic deterioration in stroke patients.[27]

The present as well as the previous studies showed that in patients with acute ischemic stroke, the admission-day serum ferritin was significantly higher in patients who deteriorated after admission, as compared to patients who did not deteriorate. There are many proposed mechanisms for this correlation. Higher serum ferritin levels indicate higher body stores of iron. This is also reflected on the iron stores in the brain. When brain ischemia occurs during CVA, more iron will be released from the injured brain cells due to larger iron stores present in them. When more iron is released, there is more oxidative stress in the local environment of the injured tissue, through generation of free radicals, especially hydroxyl radical. This results in aggravation of tissue injury during ischemia. Further, during reperfusion, this tissue insult is further augmented because of reperfusion injury that causes even more iron release and even higher oxidative stress.[1] Another proposed mechanism is that brain cells with higher iron stores release more glutamate when injured during ischemia; the released glutamate in turn causes further tissue injury.[1]

| Table 11: Correlation of serum ferritin at admission with Canadian stroke scale on the 6th day |
| Variable | Pearson correlation | Type of correlation | P |
| Admission serum ferritin versus CSS on 6th day | −0.899 | Negative correlation | <0.001 |
| CSS=Canadian stroke scale |

| Table 12: Relationship of mean serum ferritin levels on the 6th day with severity of stroke on the 6th day |
| Variables | CSS on 6th Day | Number of subjects | Mean ferritin | SD | T value (t-test) | Cohen’s D |
| Serum ferritin on 6th day | ≤7 (poor) | 25 | 349.48 | 48.720 | 9.534, P<0.001 | 2.69 |
| | >7 (good) | 25 | 169.68 | 80.728 | |
| CSS=Canadian stroke scale, SD=Standard deviation |
In our study, the mean serum ferritin levels at admission and on the 6th day were significantly higher in the “poor outcome” group (CSS score on the 6th day ≤7) than in the group with “good outcome” (CSS score on the 6th day >7) (P < 0.001). In a similar study conducted on 67 patients with acute ischemic stroke of <24 hours duration, patients were classified into two groups according to their CSS score on day 30; good outcome group (alive and CSS score >7) and poor outcome group (dead or CSS score ≤7). Serum ferritin values were greater in the poor outcome group (218 ± 156 vs. 133 ± 125 mg/L in the good outcome group; P = 0.004), and a correlation between serum ferritin values and degree of worsening or improvement of the CSS score on day 30 was found in this study (P = 0.002). Therefore, it can be concluded that serum ferritin correlates with the outcome of the disease.

The present study depicts that monitoring of serum ferritin levels during follow-up offers no significant benefit in prognostication of patients, as there was no significant difference in serum ferritin levels between day 1 and 6 of hospital admission.

Strength of the study
Very few studies from India have focused on the role of serum ferritin as a prognostic marker in acute ischemic stroke. This study highlights the positive correlation between serum ferritin level and the severity of acute ischemic stroke. Role of serum ferritin in prognostication of acute ischemic stroke is also supported by the observations in this study.

Limitations of the study
This was a single-center study with a small sample size.

Conclusions
Acute ischemic stroke is a cause of significant morbidity and mortality in both developed and developing nations. The present study reveals significant correlation of serum ferritin with the severity of acute ischemic stroke, depicting higher levels in patients with more severe disease. Serum ferritin measured at admission also correlates with the outcome of the disease; patients with higher levels of serum ferritin at admission tend to deteriorate more as compared to those with lower serum ferritin levels. Thus, serum ferritin can be used as a prognostic marker in patients with acute ischemic stroke. However, monitoring of serum ferritin levels during follow-up offers no significant benefit in prognostication of patients, as compared to a single measurement at admission. This study highlights the utility of a simple, easily available serum marker in prognostication of acute ischemic stroke.

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Conflicts of interest
There are no conflicts of interest.

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