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Original Research Article

Association of serum ferritin in patients with acute ischemic stroke in tertiary care hospital

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ABSTRACT

Background: Stroke is a major cause of mortality and morbidity globally. Identifying prognostic markers and mortality predictors is essential for successful intervention and treatment of ischemic stroke. The study aims to examine the role of serum ferritin as a prognostic indicator for stroke severity in conjunction with national institute of health stroke scale (NIHSS) and MRS stroke scales. Furthermore, the association of serum ferritin and several associated risk factors for stroke was also studied.
Methods: This study conducted was cross-sectional. 143 patients with acute ischemic stroke who attended the general medicine OPD within 24 hours of admission after the onset of stroke were taken into consideration. Only those patients who matched the inclusion and exclusion criteria were taken for analysis. Acute ischemic stroke patients were admitted with verbal consent, medical background, routine blood, neurological examination, and CT scan, NIHSS scoring, treatment protocols, anti-edema measures, and modified Rankin scale for functional recovery after four weeks.
Results: In the present study, 80% were males, and 20% were females. Most study participants were 51-60 years (38%). The mean age is 58.87 years, and the standard deviation is 11.41. About 35% were smokers, 38% were alcoholics, 56% were diabetic, 68% were hypertensives, and 35% had lipid disorders. There is a statistically significant correlation between serum ferritin and the severity of stroke based on the NIHSS scale and the Modified Rankin scale.
Conclusions: The study demonstrates the use of serum ferritin as an indicative marker for prognosis patients having an acute ischemic stroke. However, monitoring during follow-up did not show any benefit. The current study glorifies the simplistic use of a serum marker.

Keywords: Serum ferritin, Ischemic stroke, Modified Rankin scale, Stroke severity, NIHSS scale, Mortality predictors

INTRODUCTION

Stroke is one of the primary etiology for mortality and morbidity globally. A stroke is a cerebrovascular event that results in the abrupt death of specific brain cells from a lack of oxygen when a blood vessel blockage or rupture cuts off the blood supply to the brain.[1] WHO defines stroke series of quickly growing clinical indications of a localized or global disruption of brain function, longer than one day or resulting in mortality, with no clear etiology other than a vascular origin.[2] Acute ischemic stroke is also regarded as a neurological dysfunction event brought on by localized brain, spine, or retinal infractions.[3] The burden is worse globally in the developing world, accounting for 70% of mortality and morbidity. The burden of these cases doubled over the past several years. The new stroke caseload has been reduced by 42% in the developed world.[4] WHO reports fifteen million individuals get a stroke annually. Five million pass away, and the remaining is crippled, burdening the family and society.[5]

Stroke incidence in India is now 119-145/100,000 people. Since they cannot pay the costs and many continue to live with disabilities, the low-income group is heavily impacted by stroke.[6] Although the death rate associated with acute ischemic strokes is down, its morbidity is rising, making it a challenging condition to treat. An acute ischemic stroke is a neurological dysfunction brought on

by an infraction. In the pathophysiology of ischemic stroke, plaque in blood vessel linings blocks blood flow to the brain. The artery blockage in the neck or brain can lead to a condition where the flow of oxygen and glucose within a portion of the brain is prevented, leading to impaired brain function. Identifying the prognostic markers as soon as possible is crucial since this is the most beneficial time for successful intervention. Additionally, it is crucial to identify mortality predictors so that we may quickly provide treatment procedures to enhance results. The prognostic significance of many laboratory measures has been established by various research.[7-9]

Serum ferritin is an iron-carrying protein essential for maintaining iron homeostasis and is used to identify and manage iron excess and deficiency. It has been linked to poor stem cell transplant outcomes, cancer, and coronary artery disease. Ferritin is associated with rare but life-threatening human disorders such as hemophagocytic syndrome, sideroblastic anemias, and neurological conditions. By holding and releasing iron, it serves as a buffer against both excess and insufficiency.[10]

Numerous studies described the potential relevance of serum ferritin for the prediction of harmful effects of iron-mediated free radicals in the etiology of cerebrovascular disorders.

In earlier studies, iron excess encourages thrombosis following arterial damage, which in turn aids in the development of vascular disease. High blood ferritin levels in hospitals are positively connected with poor outcomes in acute stroke patients. This suggests a potential mechanism by which a rise in the body's iron reserves before the beginning of a stroke exacerbates the cytotoxicity associated with brain ischemia.[11] Therefore, the study aims to investigate the prognostic significance of serum ferritin in terms of stroke severity, and in correlation with stroke NIHSS and MRS scales. Moreover, the relationship between serum ferritin with numerous other associated risk factors for stroke was also analyzed.

METHODS

This cross-sectional study was conducted at the department of general medicine of Sree Balaji medical college and hospital, Chennai, for two years (2020 November-2023) January. The study was conducted on 143 patients with a condition of acute ischemic stroke who attended the general medicine OPD. Importantly, the patients with the onset of stroke within 24 hours. Only those patients who matched the inclusion and exclusion criteria were taken for analysis.

The inclusion criteria for this study are as follows: all patients who are above 14 years of age, regardless of their gender. These patients should have experienced a focal neurological deficit that is newly developed, followed by an ischemic stroke within a period of 48 hours. Additionally, patients should have a history of hypertension, dyslipidemia, diabetes mellitus, as well as a history of alcohol consumption and smoking.

Patients who are over 80 years of age will be excluded, as well as those with a history of malignancy. Patients with blood reports indicating infection, connective tissue disorders, and rheumatic heart disease will also be excluded. Patients with coronary artery diseases, previous transient ischemic attacks or reversible ischemic neurological deficits, a history of cerebrovascular accidents, or subdural hemorrhage will not be included. Additionally, patients with intracerebral hemorrhage, sub-arachnoid hemorrhage, recent surgery or trauma, and central nervous system tumors will be excluded.

The study proposal was submitted for approval by the ethics review committee of the institution. The purpose of the study along with the study protocol was elucidated to the patient in simple language, and written informed consent was obtained (Only if the patient was willing to participate in the study).

Verbal consent was taken soon after the patient got admitted. Thereafter, pertinent medical history, routine blood, neurological examination, and CT scan were taken into account, and the whole data were documented in a prescribed proforma. A CT scan was recorded to eliminate the stroke (Hemorrhagic). Serum ferritin was administered immediately after the admission of the patient to the hospital. Further, during the admission time of the patients, the NIHSS scoring was applied. They were categorized into mild, moderate, and severe. The treatment of these patients was carried out according to the standard treatment protocols.

There was no case of thrombolysis patients in the study group. Importantly, anti-edema measures were taken into consideration with any one of the oral glycerol or intravenous Mannitol. To know the patient's functional recovery during follow-up after four weeks, a modified Rankin scale was used.

The data was coded and entered into a computer using Microsoft excel, and the analysis was done using SPSS. Statistical tests, including descriptive statistics, the Chi-square test, and the Fisher exact test, were applied whenever the data, in terms of frequency was presented. Further, the student t test was used to estimate the significance of the results were shown as mean ± standard deviation (SD). $P<0.05$ was considered statistically significant.

RESULTS

In the present study, 80% were males, and 20% were females. Most study participants were 51-60 years (38%). About 24% were 61-70 years old, and 15.4% were 41-50. 15% were aged over 71 years, and only 8% were less than 40 years. The mean age is 58.87 years, and the standard deviation is 11.41.

Table 1: Demographic record of the patients in study.

Variables		N	Percent (%)
Gender	Male	113	79
	Female	30	21
Age group (Years)	≤40	12	8.3
	41-50	22	15.4
	51-60	54	37.7
	61-70	34	23.6
	≥71	21	15
Smoking	Yes	50	35
	No	93	65
Alcohol	Yes	54	38
	No	89	62
Diabetes mellitus	Yes	80	56
	No	63	44
Hypertension	Yes	97	68
	No	46	32
Dyslipidemia	Yes	50	35
	No	93	65
NIH stroke scale score	No stroke	0	0
	Minor	40	28
	Moderate	82	57
	Moderate to severe	19	13
	Severe	2	2
Modified Rankin scale score	No symptoms	0	0
	No disability	31	22
	Slight disability	30	21
	Moderate disability but able to walk	37	26
	Moderate disability but not able to walk	32	22
	Severe disability	13	9

About 35% were smokers, 38% were alcoholics, 56% were diabetic, 68% were hypertensives, and 35% had lipid disorders. Based on the NIH stroke scale, 57% had moderate disabilities, and 28% had minor disabilities, 13% had moderate to severe disability, and only 2% had severe disability.

Based on the modified rankin scale, 26% had a moderate disability but could walk, and 22% had a moderate disability but could not walk, 22% had no significant disability, 21% had a slight disability, and only 9% had a severe disability (Table 1).

There is a statistically significant association between serum ferritin and the severity of stroke based on the NIHSS scale ($p<0.05$). Based on the modified Rankin scale, serum ferritin and stroke severity showed a statistically significant ($p<0.05$) (Table 2) relationship among them.

After adjusting for confounding factors, the multivariate, dyslipidemia and hypertension are associated with poor outcomes, and the association is statistically significant ($p<0.05$) (Table 3).

Table 2: Mean NIHSS and MRS.

Variables		Mean	STD	P value
NIHSS severity	No to mild disability	360.8	21.67	0.001
	Moderate to severe disability	101.2	10.24	
MRS scale	Poor outcome	328.4	17.67	0.001
	Good outcome	87.6	8.24	

Table 3: Regression analysis of predictors of outcome.

Variables	Univariate analysis OR (95% CI)	P value	Multivariate analysis adjusted OR (95% CI)	P value
Age ≥65 years	1.91 (0.92-3.97)	0.08	1.87 (1.23-9.13)	0.06
Sex (male)	1.55 (0.67-3.56)	0.29	0.55 (0.17-1.80)	0.41
HT	1.38 (0.66-2.86)	0.38	2.48 (0.94-6.57)	0.035
DM	0.58 (0.28-1.1)	0.14	0.39 (0.155-0.97)	0.19
Dyslipidemia	1.32 (0.63-2.78)	0.45	2.42 (0.95-6.18)	0.033
Smoker	0.79 (0.39-1.60)	0.52	0.88 (0.31-2.47)	0.969
Alcoholism	0.79 (0.39-1.61)	0.53	0.44 (0.14-6.30)	0.096

DISCUSSION

According to available literature, a higher amount of iron promotes thrombosis post arterial injury and contributes to the onset of vascular diseases.[12] Furthermore, a high amount of serum ferritin has been already stated to forecast a substandard diagnosis in patients with acute stroke at admission to the hospital. This suggests that elevated body iron gets stored before the stroke's inception and can intensify brain ischemia cytotoxicity.[13] Hence, it has been proposed that a high amount of serum ferritin impacts the prediction of ischemic stroke. Moreover, it enhances atherogenesis and is a responsible factor for ischemic episodes.

A study conducted by Van et al. found that there is an increased risk of ischemic stroke in post-menopausal women with higher levels of serum ferritin.[14] This finding is consistent with the studies conducted by Egovindarajulu et al and Koul et al where the mean serum ferritin levels at

admission were calculated to be 241.39±120.16 ng/mL and 278.20±141.90 ng/mL, respectively.[15,16] Interestingly, no significant difference in serum ferritin levels was observed between two age groups, namely those aged 50 years or younger and those older than 50 years.

Similarly, Pankaj et al showed the mean serum ferritin (458.7 ng/mL) of the clinically deteriorated patients' group on admission day was significantly higher (87.01 ng/mL) than the clinically improved group.[17]

Narayan et al reported the mean serum ferritin of deteriorated patients was significantly higher (463.91 ng/mL) than the recovered patients (96.44 ng/mL).[18]

In another study, a significant increase ($p<0.01$) in serum ferritin concentration was observed in patients with large-sized lesions.[19] This finding aligns with a similar study by Demerdash et al where they also reported significantly higher serum ferritin levels ($p<0.01$) in patients with larger-sized lesions, and these patients experienced worsened neurological conditions during follow-up. Additionally, there was a close correlation ($r=0.50$, $p<0.001$) between cerebrospinal fluid (CSF) levels and serum ferritin, indicating that elevated levels of CSF and serum ferritin are associated with stroke severity. These findings suggest that the increased levels of CSF and serum ferritin may serve as indicators of an unfavorable prognosis, specifically in terms of neurological deterioration, in stroke patients.[20]

Limitations

A small sample size was utilized, and the study was conducted at a single medical center, restricting generalizability. Causal relationships could not be established due to the cross-sectional design. Additional insights were not provided through the follow-up monitoring.

CONCLUSION

The study reveals a notable connection between serum ferritin levels and the severity of acute ischemic stroke. It was observed that severely affected patients had higher levels of serum ferritin. Furthermore, individuals with elevated serum ferritin upon admission exhibited a greater decline compared to those with lower concentrations. This suggests that serum ferritin could serve as a potential prognostic marker for acute ischemic stroke patients. However, monitoring serum ferritin during follow-up sessions did not demonstrate any beneficial effects. The study highlights the utility of a readily accessible serum marker for prognosticating acute ischemic stroke.

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