Role of Serum Ferritin and Prediction of Neurological Outcome in Acute Ischemic Stroke Patients

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KEYWORDS
Acute ischaemic stroke, Serum ferritin, Neurological scales, GCS, Canadian Stroke Scale score, mRS.

ABSTRACT
Background: Stroke, also known as cerebrovascular accident (CVA), is an abrupt onset of neurological deficiency caused by a specific vascular aetiology. Aim: This study aimed to assess the role of serum ferritin in acute ischaemic stroke patients to correlate serum ferritin and neurological scales on the day of admission and during follow-up and to predict neurological outcomes. Methods: This prospective observational study included 100 patients who presented with acute ischaemic stroke clinically and with radiological imaging in the General Medicine and Neurology departments of Saveetha Medical College and Hospital for 18 months. Functional disability was assessed for all patients after 3 months based on the correlation of serum ferritin levels with the neurological scales, and the outcome was estimated. Results: The mean age of the patients was 59.45 ± 14.39. The serum ferritin level and Canadian Stroke Scale score during admission on day 7th and day 30th, were significantly different ($p < 0.01$). Serum ferritin levels were positively associated with the Glasgow Coma Scale score at admission and on the 7th and 30th days after admission. Ferritin levels were significantly higher in the moderate category under all circumstances ($p < 0.01$). Patients with mRS scores of 2, 3, and 4 were compared with serum ferritin levels and found to be significantly associated with serum ferritin levels. Conclusion: This study found that patients with higher serum ferritin levels experienced increased stroke severity and lower GCS and mRS scores, which correlated with increased morbidity.

1. Introduction

A stroke, also known as a cerebrovascular accident (CVA), is the abrupt onset of a neurological deficiency brought on by a specific vascular aetiology.[1] After heart conditions and cancer, CVA is the third leading cause of death in the world today. Owing to variable and non-modifiable risk factors, ischaemic stroke has a varied aetiology. Age, sex, and genetic variables were not modifiable factors. Diabetes mellitus (T2DM), hypertension, dyslipidaemia, and smoking are modifiable risk factors.[2] Excessive calcium load, acidosis, and enhanced free radical generation are the three main causes of brain damage caused by cerebrovascular occlusion. The main time when this oxygen-free radical activity exhibits an elevated effect is during reperfusion following ischaemia. The deadly hydroxyl radical is accelerated by ferrous iron, which is generated from intracellular reserves during ischaemia. The amount of iron present in the ischemic focus affects the neurons' sensitivity.[3]

Ischaemic and haemorrhagic strokes are the two main forms of stroke. Ischaemic stroke is caused by blood vessel obstruction, which lowers blood flow to the areas of the brain that supply blood vessels. Haemorrhagic stroke is characterised by vascular ruptures that allow blood to seep into the cerebral cavity.[4] Atherothrombosis is one of the most prevalent causes of cerebrovascular illness. Most cerebral infarctions are caused by the superimposition of atherosclerotic plaques; however, thrombus-related occlusions can also result from extension anterogradely, thrombus dislodging, and distant embolization.[5,6]

Different Neurological scales help assess stroke severity and prognosis. The Canadian Stroke Scale (CSS) is a simple and validated score to assess stroke severity.[7] It includes the following components: level of consciousness, orientation, speech, and motor functions range from 1.5 to 11.5 and its severity is categorised as follows. Mild (≥ 8), moderate (5–7), or severe (1–4). The lower the CSS score, the greater the stroke severity. The modified Rankin Scale (mRS) is used to measure the degree of disability in patients with stroke or other neurological disability.[8] mRS is divided into 7 categories. Zero with no symptoms and 6 for patients who died. Currently, this is the preferred method for evaluating outcomes in patients with acute ischaemic stroke (AIS).

Glasgow Coma Scale (GCS) helps to estimate the extent to which consciousness is affected in acute medical conditions and trauma patients.[9] This scale has 3 components: Eye-opening (E), Verbal component (V), and Motor (M) responses. In the Glasgow Coma Scale, the scores ranged from 1 (no response) to normal values of 4 (eye-opening response), 5 (verbal response), and 6 (motor response). The score was calculated as the sum of all scores and individual components. This scale ranges from 3 (E1V1M1) to 15 (E4V5M6) being the highest.

AIM

This study aimed to assess the role of serum ferritin in acute ischaemic stroke patients to correlate serum ferritin and neurological scales on the day of admission and during follow-up, and to predict neurological outcomes.

2. Materials and Methods

This prospective observational study was conducted on 100 patients who presented with acute ischaemic stroke clinically and radiologically in the General Medicine and Neurology departments of Saveetha Medical College for 18 months. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion criteria

Patients aged >18 years who were diagnosed with ischaemic stroke clinically with symptoms > 24 hours and with radiologically proven ischaemic stroke were included in the study.

Exclusion criteria

Patients not fulfilling the inclusion criteria with a history of recent infection or inflammation in the previous month and those with a history of malignancy, anaemia, or transient ischaemic attack who had already suffered from a stroke with haemorrhagic stroke were excluded.

Radiological imaging of either the CT or MRI of the brain was performed. Serum Ferritin levels were done on the day of admission. Neurological scales such as the Canadian Stroke Scale which has a minimum score of 1.5, to a maximum score of 11.5 done for all patients on the day of admission, and the Glasgow Coma Scale, in which factors such as eye movements, verbal, and motor components were considered, in which a minimum score of 3 and a maximum score of 15 were scored on the day of admission. A modified Rankin Scale was used for all patients on admission, with a score ranging from 0 to 6. Serum Ferritin levels were repeated on Day 7 and Day 30 for all these patients. The Canadian Stroke Scale was used on the day of admission and on days 7 and 30. Functional disability was assessed for all patients after 3 months based on the correlation of serum ferritin levels with the neurological scales, and the outcome was estimated.

Statistical analysis

Statistical analyses were performed using SPSS software (SPSS 20.0, IBM Corp., Armonk, NY, USA). Qualitative data were analysed using the chi-squared test. Continuous data of the three groups were analysed using one-way ANOVA. An independent Student's t-test was used to analyse the means between the two independent groups. Statistical significance was set at $p < 0.05$.

3. Results

Table 1. Demographic data of the study

			Percentage (%)
Age		30 - 40	10
		41 - 50	16
		51- 60	33
		61 -70	15
		71 -80	14
		81 -90	12
Gender		Male	49
		Female	51
Habits	Smoking	Yes	30
		No	70
	Alcohol	Yes	36
		No	64
Complication	Diabetes Mellitus	Yes	50
		No	50
	Hypertension	Yes	48
		No	52
	Dyslipidemia	Yes	49
		No	51
Canadian Stroke Scale at different time	During Admission	Mild	58
		Moderate	25
		Severe	17
	7th day after admission	Mild	63
		Moderate	21
		Severe	16

	30th day after admission	Mild	68
		Moderate	20
		Severe	12

The mean age of our patients was 59.45 ±14.39. The maximum number of patients ranged from to 51-60 years comprising (33%) and the minimum was 30-40 years. The sex distribution of ischaemic stroke patients was mostly female (51%). Of the 100 patients, 30% were smokers, and 36% were alcoholics. Smoking and Alcohol consumption were observed in 20% of patients. Fifty per cent of the patients had diabetes mellitus, 48% had hypertension, and 49% had dyslipidaemia. The percentage of patients with Diabetes and HTN together was 23%, and all three 3 comorbidities together were observed in 8% of the patients. The Canadian Stroke Scale scores during admission were as follows: mild, 58%; moderate, 25%; severe, 17% (Table 1).

Table 2. Descriptive statistics of serum ferritin at different times in Acute Ischemic Stroke patients

Serum ferritin at different time	Mean ± SD
Day 0	235.20 ± 183.243
Day 7	257.34 ± 179.273
Day 30	261.90 ± 176.320

The mean serum ferritin at day 0 was 235.20 ±183.243, at day 7 was 257.34 ±179.273, and day 30 was 261.90 ±176.320 (Table 2).

Table 3. Comparison of serum ferritin level with the Canadian stroke scale, Glasgow Coma scale, and modified Rankins's scale

Serum Ferritin level	Mean ± SD			P value
	Canadian Stroke Scale			
	Mild	Moderate	Severe	
During Admission	96.10 ± 85.50	403.51 ±75.03	468.14 ±50.1	0.000***
7th day after admission	136.97±101.13	444.6 ± 31.9	490.25±48.64	0.000***
30th day after admission	163.8 ± 120.7	458.51±25.51	496.58±32.51	0.000***
Serum Ferritin level	Glasgow coma scale			P value
	Mild	Moderate	-	
During Admission	102.82 ± 97.07	436.27 ± 56.19	-	0.000***
7th day after admission	128.05 ± 9.80	453.22 ± 67.00	-	0.000***
30th day after admission	135.67 ± 92.19	453.8 ± 65.61	-	0.000***
Serum Ferritin level	Modified Rankins Scale			P value
	2	3	4	
0th day	78.39 ± 36.00	359.09 ± 138.44	422.22 ± 95.20	0.000***

Serum ferritin level and Canadian stroke scale during admission of the patients showed that the serum ferritin level was very high in the severe category, followed by moderate and then mild. In the mild it was 96.10 ±85.50, moderate it was 403.51 ±75.03, in the severe it was 468.14 ±50.1, and this value was statistically significant (p=0.000).

On the 7th day after admission, the Canadian Stroke Scale score was positively associated with serum ferritin levels. As the serum ferritin level increased, the stroke scale score also increased from mild to severe. In mild ferritin was 136.97 ±101.13, in moderate ferritin, was 444.6 ±31.9 and in the severe ferritin group, the ferritin level was 490.25 ±48.64, and it was found to be highly statistically significant (p=0.000).

On the 30th day after admission, the Canadian Stroke Scale score was positively associated with serum ferritin level. As the serum ferritin level increased, the stroke scale score also increased from mild to severe on the 30th day. In mild ferritin was 163.8 ±120.7, the ferritin, was 458.51 ±25.51 and in the severe ferritin group, the ferritin level was 496.58 ±32.51, which was found to be highly statistically significant (p=0.000).

Serum ferritin levels were positively associated with the Glasgow Coma Scale score at admission, on the 7th day, and on the 30th day after admission, and ferritin levels were significantly higher in the moderate category under all circumstances (p=0.000). Patients with mRS scores of 2, 3, and 4 were compared with serum ferritin levels and were found to be significantly correlated with serum ferritin levels. The mRS scores of 0, 5, and 6 were nil (Table 3).

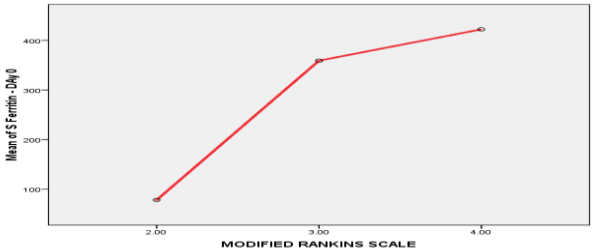

Figure 1. Comparison of modified the Rankins scale on admission between serum ferritin levels at different time

4. Discussion

In our study, most patients were aged between 51 and 60 years. Age in years had a mean and standard deviation of 59.45 ±14.39. Male patients comprised 49% of the 100 patients with acute ischaemic stroke, whereas 51% were female. Alcohol use was 36%, and smoking habit was 30%. Stroke risk factors include diabetes, which affects 50% of people; hypertension, which affects 48% of patients; and dyslipidaemia, which affects 49% of patients.

Banks and Marotta conducted a study on the validity and reliability of the modified Rankin Scale in patients with ischaemic stroke. This study found that, in addition to other impairments and endpoints, the mRS demonstrates a substantial connection with clinical assessments of stroke severity.[10] A study on the evolution of the modified Rankin Scale and its application in future trials was conducted by Broderick et al. The Modified Rankin Scale is useful for measuring the main outcome of stroke, according to this article's conclusion.[11]

Elhabr et al. studied the prediction of mRS score 90 days after treatment in patients with acute ischaemic stroke. The mRS score does not alter until 30 days, whereas between one month and three months, it significantly changed.[12]

Sultana et al. conducted a study on the comparison of serum ferritin in ischemic stroke patients and its correlation with the modified Rankins scale after 4 weeks. This study concluded that patients with higher serum ferritin levels had more severe disease than those with lower serum ferritin levels, and there was a significant association of serum ferritin with a modified Rankin scale. Patients with higher ferritin levels have increased scores of mRS.[13]

Koul et al. conducted a cross-sectional observational study in Srinagar on serum ferritin to determine its prognosis and severity of stroke. This study concluded that patients with higher mRS scores had more severe strokes than those with lower mRS scores.[14] Goldstein and Chilukuri performed a retrospective assessment of stroke severity using CSS. It concluded that retrospective stroke severity rating utilizing a CNS-based methodology is valid and practically applicable.[15]

In our study, serum ferritin levels ranged from 35 to 567 mg/dL on the day of admission, 46 to 580 mg/dL on day 7, and 60 to 561 mg/dL on day 30. The results showed that the patients with CSS of Mild had serum ferritin values of 96.10 ±85.50, moderate had values of 403.51 ±75.03, and severe had values of 468.14 ±50.1, which were significant. The serum ferritin level and Canadian Stroke Scale score during admission on day 7th and day 30th, showed a significant difference ($p=0.000$). The modified Rankin scale was compared with serum ferritin on the day of admission and found to be significant ($p < 0.000$). Patients with significant disabilities have higher ferritin levels than those with mild disabilities.

Nilanot et al. conducted a study in comparison of CSS with mRS in stroke patients. This study concluded that there is a significant relation between CSS and mRS and there is a significant reliability in the severity of strokes with these scales.[16] Erdemoglu and Ozbakir conducted a study on serum ferritin levels in ischaemic stroke patients and compared CSS with ferritin and cortisol levels with ferritin levels. This study concluded that there is a significant correlation between higher serum ferritin levels and infarct size. Patients with higher ferritin levels had higher ferritin levels. This study also concluded that there is no correlation between s. cortisol and serum ferritin in stroke patients.[17]

Simon et al. conducted a study on the correlation of serum ferritin with the Glasgow Coma Scale and the outcome of stroke. This study concluded that the Increased serum ferritin levels were found to have lower GCS scores and increased severity of stroke and had poorer outcomes in these patients.[18] Singh and Khatua conducted a prospective study on the correlation of serum ferritin in acute stroke patients and concluded that the increase in ferritin levels on admission has poorer outcomes than in patients with lower ferritin levels.[19]

Our study revealed that patients with elevated serum ferritin levels had a higher severity of stroke than those with lower ferritin levels. In comparison with the Glasgow coma scale, it was found that a lower GCS score correlated with higher ferritin levels and an increase in the severity of stroke. Patients with poorer CSS scores had a more severe stroke and were correlated with serum ferritin levels. Patients with lower CSS scores and high ferritin levels had an increased stroke severity. Our study also revealed that, when ferritin levels were compared with the modified Rankin disability scoring system, patients with higher mRS scores had increased stroke severity and higher serum ferritin levels. Our study showed that patients with higher serum ferritin levels had higher morbidity, and those with increased ferritin levels during admission had longer hospital stays than those with lower ferritin levels.

5. Conclusion

Our study revealed that patients with higher serum ferritin levels had a higher stroke severity. Patients with higher serum ferritin levels on admission had lower GCS scores and increased stroke severity. Patients with

higher mRS scores had higher serum ferritin levels and increased stroke severities. Patients with lower CSS have an increase in stroke severity, and these scores correlate with higher ferritin levels. Increased Serum Ferritin levels on admission correlated with increased morbidity.

Limitations

Patient follow-up is difficult, as is an increase in ferritin levels under other stressful circumstances. Patients who were admitted to the hospital after their symptoms had already started.

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