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Study of Serum Ferritin in Acute Ischemic Stroke and Correlation with its Outcome - A Prospective Observational Study

Shital D. Ghadge*, Deepti P Deshmukh[1], Abhinav M Wankhede[2]

[1]Senior Resident, Department of General Medicine, Punyashlok Ahilyadevi Holkar Government Medical College and General Hospital, Baramati, Pune, Maharashtra, India
Mobile No.: +91 9922516925
Corresponding Author Email: *shital6ghadge[at]gmail.com*

[2]Head of Department of General Medicine, IGGMCH, Nagpur, Maharashtra, India

[3]Senior Resident, Department of General Medicine, IGGMCH, Nagpur, Maharashtra, India

Abstract: ***Background and aim**: Acute Ischemic stroke (AIS) is an important health problem causing morbidity and mortality globally. Initially, considered only as a stress response to stroke, serum ferritin is now under research as a prognostic marker of stroke. The aim of this study was to ascertain serum ferritin levels in acute ischemic stroke and correlate its levels with severity and outcome of acute ischemic stroke. **Methodology**: This was a prospective observational study conducted in 100 patients with acute ischemic stroke admitted in the general medicine ward of a tertiary care teaching hospital in central India. **Results**: Mean serum ferritin was 227 ±73.35 µg/l in males and 131.52 ± 84.45 µg/l in females. High serum ferritin levels were found in 45.2% of males and 39.5% of females. Serum ferritin levels in patients with mRS score ≥ 3 was found to be significantly higher as compared to those with mRS score <3 (p=0.03). **Conclusion**: This study demonstrates the significant rise in serum ferritin in patients with acute ischemic stroke and correlates with high NIHSS score. Patients with lower serum ferritin levels had better outcomes as compared to those with high serum ferritin levels and this difference was statistically significant.*

Keywords: Ferritin, Prognostic marker, Acute ischemic stroke, NIHSS score, mRS score

1. Introduction

Cerebrovascular disease is the third most common cause of death in high - income countries after cancers and ischemic heart disease, and the most common cause of severe physical disability. [1] The current gold - standard approach to assessment of stroke requires brain and neurovascular imaging, in addition to the clinical assessment of stroke severity using National Institute of Health Stroke Scale (NIHSS). Modified Rankin Scale (MRS) score is used to measure the degree of disability in patients who have had a stroke. [2]

It has been suggested that ferritin influences the prognosis of Ischemic stroke and acts as a risk factor for ischemic episodes by enhancing atherogenesis. [3] Thus this study aimed to ascertain serum ferritin levels in acute ischemic stroke and correlate its levels with severity and outcome of acute ischemic stroke.

2. Methodology

This was a prospective observational study conducted in patients diagnosed with acute ischemic stroke and admitted in the general medicine department of Indira Gandhi medical college and hospital from January 2021 to September 2022.

Patients of acute ischemic stroke who presented within 48 hours of the onset of symptoms, >18 years of age, with valid telephone number and address and willing to participate in the study by giving informed consent were included. Patients with age more than 80 years, malignancy and clinical findings and blood investigations suggestive of infection, connective tissue disorders and rheumatic heart disease, features of hemorrhagic stroke, with history of recent surgery and trauma, CNS tumours, pregnant females, patients with anaemia or those who have received blood /blood component transfusion in the previous 7 days, receiving iron preparations were excluded from study.

Permission was obtained from the institutional ethics committee. On admission, a physical examination was conducted. NIHSS score was calculated. Laboratory investigations, ECG and CT scan were conducted.

Statistical analysis

All descriptive data was presented as mean ± standard deviation and percentages. Comparisons between groups were done using a two - sided student's 't' test. Correlation

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between serum ferritin levels and severity of stroke and outcome were studied.

3. Results

Mean age of the patients was found to be 63.28 ± 8.47 years. Majority of the patients were in the age group of 61 - 70 years (41%).

Table 1: Distribution of cases according to age group and gender

Age group (years)	Total n (%)	Males n (%)	Females (%)
41 - 50	7 (7)	4 (4)	3 (3)
51 - 60	29 (29)	19 (19)	10 (10)
61 - 70	41 (41)	20 (20)	21 (21)
71 - 80	23 (23)	19 (19)	4 (4)
Total		62 (62)	38 (38)

Table 2: Distribution of cases according to symptoms of ischemic stroke

Symptoms	N (%), n=100
Focal neurological deficit – total	98 (98)
Motor impairment	90 (91.8)
Speech impairment	82 (83.7)
Sensory impairment	42 (42.9)
Vision disturbances	18 (18.4)
Headache	35 (35)
Vomiting	17 (17)
Loss of consciousness	9 (9)
Seizures	8 (8)

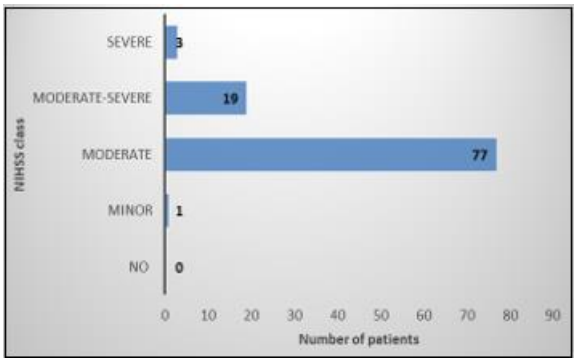

Figure 1: Distribution of cases according to stroke (OCSP) classification

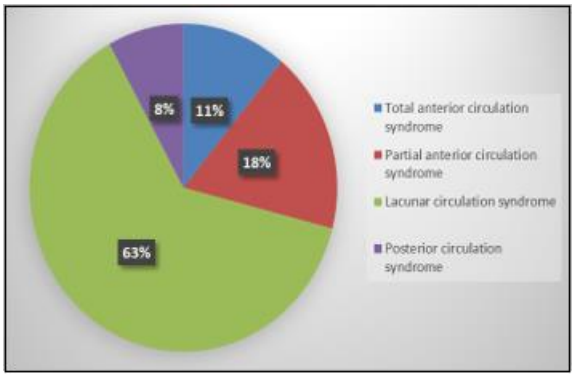

Figure 2: Oxfordshire community stroke project severity by NIHSS

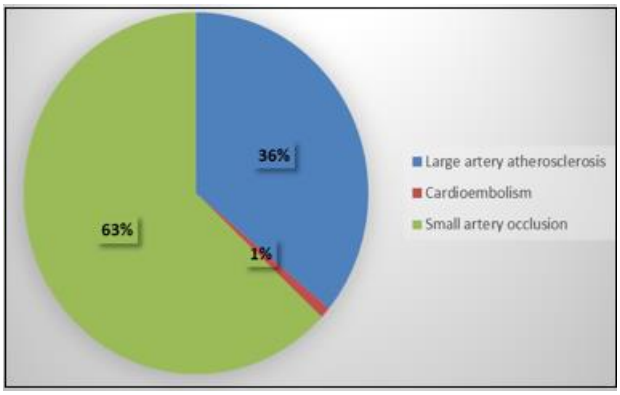

Figure 3: Distribution of cases based on clinical findings according to TOAST classification

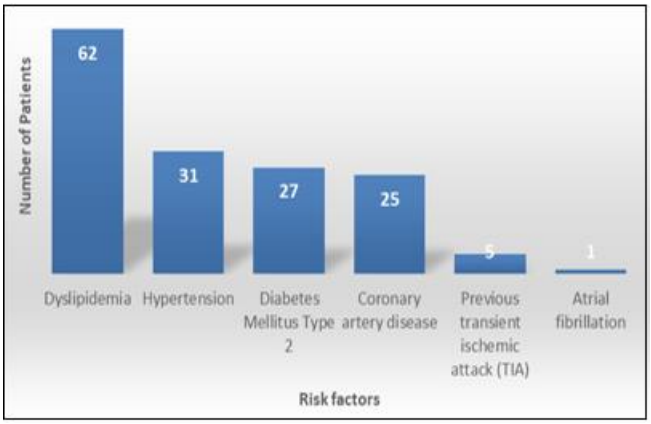

Figure 4: Distribution of cases according to risk factors contributing to Acute ischemic stroke

Serum ferritin

Serum ferritin levels were evaluated in all patients at admission, mean (±SD) serum ferritin levels were found to be; males (227 ±73.35) µg/l and females (131.52 ± 84.45) µg/l. It was found that 45.2% of males and 39.5% of females had high serum ferritin levels.

Table 3: Distribution of cases according to serum ferritin level on admission

Gender	Serum ferritin	N (%)
Males (n=62)	< 220 (Normal)	34 (54.8)
	≥ 220 (High)	28 (45.2)
Females (n=38)	< 110 (Normal)	23 (60.5)
	≥ 110 (High)	15 (39.5)

Table 4: Complications observed in study population

Complications	N (%), n=100
Fever	26 (26)
Urinary tract infection	11 (11)
Bed sores	8 (8)
Pneumonia	7 (7)
Deep vein thrombosis	1 (1)

Table 5: Distribution of outcome of cases according to Modified Rankin scale

Modified Rankin scale score	On Discharge n (%), n=100	At the end of 3 months n (%), n=100
0	0 (0)	6 (6)
1	9 (9)	23 (23)
2	26 (26)	9 (9)
3	16 (16)	33 (33)
4	28 (28)	20 (20)
5	20 (20)	5 (5)
6	1 (1)	4 (4)

Table 6: Comparison of mean serum ferritin level of patients with good vs poor outcome according to modified Rankin scale.

Variable	mRS <3	mRS ≥3	P value
Serum ferritin (mg/dl)			
mean ±SD	137.96 ± 68.15	230.62 ± 84.89	P=0.031
Range	45.2 - 311.7	42.1 - 479.3	

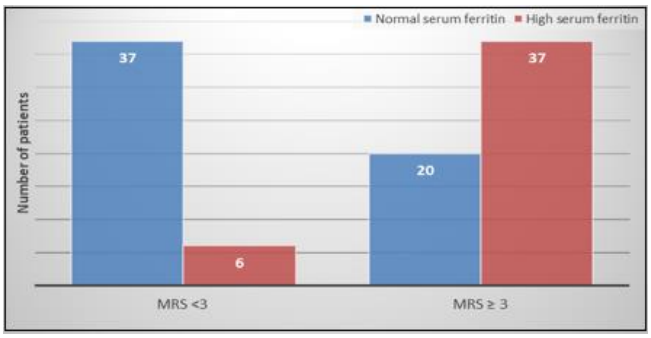

Figure 5: Number of patients with normal or high serum ferritin levels

Table 7: Multivariate logistic regression to assess the risk factor of mRS ≥3

	B	SE	P value	Odds ratio	95% C. I. for odds ratio	
					Lower	upper
High serum ferritin	1.34	0.78	0.01	3.01	- 0.22	3.90
Hypertension	0.78	- 0.73	0.05	1.83	- 0.22	2.16
Dyslipidaemia	1.46	- 0.74	0.036	1.74	0.76	2.12

4. Discussion

The mean age of the patients was found to be 63.28 ± 8.47 years NIHSS score on admission was found to represent moderate stroke in 77%, Moderate to severe stroke was found in 19% and severe stroke in 3% of the patients. Study conducted by Thanikachalam et al[4] showed that the mean NIHSS score at admission up to 50 years was 8.16±1.81, 9.41±2.32 in 51 to 70 years and it was 7.98±1.52 in 70 years and above and was statistically not significant (p=0.07). Oxfordshire Community Stroke Project (OCSP) classification found that LACI syndrome was most frequently occurring, and that TACI subtype was associated with poor outcomes. Iłzecka J et al conducted a study in Poland, in 346 hospitalized patients of ischemic stroke found that PACI syndrome was most frequently occurring, and that TACI subtype was associated with the highest frequency of complications and risk factors, and worst prognosis. The prognosis was found to be best in the LACI subtype. [5] Study conducted by WA Szlachetka reported that a total of 3534 (38.0%) patients suffered a Partial Anterior Circulation Stroke (PACS), 2401 (25.8%) of them had a Lacunar Stroke (LACS), 1830 (19.7%) patients had a Total Anterior Circulation Stroke (TACS) and 1533 (16.5%) patients had a Posterior Circulation Stroke (POCS). [6] Present study found that the majority of the patients had small artery occlusion (63%) followed by large artery atherosclerosis (36%). Salim Harris et al conducted study in Indonesia in 235 patients and found that the most common stroke subtypes were large artery atherosclerosis (n=140; 59, 6%), followed by small vessel disease (n=65, 2; 27, 7%), undetermined etiology (n=23; 9, 8%), cardioembolism (n=5; 2, 1%), and other determined etiology (n=2; 0, 9%). A retrospective study in Kingdom of Saudi Arabia by Zafar et al. showed that small vessel disease was the first etiologic ischemic stroke subtype (32, 1%), followed by cardioembolism (21, 9%) and large artery atherosclerosis (14, 6%). [7]

Present study found that a significantly greater number of patients with hypertension had a poor outcome (35.08%) compared to those with a good outcome (25.58), (p=0.03). Salim Harris also evaluated risk factors to find hypertension in 85, 3% (n=118) of patients but it was not statistically significant (p=0, 66). [8] Mohan et al reported 61 (70.1%) of ischemic stroke to have hypertension and was identified as an independent risk factor for the same (p<0.01). [9] In the present study, dyslipidemia was associated with poor outcome in significantly more patients (61.4%). Diabetes and ischemic stroke are common diseases that frequently occur together. Zafar et al[7] also found diabetes to be more prevalent in SVO (78%) than LAA (60%). Present study noted that a greater

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number of patients with diabetes had poor outcomes (38.59%), (p=0.03).

Complications such as pneumonia and bed sores were found to be more in patients with mRS score ≥ 3.

In this study, serum ferritin levels were evaluated in all patients at admission, and it was found that 45.2% of males and 39.5% of females had high serum ferritin levels. Mean (±SD) serum ferritin levels were found to be 227±73.35 µg/l in males and 131.52 ± 84.45 µg/l in females. Thanikachalam et al[4] reported that the mean serum ferritin levels at admission and on the seventh day were 247.50±123.3 and 206.34±113.28 ng/ml, respectively. In a similar study by Garg et al[10] the mean serum ferritin levels at admission and on the seventh day were 245.50 ±121.36 and 259.58±112.25 ng/ml, respectively. Narayan et al[11] reported mean serum ferritin level of the group of patients improved to be 85.01 and those deteriorated 458.70 with statistically significant difference in means of the two groups (p<0.001).

Modified Rankin scale scores were used as initial assessment and for assessment of outcome at the end of 3 months. Outcomes in the patients were categorized according to mRS score; score < 3 (good outcome) and score ≥ 3 (bad outcome) and mean serum ferritin levels were 137.96 ± 68.15 µg/l and 230.62 ± 84.89 µg/l respectively. Serum ferritin levels were significantly high in patients with bad outcomes or those who showed deterioration (p=0.03). Mohan et al[9] reported mean serum ferritin levels to be 144.48±134.65 µg/l and 362.45±153.41 µg/l in patients with ischemic stroke who improved and deteriorated respectively. The difference was found to be significant (p=0.001). Another study by Koul et al[12] revealed that there was a significant correlation between the serum ferritin values and NIHSS (p<0.001) and modified Rankin score (p<0.001), both of which are used to evaluate the stroke severity. Therefore, it is suggested that the admission day serum ferritin correlates with the severity of stroke on admission.

Rajendran et al[13] reported that hospitalization, elevated ferritin levels, ICH volume together with decreased GCS, characterized the groups with adverse prognosis. Serum ferritin moderately correlated with GCS (r = –0.643), ICH volume (r = 0.562), and had significantly higher correlations with long - term prognostic scores of 7th day mRS (r = 0.802) and 30th day mRS (r = 0.916). Koul et al[12] also concluded that a statistically significant correlation existed between NIHSS and MRS scores and serum ferritin levels in acute stroke patients. Study conducted by Garg et al[10] found that 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. This study also found that high serum ferritin (both males and females), hypertension and dyslipidaemia were found to be independent risk factors associated with poor outcomes in patients with acute ischemic stroke

5. Conclusion

The study demonstrates the significant rise in serum ferritin in ischemic stroke patients in correlation with high scores with NIHSS. Patients with lower serum ferritin levels had better outcomes as compared to those with high serum ferritin levels and the difference was statistically significant. The present study revealed a significant association between serum ferritin and poor outcome in ischemic stroke patients. Old age (71 - 80 years), hypertension, diabetes, and dyslipidemia were found to be associated with poor outcome (mRS ≥ 3). Elevated serum ferritin was found to be associated with early neurological deterioration in patients of stroke and is a definite poor prognostic marker of acute ischemic stroke.

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