



## Original Research Article

## A cross sectional study of correlation of serum ferritin levels with NIHSS scoring scale in patients of acute ischemic stroke

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## ABSTRACT

**Introduction:** Stroke is one of the leading causes of mortality and morbidity in the world. The National Institutes of Health Stroke Scale (NIHSS) is one of the most common stroke scale used by neurologist around the world. Serum Ferritin is an acute phase reactant, which increases during acute conditions like inflammation and also in vascular events.

This is a study that correlates the S.Ferritin levels with NIHSS scoring scale to assess the severity of stroke, which can also be used as an adjuvant tool for better assessment of severity of stroke in patients, which further helps in improving the management of patients with stroke.

**Aims:** This study aims to estimate serum ferritin and the NIHSS stroke scale in patients with acute ischemic stroke, and then to correlate serum ferritin with NIHSS stroke scale.

**Materials and Methods:** A cross sectional study was done during the period of November 2017-May 2019 in hospitals affiliated to Bangalore Medical College & Research Institute, Bangalore on 106 patients with acute ischemic stroke at the time of admission. NCCT brain was done and Serum Ferritin levels determined for patients who fit into the inclusion and exclusion criteria. Data was analyzed using SPSS 21.0 software by descriptive statistics in the form of mean values, standard deviation and percentages. Chi Square test was used for association of qualitative variables.

**Results:** There was linear increase of S.Ferritin with increase in severity of stroke (As determined by NIHSS scoring scale). It was found that male sex had a higher increase in S.Ferritin levels compared to females, with statistically significant correlation. It was also found that the maximum number of patients with increase in S.Ferritin levels belonged to severe stroke category.

**Interpretation and Conclusion :** As there was a linear increase of S.Ferritin with increase in severity of stroke (NIHSS scoring scale), we can conclude that Serum Ferritin level had a positive correlation with the severity of ischemic stroke indicating that S.Ferritin levels can also be used as an adjuvant tool for assessing the severity of stroke along with other tools and facilitate adequate and timely management of these patients.

**Key message:** S Ferritin can be used as a Prognostic marker in predicting the severity of Acute Ischaemic stroke.

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### 1. Introduction

As per World Health Organization, Stroke is defined as a clinical syndrome consisting of 'rapidly developing clinical signs of focal (at times global) disturbance of cerebral

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function, with duration lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.<sup>1</sup>

Ischemic stroke is the third leading cause of death and also leading cause of hospitalization causing disability. Acute Ischemic stroke has a higher chances for rapid recovery and good outcome.<sup>2</sup>

The National Institutes of Health Stroke Scale (NIHSS) is one of the most common stroke scale used by neurologist around the world.<sup>3</sup> It allows multiple acceptable answers for questions on the NIHSS certification test, introducing scoring variability. Wider the range of acceptable answers in the certification test, the greater the variability in the performance of the test in trials and clinical practice by certified examiners.<sup>4</sup> Hence the need for a search for alternative tests.

Serum Ferritin is an acute phase reactant, which increases during acute conditions like inflammation and also in vascular events.<sup>2</sup>

In this study we try to assess the NIHSS stroke scale in patients with acute ischemic stroke and correlate with serum ferritin level for the prediction of stroke severity.

## 2. Materials and Methods

### 2.1. Source of data and study design

It's a cross sectional study, was conducted on patients with acute ischemic stroke admitted to hospitals which are attached to Bangalore Medical Collage & Research Institution during the study period of November 2017-May 2019

### 2.2. Inclusion criteria

1. All patients with new onset ischemic stroke, confirmed by CT presented within 48 hours of onset of stroke are taken into study.
2. Acute ischemic stroke patients willing for examination after signing the informed consent.

### 2.3. Exclusion criteria

1. Acute ischemic stroke patients not willing for examination, not giving the informed consent
2. Patients with known infectious disease were excluded
3. Individuals with known Connective Tissue disorders were excluded
4. Patients with features of hemorrhagic stroke were excluded with the aid of CT scan
5. Patients with acute stroke below 45 years (to exclude patients with stroke in young

### 2.4. Sample size estimation

Based on previous study Egovindarajulu.K et al<sup>2</sup> sample size calculated was as follows:

$$\text{Sample Size : } n = \frac{Z\alpha^2\sigma^2}{d^2}$$

Where  $Z\alpha = 1.96$

$\alpha = 120.16$

$$n = \frac{(1.96)^2 \times (120.16)^2}{(23)^2}$$

= 106 patients of acute ischemic stroke

After obtaining institutional ethics committee clearance and written informed consent, 106 patients with acute ischemic stroke admitted as inpatients were included in this study. Detailed history was taken and clinical examination done. Relevant investigations were obtained including NCCT brain in all cases. Serum ferritin levels were determined through blood investigations and correlated with NIHSS scoring scale (through which severity of stroke was assessed)

### 2.5. Ethics

Ethical committee clearance was taken on 26/10/2017, Ref no BMC/PG/170/2017-18.

### 2.6. Statistical analysis

Data was entered in Microsoft Excel and exported into SPSS version 21.0.

Data was analysed by descriptive statistics in the form of mean values, standard deviation and percentages. Chi Square test was used for association of qualitative variables. A p value < 0.05 was considered statistically significant.

## 3. Results

During the study period, a total of 106 patients who fit into the inclusion criteria were studied. Of these, most were in the age group of 51-70 years (52.8%) (Table 1). Most of the study population were males (65.1%) and the remaining 34.9% were women (37 out of 106).

The Study population was categorized based on severity of stroke using NIHSS scoring scale. Total no of patients who fell in the minor category of NIHSS stroke scale included 10 patients, moderate category of NIHSS stroke scale included 39 patients, moderate to severe category of NIHSS stroke scale included 12 patients and severe category included 45 patients.

Out of the 106 patients, the maximum number belonged to severe stroke. This included 45 patients (42.5%) of the total study population. Serum Ferritin levels were assessed in the different groups of patients with different mean values which were statistically significant as depicted in Table 2.

As per Table 2, it was also found that serum ferritin levels increased with severity of the stroke.

Correlational analysis was done between the stroke severity and Serum Ferritin levels as depicted in Table 3.

The above chart shows that as the NIHSS score increase linearly as the S.Ferritin levels increase. A positive correlation hence exists between these 2 variables with

**Table 1:** Distribution of the patients based on age

Stroke		Age classified (in yrs.)					Gender		Total	
		46-50	51-60	61-70	71-80	>80	Female	Male		
Minor stroke	Count	0	4	2	2	2	6	4	10	
	% of Total	0.0%	3.8%	1.9%	1.9%	1.9%	5.7%	3.8%	9.4%	
Moderate stroke	Count	12	8	11	4	4	17	22	39	
	% of Total	11.3%	7.5%	10.4%	3.8%	3.8%	16%	20.8%	36.8%	
Moderate to severe stroke	Count	4	2	3	3	0	5	7	12	
	% of Total	3.8%	1.9%	2.8%	2.8%	0.0%	4.7%	6.6%	11.3%	
Severe stroke	Count	4	13	13	8	7	9	36	45	
	% of Total	3.8%	12.3%	12.3%	7.5%	6.6%	8.5%	34%	42.5%	
Total	Count	20	27	29	17	13	37	69	106	
	% of Total	18.9%	25.5%	27.4%	16.0%	12.3%	34.9%	65.1%	100.0%	
Chi-square value P value		Age distribution - 14.65					Gender distribution - 8.70		Age distribution – 0.26	Gender distribution – 0.033

**Table 2:** Comparison of serum ferritin levels among stroke groups

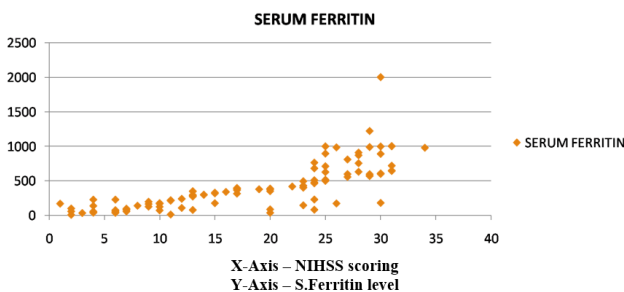
Stroke severity	N	Minimum Micrograms/L	Maximum Micrograms/L	Mean	Std. Deviation	Kruskal-wallis	P value
Minor stroke	10	10.40	230.00	90.08	69.94		
Moderate stroke	39	15.50	393.10	184.92	103.72	65.12	<0.001*
Moderate To Severe Stroke	12	40.00	403.00	320.25	122.29		
Severe Stroke	45	84.70	1222.00	636.60	268.70		

\*significant

**Table 3:** Spearmans correlation between serum ferritin levels and NIHSS scoring scale

S. Ferritin v/s NIHSS	r value	P value
S. Ferritin v/s NIHSS	0.83	<0.001*

\*significant



**Fig. 1:** Correlation of S.Ferritin level with NIHSS scoring scale

a statistically significant ‘p’ value. Scatter plot analysis reveals the positive correlation between serum ferritin & NIHSS.

However, there was no significant difference in the number of patients affected with stroke in the male-female ratio in the different groups based on severity. However, Serum Ferritin was significantly higher in male patients as shown in Figure 1.

From the above data (Table 4) we could analyze that in the minor category of stroke the no of patients whose S.Ferritin levels were with normal limits were 9 (8.5%) and

the number of patients whose S.Ferritin levels were more than the normal limits were 1 (0.9%).

In the moderate category of stroke the no of patients whose S.Ferritin levels were with normal limits were 33 (31.1%) and the number of patients whose S.Ferritin levels were more than the normal limits were 6 (5.7%).

In the moderate to severe category of stroke the no of patients whose S.Ferritin levels were with normal limits were 2(1.9%) and the number of patients whose S.Ferritin levels were more than the normal limits were 10 (9.4%).

In the severe category of stroke the no of patients whose S.Ferritin levels were with normal limits were 6 (5.7%) and the number of patients whose S.Ferritin levels were more than the normal limits were 39 (36.8%). Therefore 86.67 % of patients who fall into the category of severe stroke had elevated S.Ferritin level.

#### 4. Discussion

K Egovindarajulu et al<sup>2</sup> a cross sectional observational study conducted in Vellore on 2016 found that significant rise in serum ferritin in ischemic stroke patients associated with high scores with NIHSS which indicates the severity and poor outcome in correlation with high serum ferritin

**Table 4:** Comparison of serum ferritin levels between gender using mann-whitney test

Gender	N	Minimum	Maximum	Mean	Std. Deviation	Mean difference	P value
Females	37	10.40	990.00	249.41	235.09	-205.29	<0.001
Males	69	40.00	1222.00	454.70	299.98		

**Table 5:** Cross-tabulation of strokes and S.Ferritin levels

Stroke Severity		S. Ferritin classified		Total
		Abnormal	Normal	
Minor stroke	Count	1	9	10
	% of Total	0.9%	8.5%	9.4%
Moderate stroke	Count	6	33	39
	% of Total	5.7%	31.1%	36.8%
Moderate to severe stroke	Count	10	2	12
	% of Total	9.4%	1.9%	11.3%
Severe stroke	Count	39	6	45
	% of Total	36.8%	5.7%	42.5%
TOTAL	Count	56	50	106
	% of Total	52.8%	47.2%	100.0%

Chi-square value- 54.46  
P value-<0.001\*

level as opposed to low S ferritin.

Emilie Millerot et al<sup>5</sup> is a study conducted in rats in 2005, evaluated the effect of body of body iron stores on the vulnerability of the brain to ischemia, a focal permanent brain ischemia was induced by photothrombotic occlusion of cortical vessels in rats with or without chronic treatment with iron dextran (25 mg iron/kg, every other day for 20 days, intraperitoneally), it was found that increased body iron stores do not increase the vulnerability of the brain to ischemia and that brain ischemia, if severe, results in the elevation of serum Ferritin levels.

Kemal Erdemoglu A et al<sup>6</sup> a prospective study conducted in 2002 in Turkey in 51 patients found that Serum ferritin level was found to be higher in patients with large lesion size ( $P < 0.01$ ), deteriorated neurologic status during clinical follow-up ( $P \frac{1}{4} 0.03$ ) and deceased patients ( $P < 0.01$ ).

There are several other studies conducted across India shows positive correlation with severity of stroke and S ferritin . Rakesh kumar koul et al<sup>7</sup> study conducted in Srinagar in 2018 in 50 patients using Modified Rankin scale and NIHSS, another study by Ramesh Thanikachalam et al<sup>8</sup> conducted in TamilNadu in 2020 in 60 patients using NIHSS scale for severity of stroke and Ravindra Garg et al<sup>9</sup> study conducted in Punjab in 2020 in 50pts using Canadian Stroke Scale to asses the severity, All the above studies found that S ferritin levels can be used as a prognostic marker in acute Ischemic stroke.

There is also a study which shows no significant correlation with S ferritin levels it was a study by M Üstünda et al<sup>10</sup> conducted in Turkey in 2010 found that Ferritin, pro-BNP and homocysteine levels were raised in acute ischemic stroke patients. However, only serum pro-BNP level is clinically useful in predicting stroke subtype, severity and

mortality.

Among the 106 cases included in this study cases 55 (52.8%) had high S.Ferritin values [ $\geq 300$  mg/l (male) ,  $\geq 200$  mg/ml (female)] Out of these, 0.9 % of cases were under minor category and 5.7% of cases were under moderate category. 9.4 % of cases belonged to moderate to severe category and 36.8 % of cases belonged to severe category. Hence, our study also shows that more severe stroke had higher Ferritin levels.

Spearman's r correlation also revealed positive correlation between serum ferritin and NIHSS scores. With a Spearman's r value of 0.87, it is implied that any increase or decrease in S.Ferritin score linearly correlates with increase/decrease severity score of NIHSS.

## 5. Conflict of Interest

None.

## 6. Funding of Sources

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## References

1. World Health Organization. The World Health Report: 2002:Reducing risks, promoting healthy life; 2002.
2. Egovindarajulu K, Maaran AT, Prathiba P, Saiprashanth PR. A Study on prognostic Significance of Serum Ferritin in Patients with Acute Ischemic Stroke. *IOSR J Dent Med Sci*. 2016;15(10):31–9.
3. Kaviani G. Challenging comparison of stroke scales. *J Res Med Sci*. 2013;18(10):906–10.

4. Hills NK, Josephson SA, Lyden PD, Johnston SC. Is the NIHSS Certification Process Too Lenient? *Cerebrovasc Dis.* 2009;27(5):426–32.
5. Millerot E, Tessier AP, Bertrand NM, Faure PC, Mossiat CM, Giroud ME. Serum ferritin in stroke: a marker of increased body iron stores or stroke severity. *J Cereb Blood Flow Metab.* 2005;25(10):1386–93.
6. Erdemoglu AK, Ozbakir S. Serum ferritin levels and early prognosis of stroke. *Eur J Neurol.* 2002;9(6):633–7. doi:10.1046/j.1468-1331.2002.00472.x.
7. Koul RK, Yaseen Y, Amreen S, Shah PA, Hakeem MM. Role of Serum Ferritin in Determining the Severity and Prognosis of Stroke: A Hospital Based Study. *Int J Sci Stud.* 2018;6(8):142–5.
8. Kaushik R, Mittal M, Gupta A. Serum ferritin level - A predictor of haemorrhagic transformation in acute ischaemic stroke. *Int J Contemp Med Res.* 2018;5(1):24–31. [cited 2021 Aug 6].
9. Garg R, Aravind S, Kaur S, Chawla SS, Aggarwal S, Goyal G, et al. Role of serum ferritin as a prognostic marker in acute ischemic stroke: A preliminary observation. *Ann Afr Med.* 2020;19(2):95–102.
10. Üstündağ M, Orak M, Güloğlu C, Öztürk E, Tamam Y, Kale E, et al. The role of serum ferritin, pro-brain natriuretic peptide and homocysteine levels in determining ischaemic stroke subtype, severity

and mortality. *Hong Kong J Emerg Med.* 2010;17(1):13–21.

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