ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 07 | July - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF SERUM FERRITIN LEVELS AMONG PATIENTS WITH ACUTE ISCHEMIC STROKE: AN OBSERVATIONAL STUDY

General Medicine

Dr Shubhangi H Verma* Professor and Head, Department of Medicine, PDMC, Amravati, Maharashtra *Corresponding Author

Dr Akshay U Nagarkar Junior resident, Department of Medicine, PDMC, Amravati, Maharashtra

ABSTRACT

Background: Hyperferritinemia has been postulated in promoting thrombosis causing vascular injury in patients with stroke. It has also been reported that high ferritin levels at admission can aggravate the cytotoxicity of the brain ischemia. With this background, we conducted this study with a goal to understand the ferritin levels among the patients with acute ischemic stroke and to study its correlation with stroke severity using CSS and infarct volume as based on the computed tomography scan of brain. **Materials and methods:** It was prospective observational study conducted in 85 patients admitted in the department of medicine of Dr Punjabrao Deshmukh Memorial Medical College, Amravati. All the patients whose diagnosis was confirmed by CT scan or Magnetic resonance imaging (MRI) of brain and presenting to the emergency within 48 hours of the symptoms of ischemic stroke were included in the study. After detailed history and thorough clinical examination, the clinical severity of stroke was assessed using CSS at the time of admission. Outcome and ferritin levels at admission and at follow up were noted down and analysed. **Results:** The present study reported significant negative correlation between the Canadian stroke scale and serum ferritin levels at admission [r=-0.485; p value <0.001] and at follow up [r=-0.512; p value <0.001]. The average ferritin levels among the patients with good outcome was 291.41microgram/L, for those who deteriorated were 889.66 microgram/L and those who died during the first week of admission was 908.47 microgram/L. **Conclusions:** Canadian stroke scale and infarct volume has a significant correlation with serum ferritin levels. With increase in the CSS the ferritin levels were low and with increase in the infarct volume the serum ferritin levels were high. Those patients who died and who deteriorated had significantly higher ferritin levels than those who had good outcome.

KEYWORDS

Serum ferritin; Stroke; Canadian stroke scale

INTRODUCTION

Stroke or cerebrovascular accident is defined as acute onset of neurological injury in a vascular territory as a result of focal cerebrovascular disease. [1] Stroke is third common cause of death and is now emerging as a preventable neurological problem worldwide. [2,3] It is second most common cause of disability and dementia among ages more than or equal to 65 years of age. The estimated incidence rate of stroke is 119-145 per lakh based on the recent population based studies. [4] Approximately 70% of strokes and 87% of both stroke related mortality and morbidity occurs in low and middle income countries. The effects of stroke are determined by the site and severity of brain injury. [5,6] Various severity scores in assessing the patients with stroke have been sued. Some of the important ones are Canadian Stroke Scale (CSS), National Institute of Health Stroke Scale (NIHSS), and Glasgow Coma Scale (GCS). [7] Basic pathophysiological mechanism of stroke is atherothrombosis of the arteries of the brain. These occlusions lead to cerebral infarction those results in ischemic changes in the brain parenchyma. [8] Ischemic strokes are noted as the most common subtype of strokes. [9] Early diagnosis and prompt treatment remains the best approach to such neurological insults. [10] In the recent times, serum ferritin levels have gained a significant role in predicting the prognosis of the ischemic stroke. Ferritin is storage protein for iron and is an essential factor for iron homeostasis. [11] Hyperferritinemia has been postulated in promoting thrombosis causing vascular injury in patients with stroke. It has also been reported that high ferritin levels at admission can aggravate the cytotoxicity of the brain ischemia. Few studies have explored the role of serum ferritin in the predicting acute ischemic stroke [12]; hence, we conducted this study with a goal to understand the ferritin levels among the patients with acute ischemic stroke and to study its correlation with stroke severity using CSS and infarct volume as based on the computed tomography scan of brain.

MATERIALS AND METHODS:

It was prospective observational study conducted in 85 patients admitted in the department of medicine of Dr Punjabrao Deshmukh Memorial Medical college, Amravati. The study was approved by institutional ethics committee of the institute.

Inclusion criteria: Patients of both genders above 18 years of age were included. All the patients whose diagnosis was confirmed by CT scan or Magnetic resonance imaging (MRI) of brain and presenting to the emergency within 48 hours of the symptoms of ischemic stroke were included in the study.

Exclusion criteria: Those patients who presented later than 48 hours, those who have recently recovered from an infection, malignancy, anemia or liver failure were excluded from the study. Also, those patients who have received blood or blood components in previous 7 days and who have received thrombolytic therapy were excluded.

Sample size: Based on a pilot study of 30 cases of ischemic stroke admitted in our hospital, we found that 65% of the patients had higher than upper limit of serum ferritin levels. Using this, with 10% absolute error and 95% confidence interval, we found the sample size to be 84.

Data collection procedure: We conducted this study in accordance with Declaration of Helsinki. All the participants were informed about the nature of the study and were ensured strict confidentiality. Written informed consent was taken from the patients or caregivers before the enrollment in 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. The CSS score was dichotomised into less severe (≤7) and severe group (>7) for the ease of analysis. Also, necessary laboratory investigations including serum ferritin were undertaken in all the enrolled patients at admission. CT scan or MRI of brain was performed in all the patients and the size of it was noted down to calculate the infarct volume in cubic centimetres.

Statistical analysis plan: The data will be collected, compiled, and analyzed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantitative variables were both categorized and expressed in terms of percentages or in terms of mean and standard deviations. The difference between the two proportions was analyzed using chi-square or Fisher exact test. Normality of Quantative data was tested using kolmogorov smirnov test. Mann Whitney U test was used to test the difference between the two medians. To correlate between the two Quantative parameters, we used Pearson's correlation coefficient. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS: We have 85 patients of ischemic stroke included in the present study

Table 1: Demographic profile of the patients

Demographic particulars	Frequency	Percentage
Age group		
40 to 50	9	10.71
50 to 60	19	22.62

60 to 70	51	60.71
>70	5	5.95
Gender		
Female	29	34.52
Male	55	65.48
Risk factors (n=84)		
Alcohol use	31	36.90
Smoking	14	16.67
Hypertension	44	52.38
Diabetes mellitus	36	42.86
Ischemic heart disease	2	2.38
Symptom onset		
<24 hours	37	44.05
>24 hours	47	55.95
Side of involvement		
Left	49	58.33
Right	35	41.67
Canadian Stroke Scale		
≤7 (Non severe)	67	80.72
>7 (Severe)	16	19.28

The mean age of the subjects was 63.45 ± 4.56 years with male preponderance. The most common risk factors associated were hypertension (52.38%) and diabetes mellitus (42.86%). Based on the Canadian stroke scale, 80.72% of the cases were non severe type.

Table 2: Distribution based on the site and volume of infarct (Based on imaging)

Infarct	**Frequency**	**Percentage**
Site (n=84)		
Middle cerebral artery	61	72.62
Posterior cerebral artery	25	29.76
Anterior cerebral artery	12	14.29
Infarct volume (cm3)	**Mean**	**SD**
	27.07	42.04

The average infarct volume was 27.07 ± 42.04 cm^3. About 72.62% were in middle cerebral artery, 29.76% were in posterior cerebral artery and 14.29% were in anterior cerebral artery.

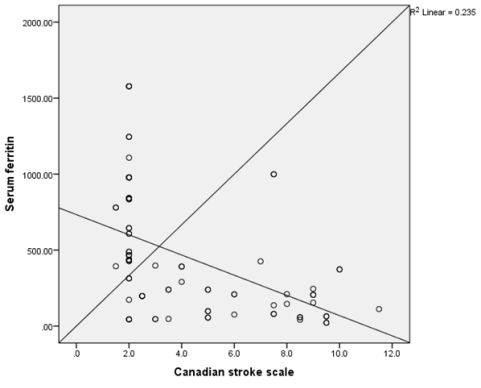

Chart 3a: Scatter diagram of correlation between serum ferritin at admission and Canadian stroke scale

We found a moderate significant negative correlation between the Canadian stroke scale and serum ferritin levels [r=-0.485; p value <0.001].

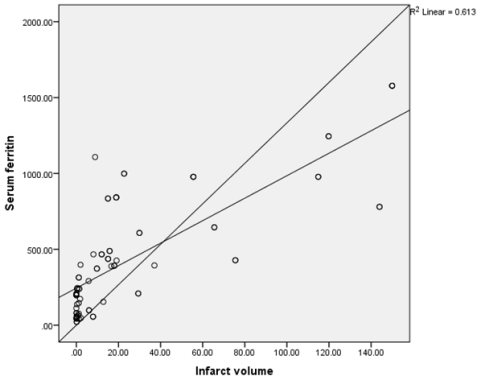

Chart 3b: Scatter diagram of correlation between serum ferritin at admission and infarct volume

We found a good significant positive correlation between the infarct volume and serum ferritin levels [r=0.783; p value <0.001].

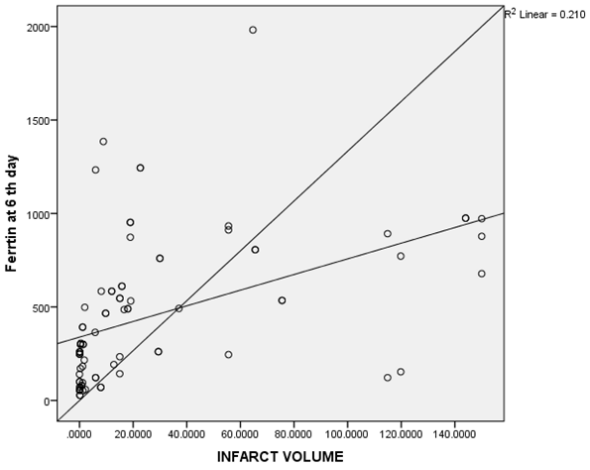

Chart 4a: Scatter diagram of correlation between serum ferritin at 6th day at admission and infarct volume

We found a good significant positive correlation between the infarct volume and serum ferritin levels at 6th day [r=0.818; p value <0.001].

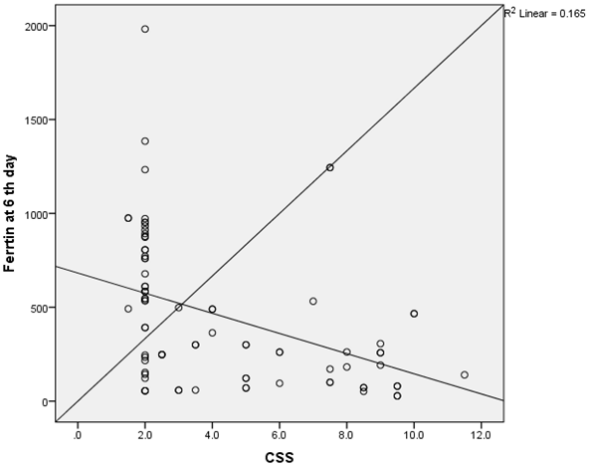

Chart 4b: Scatter diagram of correlation between serum ferritin at 6th day at admission and Canadian stroke scale

We found a moderate significant negative correlation between the Canadian stroke scale and serum ferritin levels [r=-0.512; p value <0.001].

Table 5a: Distribution based on of serum ferritin based on the outcome (n=84)

Outcome of patients	**Number**	**At admission**	
		Mean	**SD**
Good	**58**	291.41	374.52
Deteriorated	**9**	889.66	248.90
Death	**17**	908.47	396.23
P value		<0.001	

The average ferritin levels among the patients with good outcome was 291.41microgram/L, for those who deteriorated were 889.66 microgram/L and those who died during the first week of admission was 908.47 microgram/L. This difference was statistically significant (<0.001).

Table 5b: Distribution based on of serum ferritin based on the outcome (n=67)

Outcome of patients	**Number**	**At admission**	
		Mean	**SD**
Good	60	310.61	315.75
Death	7	831.90	387.46
P value		<0.001	

At one week follow up, the ferritin levels were studied on the patients who had died and had good outcome. The ferritin levels among those who died [831.90microgram/L] were significantly higher when compared to those who had good outcome [310.61microgram/L].

DISCUSSION

Hyperferritinemia has been implicated in various thrombotic conditions and is a novel marker for predicting the prognosis of stroke. [10,11] It has been postulated as an etiological factor for clinical deterioration in the patients with stroke. With this background, we conducted a study to find the ferritin levels among the patients with acute ischemic stroke in our setup.

The present study reported a significant positive correlation between the infarct volume as calculated by the CT scan of the brain of the patients with the ferritin levels at admission and 6th day of follow up ferritin levels. This signifies that as the volume of infarct increased the ferritin levels significantly increased in the patients. Rajendran SR et al [13] studied the ferritin levels among their patients and found out that there was positive correlation between the infarct size and ferritin levels in their study.

We also found the CSS score to be having negative correlation with ferritin levels in the patients. As the score increased the prognosis of the patients was good and the ferritin levels were less and vice versa. Rajendran SR et al [13] reported that ferritin levels had significantly higher correlations with long-term prognostic scores of 7th day mRS (r = 0.802) and 30th day mRS (r= 0.916). Based on the outcome of the patients immediately post intervention, the ferritin levels were significantly higher among those who died and deteriorated compared to those who had good outcome. ($p<0.001$) 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 ± 110.96ng/mL, respectively in a study conducted by Garg R et al. [14] Further, they reported that 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 6 day were 193.29 ± 101.88 and 343.95 ± 52.34 ng/mL in subjects who did not deteriorate and those who deteriorated, respectively. Among the 61 cases studied by Sultana J et al [15] reported that cases having high serum ferritin levels, 26(40%) were in moderate category and 35(60%) were in severe category of NIHSS. On the other hand, among the remaining 39 cases who had normal serum ferritin, all the 39 cases come under moderate group and none in severe group. Out of 61 cases with high serum ferritin, 12 cases were in good outcome category and 49 cases in poor outcome category of MRS scores. In another study conducted by Mehrpour M et al [16] revealed that the incidence of hemorrhagic transformation was two persons (13.3%) in the group with the serum ferritin level of lower than 164.1ng/ml, and eight persons (53.3%) in the other group. This difference was statistically significant between the two groups. Similar inferences were reported by Mandal SK et al, Thanikachalam R et al, Giri R et al and Gopinathan R et al.

CONCLUSIONS

Canadian stroke scale and infarct volume has a significant correlation with serum ferritin levels. With increase in the CSS the ferritin levels were low and with increase in the infarct volume the serum ferritin levels were high. Those patients who died and who deteriorated had significantly higher ferritin levels than those who had good outcome.

REFERENCES

1. Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol. 2003 Jan;2(1):43-53. doi: 10.1016/s1474-442 2(03)00 266-7. PMID: 12849300.
2. Béjot Y, Daubail B, Giroud M. Epidemiology of stroke and transient ischemic attacks: Current knowledge and perspectives. Rev Neurol (Paris). 2016 Jan;172(1):59-68. doi: 10.1016/j.neurol.2015.07.013. Epub 2015 Dec 21. PMID: 2 6 7 1 8 592.
3. Pandian JD, Sudhan P. Stroke epidemiology and stroke care services in India. J Stroke. 2013 Sep;15(3):128-34. doi: 10.5853/jos.2013.15.3.128. Epub 2013 Sep 27. PMID: 24396806; PMCID: PMC3859004.
4. Ovbiagele B, Nguyen-Huynh MN. Stroke epidemiology: advancing our understanding of disease mechanism and therapy. Neurotherapeutics. 2011 Jul;8(3):319-29. doi: 10.1007/s13311-011-0053-1. PMID: 21691873; PMCID: PMC3250269.
5. Donkor ES. Stroke in the 21st Century: A Snapshot of the Burden, Epidemiology, and Quality of Life. Stroke Res Treat. 2018 Nov 27;2018:3238165. doi: 10.1155/2018/3238165. PMID: 3059 874 1 ; P M CID: PMC6288566.
6. Kamalakannan S, Gudlavalleti ASV, Gudlavalleti VSM, Goenka S, Kuper H. Incidence & prevalence of stroke in India: A systematic review. Indian J Med Res. 2017 Aug;146(2):175-185. doi: 10.4103/ijmr.IJMR_516_15. PMID: 29265018; PMCID: PMC5761027.
7. Rost NS, Bottle A, Lee JM, Randall M, Middleton S, Shaw L, Thijs V, Rinkel GJ, Hemmen TM; Global Comparators Stroke GOAL collaborators. Stroke Severity Is a Crucial Predictor of Outcome: An International Prospective Validation Study. J Am Heart Assoc. 2016 Jan 21;5(1):e002433. doi: 10.1161 /JAHA.1 15.002433. PMID: 26796252; PMCID: PMC4859362.
8. Tadi P, Lui F. Acute Stroke. [Updated 2022 Apr 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
9. Chugh C. Acute Ischemic Stroke: Management Approach. Indian J Crit Care Med. 2019 Jun;23(Suppl 2):S140-S146. doi: 10.5005/jp-journals-10071-23192. PMID: 31485123; PMCID: PMC6707502.
10. Hui C, Tadi P, Patti L. Ischemic Stroke. [Updated 2022 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
11. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: Past, present and future. Biochim Biophys Acta. 2010 Aug;1800(8):760-9. doi: 10.1016/j.bbagen.2010.03.011. Epub 2010 Mar 19. PMID: 20304033; PMCID: PMC2893236.
12. Sandnes M, Ulvik RJ, Vorland M, Reikvam H. Hyperferritinemia-A Clinical Overview. J Clin Med. 2021 May 7;10(9):2008. doi: 10.3390/jcm10092008. PMID: 34067164; PMCID: P M C 8125175.
13. Rajendran SR, Periyasamy S, Manjuladevi MT, George N. Evaluation of Serum Ferritin as a Prognostic Marker in Acute Hemorrhagic Stroke. J Neurosci Rural Pract. 2020 Jan;11(1):72-77. doi: 10.1055/s-0039-1700597. Epub 2019 Dec 11. PMID: 32140006; PMCID: PMC7055639.
14. Garg R, Aravind S, Kaur S, Singh Chawla SP, Aggarwal S, Goyal G. Role of serum ferritin as a prognostic marker in acute ischemic stroke: A preliminary observation. Ann Afr Med. 2020 Apr-Jun;19(2):95-102. doi: 10.4103/aam.aam_35_19. PMID: 32499465; PMCID: PMC7453951.
15. Sultana J, Sharma DJ. Evaluation of Serum Ferritin as a Prognostic Marker in Acute Ischemic Stroke Patients-A Prospective Cohort Study. J Assoc Physicians India. 2022 Apr;70(4):11-12. PMID: 35443413.
16. Mehrpour M, Mehrpour M. Is the serum ferritin level a considerable predictor for hemorrhagic transformation of ischemic stroke? Med J Islam Repub Iran 2016 (4 May). Vol. 30:363.
17. Mandal SK, Majumder M, Hossain MS. Serum ferritin and plasma fibrinogen levels in acute ischemic stroke. Bangladesh J Med Biochem 2017; 10(1): 16-20.
18. Thanikachalam R, Elangovan S, Srivijayan A. Evaluation of serum ferritin as a prognostic marker in acute ischemic stroke: aprospective observational study. Int J Res Med Sci 2020;8:4282-7.
19. Giri R, Ahamed F, Agarwal S, Kumar L. Assessment of serum ferritin and thyroid hormones level in acute ischemic stroke and their association with hemorrhagic conversion. Int J Adv Med 2021;8:672-8.
20. Gopinathan R, Gopalakrishna D, Beegum S, et al. Serum Ferritin levels in Acute Ischemic Stroke patients - A cross sectional study from Thiruvananthapuram, Kerala. J Evid Based Med Healthc 2021;8(20):1516- 1520. DOI: 10.18410/jebmh/2021/287.