International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Serum Ferritin Levels as a Prognostic Indicator in Acute Ischemic Stroke: A Comprehensive Clinical Study

Dr. Nasiba Khan[1], Dr. Mukesh Kumar Samota[2], Dharam Singh[3], Dr. Sudhir Bhandari[4]

[1]Post Graduate Student, Department of Medicine, SMS Medical College, Jaipur (Raj.), India

[2]Senior Resident, Department of Medicine, SMS Medical College, Jaipur (Raj.), India (Corresponding Author)

[3]Post Graduate Student, Department of Medicine, SMS Medical College, Jaipur (Raj.), India

[4]Vice Chancellor, Rajasthan University of Health Sciences, Jaipur (Raj.), India

Abstract: ***This comprehensive clinical study investigates the potential of serum ferritin levels as a prognostic indicator in acute ischemic stroke. With stroke emerging as a significant global health concern, reliable prognostic markers are crucial for patient management. The study assesses the correlation between serum ferritin levels and various clinical parameters, including stroke severity, consciousness status, and disability outcomes. Results reveal a significant association between elevated serum ferritin levels and severe stroke, as well as unfavourable outcomes. The findings suggest that serum ferritin could serve as a promising prognostic index in acute ischemic stroke, aiding in patient risk stratification and clinical decision - making.***

Keywords: Serum ferritin, acute ischemic stroke, prognostic indicator, stroke severity, consciousness status, disability outcomes

1. Introduction

According to World Health Organization (WHO)[1], stroke is defined as ‘’a clinical syndrome consisting of 'rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, with duration lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin. ’’After heart diseases and cancer, stroke is now emerging as the most common preventable life - threatening neurological problem, worldwide. As per Indian Council Medical Research (ICMR) reports, Stroke and Diabetes together brings the estimated national economic loss of approximately 46 billion dollars in India between 2006 - 2015[2]. In clinical practice, cerebrovascular accident (CVAs) / Stroke (excluding subarachnoid haemorrhages) are grouped into two main groups: Ischemic and haemorrhagic. Most CVA cases (up to 80%) are ischemic, with haemorrhages being responsible for the remaining 20%. [3] An ischemic stroke occurs as a result of the occlusion of a cerebral vessel that blocks 80% or more of the vessel. On the other hand, a hemorrhagic stroke occurs following a vessel rupture. Acute Ischemic stroke (AIS) has a heterogeneous aetiology caused by modifiable (Hypertension, diabetes mellitus, dyslipidemia, smoking etc) and non - modifiable risk factors (a positive family history of strokes, age, male gender, and black or Hispanic races) [4].

Some theories suggest that coagulation cascade activation and vascular inflammation can play a role in this. According to these theories, the vascular abnormalities along with coagulopathies will work together and with other predisposing factors to enhance the initiation of stroke development (either haemorrhagic or ischemic) [6]. The presence of leucocytosis, and elevates inflammatory markers (which is a poor prognostic factor) in the setting of acute stroke supports this theory.

The brain is generally considered vulnerable to hypoxic injury when compared to other body organs. This is mainly because the presence of glutamate (a neurotransmitter) in high concentrations, and the relatively high metabolic activity. Thus, hypoxic injury can occur as a result of cerebral vascular occlusion from emboli, or an in - situ thrombus[7].

Although there has been a tremendous progress made in the field of stroke, still the exact prognostication of stroke is not possible. Several indicators such as the size of, infarct, the vessel involved, the presenting Glasgow coma scale (GCS), the amount of oedema surrounding the infarct, the intracranial pressure and serum acute Phase Reactants have been used as an index to access the severity and to prognosticate acute ischemic stroke. In 1941, Avery and Theodore J Abernethy[8] coined the term Acute Phase Reactants and also denoted that acutely ill patient’s serum contains CRP. Acute phase reactants are the markers of inflammation and they are elevated in inflammation, infection and they tend to appear or rise in the blood whenever the immune system comes in contact with proteins. This elevation of acute phase reactants indicates inflammatory burden and it gets elevated in vascular events. Some of the acute phase reactants are: α1 globulin & α2 globulin, α1antitrypsin, Fibrinigen, Fibrinonectin, Serum Amyloid A protein, Pre - Albumin, Ferritin, Transferrin. Iron can play a role in the initiation and propagation of lipid peroxidation, resulting in altered membrane fluidity, inactivation of membrane - bound enzyme complexes, and eventually disruption of cell membrane and cell death. Therefore, lipid peroxidation is considered to be related to the concentration of tissue iron[9, 10]. Ferritin (Ft) is a positive

acute phase cellular storage protein for iron. Ferritin is essentially located within cells and constitutes the main intracellular iron storage protein[11]. The principal factor that controls cellular Ferritin content is the intracellular level of free iron[12]. Thus, Ft provides a means of storing the metal within cells in available safe manner. Ferritin is also present at a very low concentration in blood but the role of circulating Ft is still unknown. However, serum Ft has been used widely in clinical medicine chiefly as an indicator of body iron stores.[13]

It is an acute - phase reactant involved in cellular defense against oxidative stress and inflammation along with transferrin. Serum Ft concentrations are normally in the range of 15–300 ng/mL and are lower in children than adults. Mean values are lower in women before the menopause in comparison to men.[14] Serum ferritin concentration decreases with blood donation and increases with alcohol intake. Previous studies have suggested that iron overload contributes to the development of vascular disease by promoting thrombosis after arterial injury. High serum ferritin at admission was reported to predict a poor prognosis in acute stroke patients (within 24–48 h after stroke onset), implicating that increase in the body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia.[15]

In a study by Garg R et al [16] showed that in patients with AIS, the admission - day serum ferritin was significantly higher in patients who deteriorated after admission, as compared to patients who did not deteriorate

Despite lot of researches in the field of stroke, accurate prognostication of an acute attack is difficult. Some of the upcoming prognostic indicators are under study e. g.; hyperglycaemia in stroke, infection in stroke, TNFa or interleukins etc. One of the prognostic indicators which have gained great clinical interest in recent times is the level of serum ferritin. Initially considered only as a stress response to stroke, serum ferritin now is under research as a prognostic indicator[17].

High levels of serum ferritin correlate well with the early neurological deterioration of stroke patients. Therefore testing of serum ferritin can be helpful in identifying high risk patients[18].

2. Materials and Methods

In this cross - sectional study, a total of 75 patients, who attended our outpatient clinic as well as those admitted in the department of General Medicine at SMS medical college and attached group of hospitals were enrolled into the study. All participants submitted informed consent before enrolment. It is a hospital based Observational Comparative study conducted in May 2020 onwards for one year. Sample Size was calculated 25 in each group (mild/moderate/severe) as per NIHSS scoring. As per previous study shows the correlation of serum ferritin r=1 and MRS 0.560 for 80% power, 0.05 alpha error. All patients with new onset focal neurological deficit following ischemic stroke, presented within 48 hours of onset of stroke were taken into study. Patients with age more than 80 years, malignancy, prior history of transient ischemic attacks or reversible ischemic neurological deficit or cerebrovascular accidents, with features of haemorrhage such, History of recent surgery and trauma, and CNS tumours were excluded. The study was approved by the Ethics Committee of our institution.
Blood samples were taken for serum ferritin level. Baseline clinical characteristics including demographic, clinical and biochemical data were collected. For each enrolled subject, detailed history as well as personal and family medical histories were obtained

Statistical Analysis
Data were analysed and statistically evaluated using Statistical Package for Social sciences (SPSS) - PC - 20 software (version 20, SPSS, Inc, Chicago, IL, USA). Data were presented as mean and standard deviation (SD) for normally distributed continuous variables and as frequencies for categorical variables. Comparisons were made for means of two sample using Student‘s t test for continuous variables and by x2 analysis for categorical variables.
All statistical analyses were performed taking level of significance at p - value<0.05.

3. Observations & Results

The total of 75 patients (25 in each group (mild/moderate/severe) were analysed.

Table 1: Distribution of Study Population according to age group

Age Groups	Group Mild		Group Moderate		Group Severe	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
<20	2	8	2	8	5	20
20 - 30	2	8	2	8	0	0
31 - 40	3	12	2	8	3	12.0
41 - 50	5	20	5	20	4	16
51 - 60	3	12	4	16	3	12
>60	10	40	10	40	10	40
Total	25	100.0	25	100.0	25	100.0
Mean Age	51.9600	18.79379	**51.4000**	**17.89786**	**49.2400**	**20.12726**
Chi Square	2.121					
P - Value	0.079*					

*p - value>0.05 is insignificant

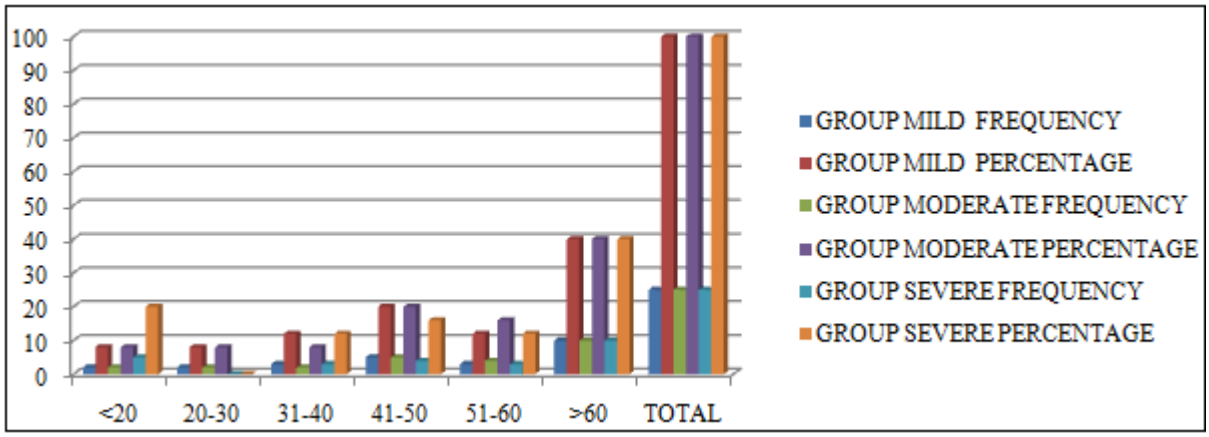


Table No.1 shows the distribution of study population according to age groups. Maximum patients 40% each were found in all the three groups, with mean age being 51.96±18.79yrs, 51.4±17.89yrs and 49.24±20.13yrs in mild, moderate and severe groups respectively. Chi square statistical analysis revealed an insignificant (p - value>0.05) statistical relation between all the three study groups in relation to age groups.

Table 2: Distribution of study population according to gender

Gender	Group mild		Group moderate		Group severe	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Female	7	28.0	8	32.0	8	32.0
Male	18	72.0	17	68.0	17	68.0
Total	25	100.0	25	100.0	25	100.0
Chi Square	1.198					
P - Value	1.09*					

***p - value>0.05 is insignificant**

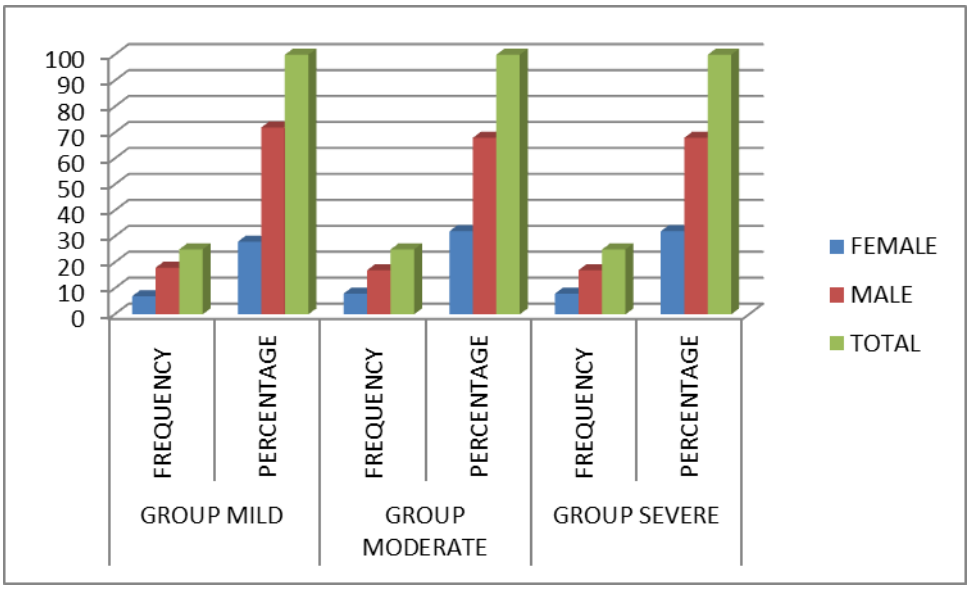
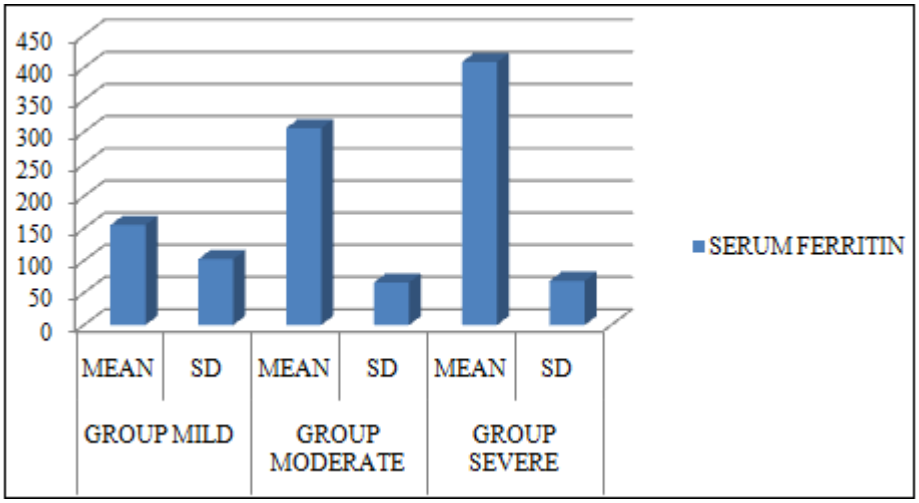


Table No. 2 shows the distribution of study population according to gender. Maximum patients 72%, 68%, and 68% were males in mild, moderate and severe groups respectively, showing a male predominance. Chi square statistical analysis revealed an insignificant (p - value>0.05) statistical relation between all the three study groups in relation to gender.

Table 3: Study Population according to Serum Ferritin Level

Parameters	Group Mild		Group Moderate		Group Severe		Anova Statistical Analysis	
	Mean	SD	Mean	SD	Mean	SD	F - statistic	p - value
Serum Ferritin	155.2000	102.17999	305.8400	66.08623	408.4800	68.63740	32.541	0.022*

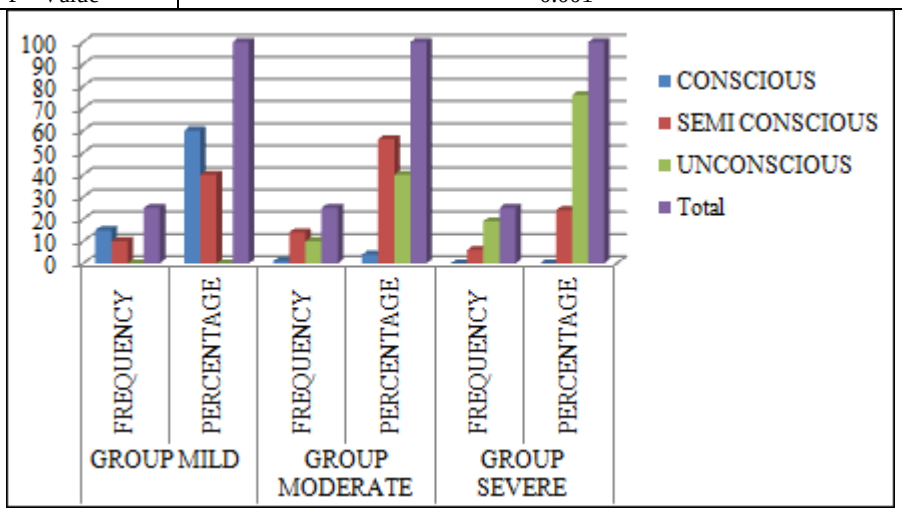


***p - value<0.05 is significant**

Table No. 3 shows study population according to serum Ferritin levels. Mean serum ferritin levels were maximum in severe group, being 408.48±68.63. ANOVA statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to serum ferritin levels

Table 4: Distribution of Study Subjects according to Loss of Consciousness

Loss of Consciousness	Group Mild		Group Moderate		Group Severe	
	Frequency	Percentage	Frequency	Frequency	Percentage	Frequency
Conscious	15	60.0	1	4.0	0	0
Semi Conscious	10	40.0	14	56.0	6	24.0
Unconscious	0	0	10	40.0	19	76.0
Total	25	100.0	25	100.0	25	100.0
Chi Square	2.207					
P - Value	0.001*					



***p - value<0.05 is significant**

Table No. 4 shows distribution of study population according to loss of consciousness. In mild group, maximum 60% patients were conscious, in moderate group, maximum 56% were semi - conscious and in severe group maximum 76% were unconscious. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to loss of consciousness

Table 5: Distribution of Study Subjects according to MRS Score

MRS Score	Group Mild		Group Moderate		Group Severe	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
<3	**25**	**100.0**	**0**	**0**	**0**	**0**
≥3	**0**	**0**	**25**	**100.0**	**25**	**100.0**
Total	**25**	**100.0**	**25**	**100.0**	**25**	**100.0**
Chi Square	1.562					
P - Value	0.011*					

***p - value<0.05 is significant**

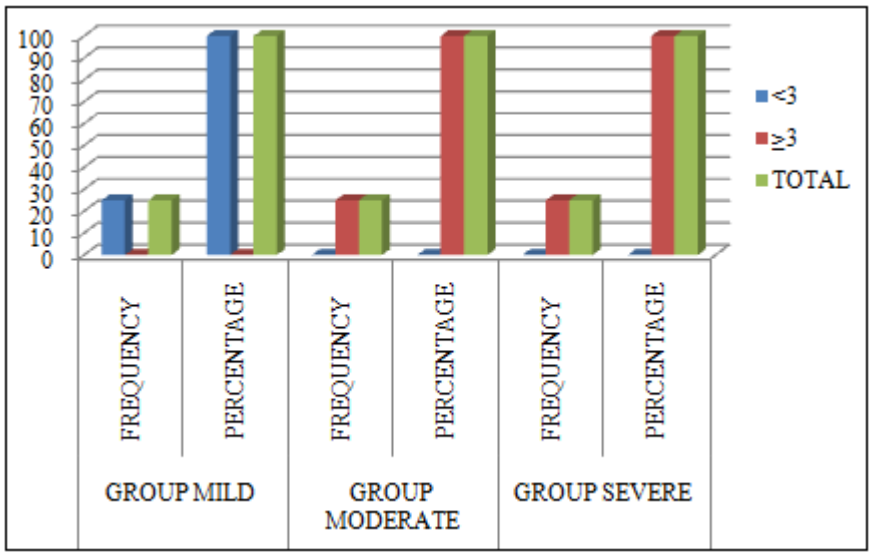


Table No.5 shows distribution of study population according to MRS score. In mild group, all 100% patients were with <3 MRS score, in moderate and severe group, maximum 100% were with >3 score. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to MRS score.

Table 6: Distribution of Study Subjects according to NIHSS Score

NIHSS Score	Group Mild		Group Moderate		Group Severe	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Mild (1 - 4)	25	100	0	0	0	0
Moderate (5 - 15)	0	0	25	100	0	0
Severe (>15)	0	0	0	0	25	100
Total	25	100	25	100	25	100
Chi Square	2.933					
P - Value	0.035*					

*p - value<0.05 is significant

Table No. 6 show distribution of study population according to NIHSS score. In mild group, all 100% patients were with mild (1 - 4) score, in moderate maximum 100% were with moderate (5 - 15) score and severe group 100% were with severe (>15) score. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to NIHSS score

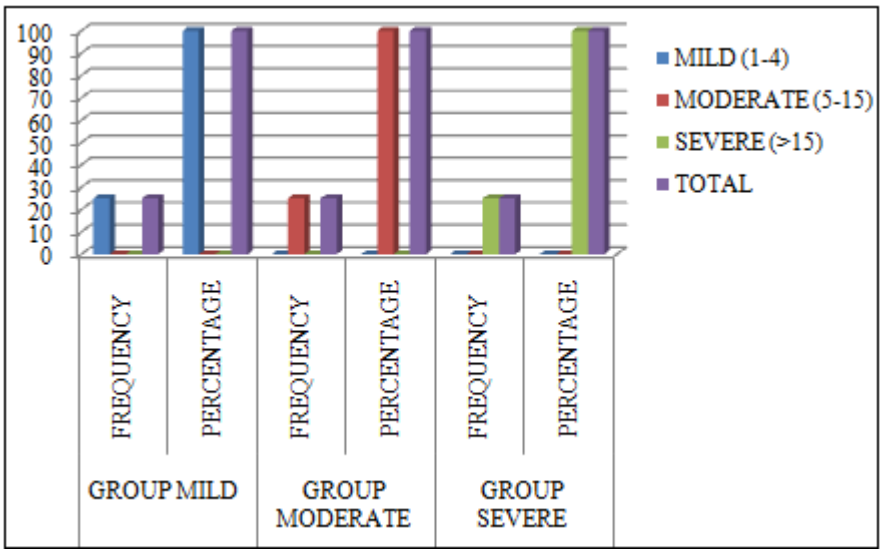


Table 7: Correlation of Loss of Consciousness and Ferritin

Loss of Consciousness	Mean Ferritin	
	Mean	SD
Conscious	87.5625	60.76728
Semi Conscious	277.4667	35.92687
Unconscious	414.2414	53.14311
F - statistics	12.009	
p - value	0.023*	

*p - value<0.05 is significant

Table No. 7 show correlation of loss of consciousness and Ferritin levels. The mean Ferritin levels were 87.5625± 60.76728, 277.4667±35.92687 and 414.2414±53.14311 in conscious, semiconscious and unconscious patients. ANOVA statistical analysis revealed a significant (p - value<0.05) statistical relation between loss of consciousness and Ferritin levels.

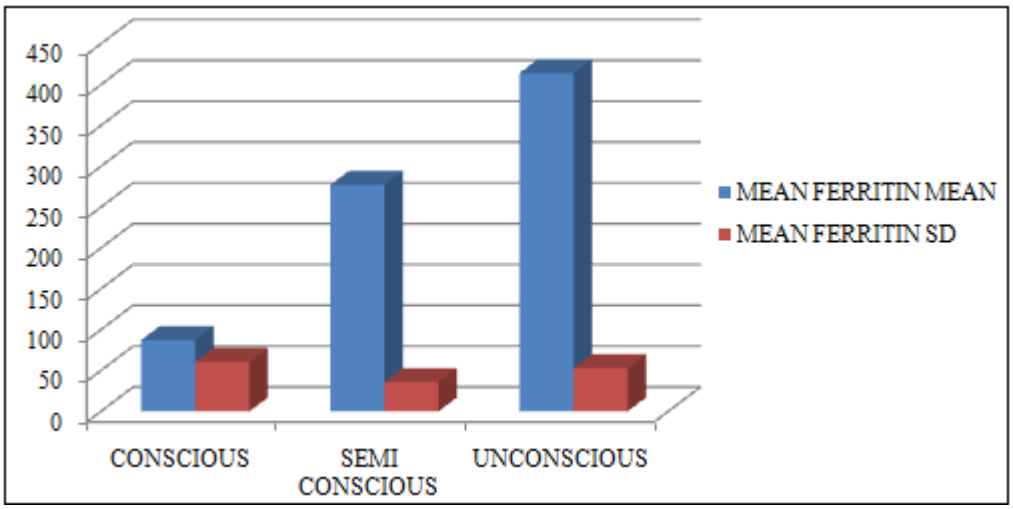


Table 8: Correlation of MRS and Ferritin

MRS	Mean Ferritin	
	Mean	SD
<3	155.2000	102.17999
≥3	357.1600	84.46358
t - test	11.709	
p - value	0.003*	

***p - value<0.05 is significant**

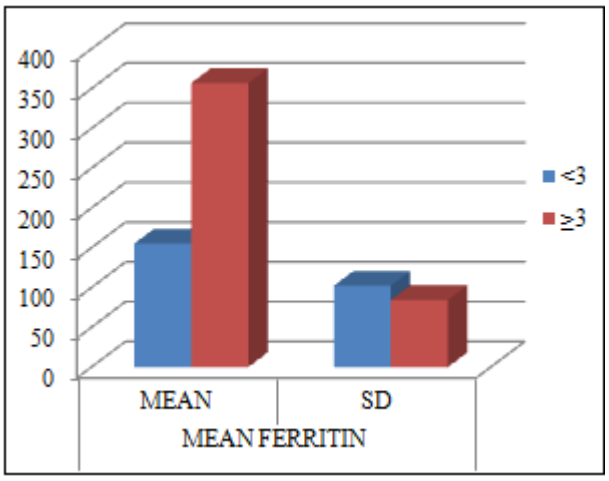


Table No. 8 shows correlation of MRS and Ferritin levels. The mean Ferritin levels were 155.2000±102.17999 and 357.1600±84.46 in <3 and >3 respectively. One sample t - test statistical analysis revealed a significant (p - value<0.05) statistical relation between MRS and Ferritin levels.

4. Discussion

The effects of a stroke depend on the site and severity of brain injury. Severity and follow - up of neurological deficit in stroke can be done with scales such as Canadian Stroke Scale (CSS), National Institute of Health Stroke Scale (NIHSS), and Glasgow Coma Scale (GCS) [19].

The risk factors namely blood pressure (BP), smoking, diabetes, dyslipidaemia, alcohol predict the happening of stroke, but still they are not completely reliable, therefore there is a continuous debate and search for prediction of occurrence of stroke and reliability of prognostic markers In stroke have gained interest in recent years[2]. It has been suggested that ferritin influences the prognosis of Ischemic stroke and also acts as a risk factor for Ischemia. In present study, in mild group, all 100% patients were with mild (1 - 4) score, in moderate maximum 100% were with moderate (5 - 15) score and severe group 100% were with severe (>15) score mic episodes by enhancing atherogenesis[16].

In present study, we found that maximum 18.67% patients were 41 - 50yrs of age, with mean age being 50.867±18.74yrs. Maximum patients 40% each were found in all the three groups, with mean age being 51.96±18.79yrs, 51.4±17.89yrs and 49.24±20.13yrs in mild, moderate and severe groups respectively. Maximum 69.3% patients were males, and 30.7% were females. Maximum patients 72%, 68%, and 68% were males in mild, moderate and severe groups respectively, showing a male predominance. Similar to our study, Mahur H et al[20]. Showed male predominance with mean age of the patients being 63.40 years.

Serum Ft has been used widely in clinical medicine chiefly as an indicator of body iron stores. Iron also plays a role in ischemic stroke by activating platelets via a protein kinase - C mechanism. High serum ferritin on admission of acute stroke patients (within 24 to 48 hours after stroke onset) had poor prognosis implicating that increase in body iron stores before stroke onset can aggravate the brain ischemia

cytotoxicity. It also acts as a risk factor for ischemic episodes by enhancing atherogenesis[21].

There are only limited studies in India to assess the serum ferritin levels on stroke prognosis. Hence, the present study investigated the prognostic significance of serum ferritin levels with the severity of ischemic stroke.

In present study, we found that mean serum ferritin levels increased with intensity of stroke. It was maximum in severe group, being 408.48±68.63. The mean Ferritin levels were 225.4348±97.39135 and 318.3269±135.30441 in female and male respectively. It has been observed that a significant (p - value<0.05) relation was observed between hypertension and Ferritin levels, whereas an insignificant statistical relation (p - value>0.05) was observed between age and Ferritin levels.

Similar results were observed in study by Thanikachalam R et al[21]. The mean serum ferritin levels at admission in patients with severe stroke, moderate stroke and mild and less stroke were 337.41±58.76, 285.56±49.37, and 197.91±111.01 ng/mL, respectively. The mean serum ferritin levels at admission were 178.76±114.70 ng/mL and 341.91±62.292 ng/mL in subjects who did not deteriorate and those who deteriorated, respectively.

Our study revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to serum ferritin levels. Thanikachalam R et al[21]. Revealed that serum ferritin has a significant positive correlation with the severity of acute ischemic stroke severity on admission (p<0.001). Thus, serum ferritin can be used as a prognostic marker in acute ischemic stroke.

Thanikachalam R et al[21]. revealed that mean serum ferritin in the group with severe stroke on admission was significantly higher than in the group with mild and moderate stroke on admission and on seventh day (p=0.001). Whereas in a study done by Garg et al[21] a statistically significantly negative correlation was observed between serum ferritin levels and NIHSS scores both at admitted and on seventh day of admission. Egovindrajulu et al[22] in their study observed positive correlation between serum ferritin and NIHSS scores (p=0.000). In another study by Koulet al[23]revealed that there was a significant correlation between the serum ferritin values and NIHSS 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.

The proposed mechanism behind this is that higher serum ferritin levels indicate higher iron stores in the brain. When brain ischemia occurs during cerebrovascular accident, injured brain cells release more iron. When more iron is released into the local environment of the injured tissue, there is more oxidative stress through generation of free hydroxyl radicals. This results in tissue injury aggravation during ischemia. Another mechanism is that the injured brain cells during ischemia, release more glutamate; the released glutamate further causes tissue injury[24 - 25].

Level of consciousness and grades of stroke were evaluated. We observed that in mild group, maximum 60% patients were conscious, in moderate group, maximum 56% were semi - conscious and in severe group maximum 76% were unconscious. The mean Ferritin levels were 87.5625±60.76728, 277.4667±35.92687 and 414.2414±53.14311 in conscious, semiconscious and unconscious patients. Thus serum Ferritin levels increased with grade of ischemic stroke and level of unconsciousness.

The modified Rankin Scale (mRS) score is the standard disability outcome measure used in both stroke patient care and clinical trials and has been found to be especially valuable when evaluated at 90 days after stroke onset. In present study we found that the mean age was 51.96±18.79 and 50.32±18.88yrs in MRS score <3 and >3 respectively. The mean Ferritin levels were 155.2000±102.17999 and 357.1600±84.46 in <3 and >3 respectively. In mild group, all 100% patients were with <3 MRS score, in moderate and severe group, maximum 100% were with >3 score.

In study by Egovindrajuluet al[22] out of 35 cases with high serum ferritin, 5 cases were in good outcome category and 30 cases in poor outcome category of MRS scores. In contrast among 25 cases with normal serum ferritin, 17 cases were in good outcome and 8 cases were in poor outcome category in MRS Score. Pearson's r correlation analysis reveals positive correlation between serum ferritin and MRS. Pearson's r value is 0.560 and is positive variable. Increase in serum ferritin will favour the poor outcome of patients in terms of death and severe disability.

The present study reveals a significant correlation of serum ferritin with the severity of acute ischemic stroke, depicting elevated admission serum ferritin levels with poor IS outcomes. Patients with high serum ferritin levels at admission tend to clinically deteriorate compared with those of lower serum ferritin levels. Hence, this study suggests that serum ferritin can be used as a possible prognostic index for acute ischemic stroke.

The patients with stroke with increased serum ferritin concentrations have a higher risk of poor clinical outcome, hemorrhagic transformation, and brain edema than patients with low ferritin values. These findings suggest that iron overload may counterbalance the benefits of thrombolytic therapy observed in patients with low ferritin levels. If these results are confirmed in future studies, iron chelators or free radical trapping agents should be used to reduce the neurotoxic effects of iron in patients with acute ischemic stroke and those who are treated with thrombolytic therapy.

5. Conclusion

Maximum patients 72%, 68%, and 68% were males in mild, moderate and severe groups respectively, showing a male predominance. Chi square statistical analysis revealed an insignificant (p - value>0.05) statistical relation between all the three study groups in relation t5. Mean serum ferritin levels were maximum in severe group, being 408.48±68.63. ANOVA statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to serum ferritin levels.

1) In mild group, maximum 60% patients were conscious, in moderate group, maximum 56% were semi - conscious and in severe group maximum 76% were unconscious. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to loss of consciousness.
2) In mild group, all 100% patients were with <3 MRS score, in moderate and severe group, maximum 100% were with >3 score. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to MRS score.
3) In mild group, all 100% patients were with mild (1 - 4) score, in moderate maximum 100% were with moderate (5 - 15) score and severe group 100% were with severe (>15) score. Chi square statistical analysis revealed a significant (p - value<0.05) statistical relation between all the three study groups in relation to NIHSS score.
4) The mean Ferritin levels were 87.5625±60.76728, 277.4667±35.92687 and 414.2414±53.14311 in conscious, semiconscious and unconscious patients. ANOVA statistical analysis revealed a significant (p - value<0.05) statistical relation between loss of consciousness and Ferritin levels.
5) The mean Ferritin levels were 225.4348±97.39135 and 318.3269±135.30441in female and male respectively. One sample t - test statistical analysis revealed a significant (p - value<0.05) statistical relation between gender and Ferritin levels.
6) The mean Ferritin levels were 155.2000±102.17999 and 357.1600±84.46 in <3 and >3 respectively. One sample t - test statistical analysis revealed a significant (p - value<0.05) statistical relation between MRS and Ferritin levels.
7) It has been observed that a significant (p - value<0.05) relation was observed between hypertension and Ferritin levels, whereas an insignificant statistical relation (p - value>0.05) was observed between age and Ferritin levels.
8) The mean age was 51.96±18.79 and 50.32±18.88yrs in MRS score <3 and >3 respectively. One sample t - test statistical analysis revealed an insignificant relation statistically (p - value>0.05) between MRS and mean age or gender

References

[1] The world health organization MONICA project (monitoring trends and determinants in cardiovascular disease): A major international collaboration. WHO MONICA project principal investigators. J ClinEpidemiol 1988; 41: 105 - 14.
[2] Indian Council Of Medical Research, Stroke. In: Assessment of the burden of non communicable diseases, New Delhi: Indian Council of Medical research (ICMR); 2012. Page no.6 - 7.
[3] Khaku AS, Tadi P. Cerebrovascular Disease. [Updated 2021 Sep 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan - . Available from: https: //www.ncbi. nlm. nih. gov/books/NBK430927/
[4] Boehme AK, Esenwa C, Elkind MS. Stroke Risk Factors, Genetics, and Prevention. Circ Res.2017; 120 (3): 472 - 495.
[5] Elkind MS. Why now? Moving from stroke risk factors to stroke triggers. CurrOpin Neurol.2007; 20: 51–57.
[6] Alrabghi L, Alnemari R, Aloteebi R, Alshammari H, Ayyad M, Al Ibrahim M, et al. Stroke types and management. Int J Community Med Public Health 2018; 5 (9): 1 - 5.
[7] Abernethy TJ, Avery OT. The occurrence during Acute Infections of a protein not normally present in the blood: I. Distribution of the reactive protein in patients' sera and the effect of Calcium on the flocculation reaction with C polysaccharide of Pneumococcus. J Exp Med.1941; 73 (2): 173 - 82.
[8] Bishop GM, Robinson SR. Quantitative analysis of cell death and ferritin expression in response to cortical iron: implications for hypoxia - ischemia and stroke. Brain Res 2001; 907: 175–187.
[9] Lesnefsky E. Tissue iron overload and mechanisms of iron catalyzed oxidative injury. In: Armstrong D, editor. Free radicals in diagnostic medicine. New York, NY: Plneum Press; 1994.129–146.
[10] Eisenstein RS. Iron regulatory proteins and the molecular control of mammalian iron metabolism. Annu Rev Nutr.2000; 20: 627 - 62.
[11] Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: Past, present and future. BiochimBiophysActa.2010; 1800 (8): 760 - 769.
[12] Worwood M. In: Iron in Biochemistry and Medicine, II. A. a. W. Jacobs M, editor. London: Academic Press; 1980. pp.204–244.
[13] Jacobs A, Worwood M. Ferritin in serum. Clinical and biochemical implications. N Engl J Med.1975; 292: 951–956
[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; 19 (2): 95 - 102.
[15] Narayan M et al. Study of Association between Serum Ferritin And Prognosis Of Patients In Acute Ischemic And Haemorrhagic Stroke. Journal of Dental and Medical Sciences.2018; 17 (4): 46 - 56.
[16] Egovindarajulu K et al. A Study on Prognostic Significance of Serum Ferritin in Patients with Acute Ischemic Stroke. Journal of Dental and Medical Sciences.2016; 15 (10): 31 - 39.
[17] Thanikachalam R et al. Evaluation of serum ferritin as a prognostic marker in acute ischemic stroke: a prospective observational study. Int J Res Med Sci.2020 Dec; 8 (12): 4282 - 4287
[18] Hornig CR, Dorndorf W, Agnoli AL. Hemorrhagic cerebral infarction - - a prospective study. Stroke.1986 Mar - Apr; 17 (2): 179 - 85.
[19] Mahur H, Ralot TK, Singh DP, Ken P, Patel J. To establish the role of serum ferritin as a prognostic marker in patients of stroke. Indian J Neurosciences 2018; 4 (2): 64 - 68.
[20] Koul RK, Yaseen Y, Amreen S, Shah PA. Role of serum ferritin in determining the severity and

prognosis of stroke: A hospital based study. Int J Sci Study.2017; 6: 142 - 5.

[21] Herbert V, Jayatilleke E, Shaw S, Rosman AS, Giardina P, Grady RW, et al. Serum ferritin iron, a new test, measures human body iron stores unconfounded by inflammation. Stem Cells.1997; 15 (4): 291 - 6.

[22] Roudbary SA, Saadat F, Forghanparast K, Sohrabnejad R. Serum C - reactive protein level as a biomarker for differentiation of ischemic from hemorrhagic stroke. Acta Med Iran.2011; 49 (3): 149 - 52.

[23] ElHabr AK, Katz JM, Wang J, Bastani M, Martinez G, Gribko M, Hughes DR, Sanelli P. Predicting 90 - day modified Rankin Scale score with discharge information in acute ischaemic stroke patients following treatment. BMJ Neurol Open.2021 Jun 24; 3 (1): e000177.

[24] Reif DW. Ferritin as a source of iron for oxidative damage. Free RadicBiol Med.1992; 12: 417–427.17. Castellanos M, Puig N, Carbonell T, Castillo J, Martı´nez JM, Rama R, Da´valos A. Iron intake increases infarct volume after permanent middle cerebral artery occlusion in rats. Brain Res.2002; 952: 1–6.

[25] Cote, R., Hachinski, V., Shurvell, B., Norris, J. &Wolfson, C. (1986). The Canadian Neurological Scale: A preliminary study in acute stroke. Stroke, 17 (4), 731 - 737.