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Serum ferritin level as a prognostic sign in cases of ischemic and hemorrhagic stroke: A prospective study

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Abstract
Humans require iron to function. In cerebral ischemia, free radicals that utilize iron cause more damage. In this study, serum ferritin levels were looked at as a potential indicator of early neurologic worsening in patients with stroke. In this study, the maximum number of patients was in the 18-90-year-old group. In total, 70 patients were admitted within 48 hours of a stroke. According to inclusion criteria, the study only included patients who were admitted within 48 hours of the onset of stroke. Of 70 patients, 34% were female and 65% were male.
A total of 32 patients with ischemic stroke were admitted, of which 25 improved and 7 deteriorated. Patients in the age group 61-70 were most likely to suffer an ischemic stroke. The mean serum ferritin level for improved patients was 211.61, while that of deteriorated patients was 316.82.
In all, 38 patients with haemorrhagic stroke were admitted, out of which 29 improved and 9 deteriorated. Patients aged 61-70 were more likely to experience haemorrhagic strokes. A mean serum ferritin level of 228.67 was found in improved patients, whereas 364.27 was found in deteriorated patients.
The mean serum ferritin level in deteriorated patients is significantly higher than that of improved patients. Early neurologic deterioration is associated with high ferritin levels within 24 hours after stroke onset. In cerebral ischemia, increased body iron stores may enhance cytotoxic mechanisms contributing to stroke progression. More research is needed to identify the underlying causes and potential therapeutic implications of serum ferritin elevations. The reduction of serum ferritin levels can be achieved with medications like Deferoxamine.

Keywords: Ischemic stroke, hemorrhagic stroke, serum ferritin

Introduction

The World Health Organization defines stroke as a clinical syndrome characterized by a rapid onset of localized (or widespread with coma) neurological disruption lasting longer than 24 hours or causes death [1]. The diagnosis of stroke requires laboratory investigations including brain imaging. The number of deaths caused by cerebrovascular diseases in developed countries is rapidly rising as it is the third most common factor responsible for death following cardiovascular disease and cancer. Strokes are classified into ischemic strokes and hemorrhagic strokes.

1. The ischemic stroke occurs due to the blockage of a blood vessel which limits the supply of blood to the brain, whereas hemorrhagic stroke results from blood vessels ruptured in the brain which leads to blood spilling in the intracranial cavity.
2. Hemorrhagic strokes may be classified as intracerebral haemorrhages or subarachnoid haemorrhages depending on where blood spills Ischemic strokes account for 60–80% of all strokes. In both developed and developing countries, it contributes to morbidity and mortality.

The impact of this disease could be reduced by improved detection and modification of risk factors.
About 80% of stroke cases are caused by ischemic strokes, while 20% are caused by hemorrhagic strokes. However, the percentages of stroke types vary by population [2]. From the first Inter stroke study, 22 countries showed that stroke proportions African countries accounted for 66.7% and 34.8%, accordingly, in comparison with 91.1% and 9.0%. For developed nations, respectively [3].

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Study data from the Stroke Investigations Research and Education Network (SIREN) study has reported a 68% ischaemic stroke rate and a 32% haemorrhagic stroke rate, in accordance with the prevalence of strokes among Africans in Inter stroke [4]. There is evidence of an evolution of stroke subtypes in few countries, including Ghana, resulting in a decline of hemorrhagic strokes while increasing the incidence of ischemic strokes [5, 7]. Research done during the 1950s and 1980s in Ghana demonstrated that haemorrhagic stroke was the most prevalent form of stroke causing the majority of stroke deaths [5, 6].

Materials and Methods
This was a Single centred observational prospective hospital based study carried out in General medicine ward and ICU of NIMS Hospital Jaipur for a duration of 18 months (January 2020 to June 2021). Patients of stroke who were admitted within 48 hrs of symptoms onset were included in the study and the diagnosis of stroke was confirmed by CT/MRI Brain. Neurological assessment was done by Canadian stroke scale. Serum ferritin levels was performed within 48 hrs of onset of symptoms. Neurological assessment was repeated on 6th day of admission by Canadian stroke scale and patients were classified into 3 categories namely clinical improvement, deterioration and death. following data were recorded for each patient of acute stroke-NCCT/MRI Brain, Serum ferritin, Age, sex, history of Diabetes, Hypertension and smoking Biochemical profile including: Haemoglobin levels, blood sugar levels(random),liver function tests, renal function tests, lipid profile, serum electrolytes. All the information were collected on a pre-designed Performa. Data thus collected were entered in MS Excel 2007 worksheet in the form of master chart. These data were classified and analysed as per aims and objectives of the study. Inferences were drawn with use of appropriate test of significance.

Results
A total of 70 patients were enrolled in the study after an informed consent, out of which 46 were males and 24 were females with a age range of 20-90. 32patients were diagnosed with ischemic stroke and 38 with hemorrhagic stroke in which percentage of female was 34.38% and 34.21% respectively. Maximum no. of patients i.e; 23 were reported with the age range of 61-70,17 patients with the age group 51-60,16 patients were from the aged range from 71-80 and 10 patients were from the age group 81-90.

The mean serum ferritin level of deteriorated patients was significantly higher as compared to those who improved in both cases i.e; 316.8271 and 364.2767 respectively. Mean statistically different with $p < 0.001$.

Patient Profile
Total sample size: 70. Males: 46.
Females: 24.
Age range: 20-90.

Demographic Details
Followings were the findings of the present study.

Patients distributed by etiological factor

Table 1: Patients distributed by etiological factor

Stroke	Nos. of Patients	Percentage
Ischemic stroke	32	45.71%
Haemorrahgic stroke	38	54.29%

Number of cases classified by type and results

Table 2: Distribution based on type and results

Nos. of cases	Ischemic stroke	Hemorrhagic stroke
Improved cases	25	29
Deteriorated cases	7	9
Total	32	38

Patients with ischemic stroke distributed on the basis of sex

Table 3: Sex distribution of patients with ischemic stroke

Sex	Count of Genders	Percentage
Male	21	65.62%
Female	11	34.38%

Patients with hemorrhagic stroke distributed by sex

Table 4: Sex distribution of patients of haemorrhagic stroke

Sex	Count of genders	Percentage
Men	25	65.79%
Women	13	34.21%

Distribution by age of stroke patients

Table 5: Distribution by age of stroke patients

Age quartile	Ischemic stroke	Haemorrahgic stroke
21-30	01	00
31-40	00	01
41-50	02	00
51-60	10	07
61-70	12	11
71-80	08	08
81-90	05	05

Age-based mean of patients with ischemic stroke on the basis of prognosis

Table 6: Age-based mean of patients with ischemic stroke on the basis of prognosis

Patient's Condition	Ischemic Stroke
Patients mean age who improved	69.88
Patients mean age who deteriorated	67.00

Age-based mean of patients with hemorrhagic stroke on the basis of prognosis

Table 7: Age-based mean of patients with haemorrhagic stroke on the basis of prognosis

Patient's condition	Hemorrhagic Stroke
Patients mean age who improved	67.06897
Patients mean age who deteriorated	64.44444

Mean serum ferritin in ischemic stroke patients

Table 8: Mean serum ferritin of patients of ischemic stroke

Patients Condition	Mean of serum ferritin
Improved subject	211.6124
Deteriorated subject	316.8271

Mean of serum ferritin in hemorrhagic stroke cases

Table 9: Mean serum ferritin of patients of haemorrhagic stroke

Patients Condition	Mean of serum ferritin
Improved subjects	228.6731
Deteriorated subjects	364.2767

Inference

- In both groups, the means are statistically different with $p < 0.001$.
- Ferritin levels are significantly higher in patients who deteriorate than those who improve.

T-test assuming disperse variances for comparison of mean serum ferritin in hemorrhagic stroke assuming unequal variances

Table 10: T-Test assuming unequal variances to compare mean of serum ferritin of improved and deteriorated groups in ischemic and hemorrhagic stroke

	Improved	Deteriorated
Mean	228.6731	364.2767
Variance	8513.476	8283.64
Observation	29	9
Hypothesized mean difference	135.6036	
Df	14	
T stat	-7.7839	
P(T<=t)one tail	9.4E-07	
T critical one tail	1.76131	
P(T<=t)two-tail	1.88E-06	
T critical two-tail	2.144787	

Inference

- In both groups, the means are statistically different with $p < 0.001$.
- Ferritin levels are significantly higher in patients who deteriorate than those who improve.

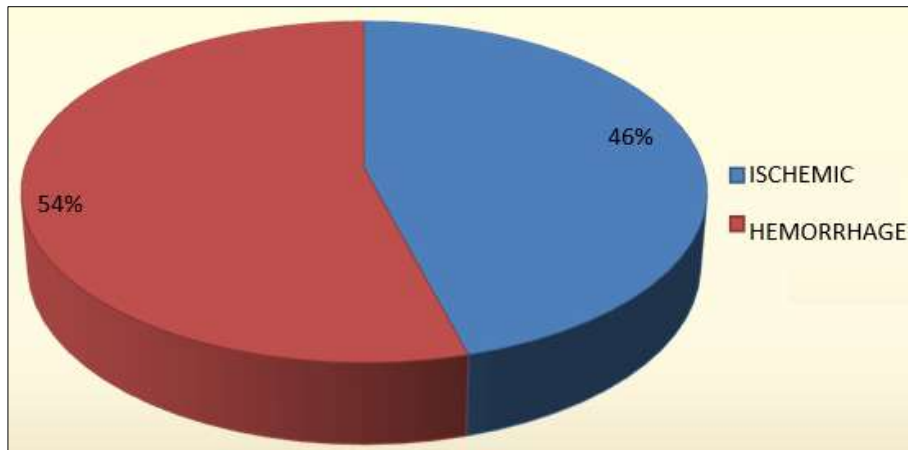**Patient distribution based on etiology**

Fig 1: Patient distribution based on etiology

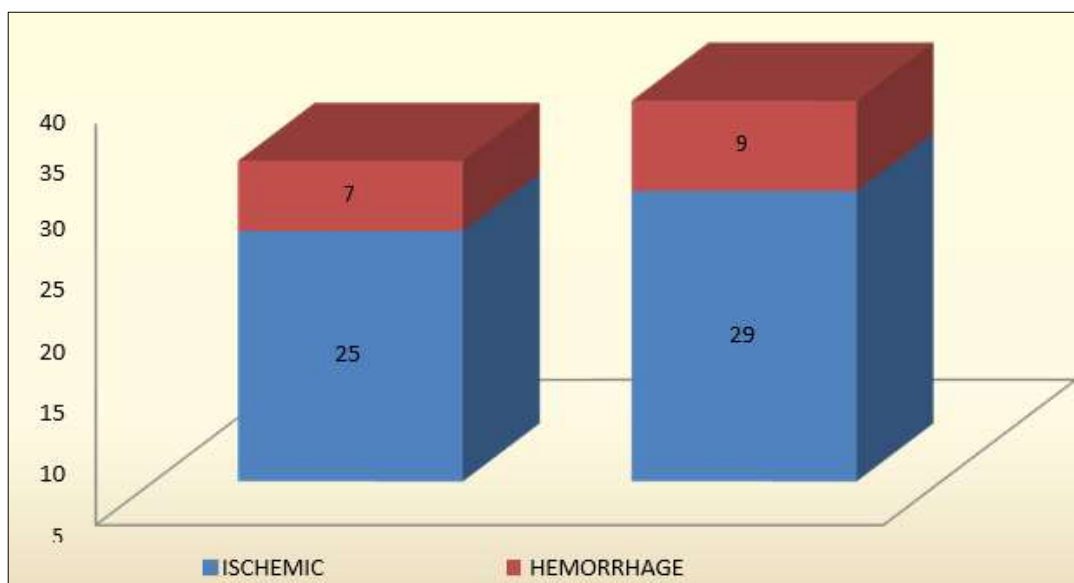**Patient's distribution on the basis of classification and results diagrammatic presentation in a bar graph**

Fig 2: Graphical presentation based on type of stroke and outcome

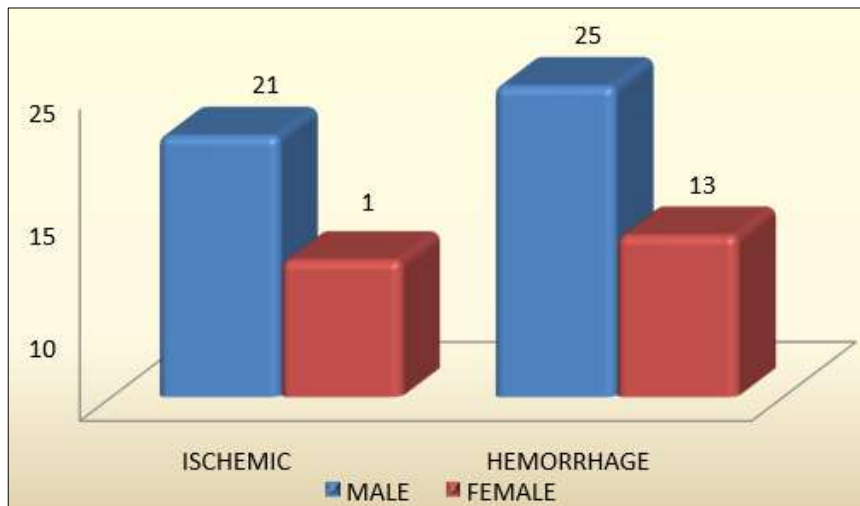**Graphical representation of sex distribution of cases**

Fig 3: Graphical presentation of patients on the basis of gender determination

On the basis of progression in individuals with ischemic and hemorrhagic stroke: mean of age
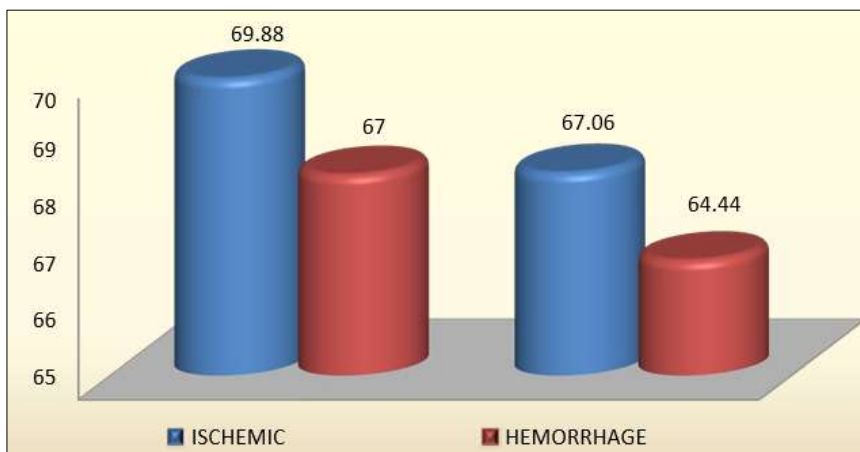

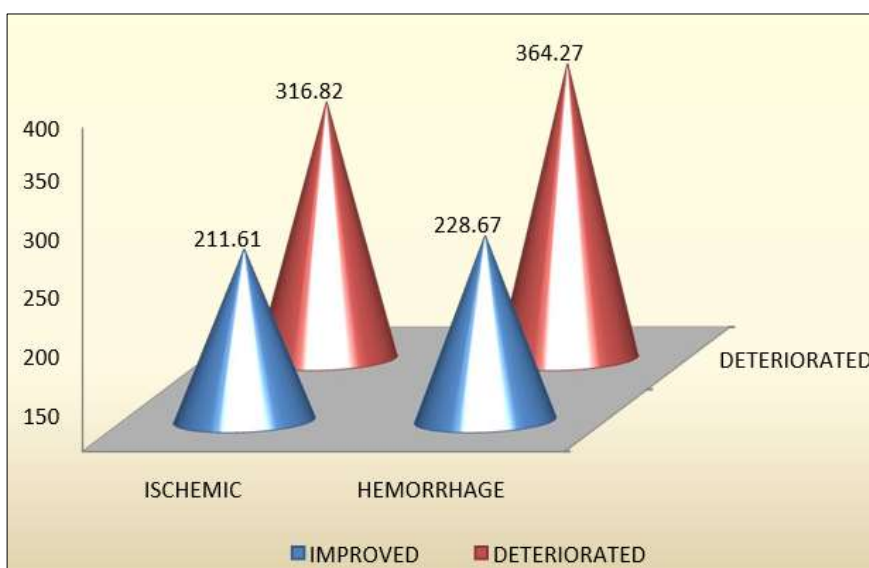**Fig 4:** Mean age of patients of ischemic and haemorrhagic stroke based on prognosis

Fig 5: Graphical representation of mean serum ferritin level of patients of stroke based on prognosis

Discussion

Study results suggest that ferritin levels could be an influential predictive criterion for strokes. There is a relationship between elevated ferritin concentration and neurodegeneration as a result of stroke. Serum ferritin measurements can thus be used to determine whether an individual is susceptible to stroke. Among the two groups with better and worsening health, the average age of the individuals was quite similar. Neither improved nor deteriorating groups differed in the prevalence of various other influences. Both the improving and deteriorating groups, nevertheless, ferritin levels were lower in the deteriorating group. It makes no difference if a stroke is Haemorrahgic or ischemic, that is true. Individuals who rapidly declined showed elevated ferritin values at the time of admission. Serum ferritin provides an indication of cellular ferritin concentrations, enabling us to discern whether infarcted tissues possess adequate iron stores [8, 9]. Studies have shown elevated serum ferritin levels as well as high cerebrospinal fluid ferritin levels contributed to worsening neurological symptoms, negative outcomes, increased infarct size, and glutamate accumulation among stroke victims [10, 11]. As a whole, the findings indicate excessive iron intake is responsible for:

1. Stroke patients experience negative outcomes neurologically.
2. Thrombolytic treatment interferes with iron overload.
3. Chlorination therapy is effective after a stroke when serum ferritin levels are high.

Conclusion

Our study has shown that increased serum ferritin levels predict stroke outcome. Serum ferritin levels above normal suggest enhanced medical protocols, indicating cognitive decline. Serum ferritin levels also aid in deciding whether to use thrombolytic therapy. There are ways to figure out whether a patient would benefit from thrombolysis. Patients with elevated serum ferritin are more likely to deteriorate following thrombolysis**.**

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