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RESEARCH ARTICLE

SERUM FERRITIN LEVEL IN PATIENTS WITH ACUTE HAEMORRHAGIC STROKE AND ITS ASSOCIATION WITH OUTCOME

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Abstract

Background: Stroke is characterized by acute onset of focal neurological deficit lasting 24 hours or longer. With the increasing incidence of hemorrhagic stroke in Indians, the use of biochemical markers like Ferritin can predict outcome. This study was undertaken to study level of Serum Ferritin levels in patients with acute hemorrhagic stroke and its association with the outcome.

Materials and Methods: This was a hospital based cross sectional observational study with 90 patients with acute hemorrhagic stroke admitted into the Department of Medicine, JMCH since 1st July 2020 till June 30th 2021. All the patients subjected to investigations and inclusion and exclusion criteria. Equal number of age and sex matched healthy individuals were included in the study as control

Results: In this study the mean age group with Acute Hemorrhagic Stroke was 63.3 \pm 7.2 years. Of the total cases 57 were males (63.3%) and 33 female (37.7%). Hypertension was the most common risk factor associated present in 67.8% patients which is 53.3. The most common site of bleed was the basal ganglia. The mean serum Ferritin value was 333.44 \pm 92.12 ng/ml in patients with acute hemorrhagic stroke. The serum ferritin values correlated with the hematoma volume and higher values were associated with increased mortality.

Conclusion: In the study Serum Ferritin values were significantly higher 445.29 \pm 97.70 ng/ml (p value < .001) in patients which deteriorated and showed a positive correlation.

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Introduction:-

A stroke is a clinically defined syndrome of rapidly developing symptoms or signs of focal loss of cerebral function with no apparent cause other than that of vascular origin, but the loss of function can at times be global (applied to patients in deep coma and to those with subarachnoid hemorrhage). Symptoms last more than 24 h or lead to death.¹ Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range, 84-262/100,000 in rural and 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population based studies. There is also a wide variation in case fatality rates with the highest being 42%.² Hypertension is considered to be one of the most important risk factor in middle aged and elderly person.³ The increased risk of intracerebral hemorrhage is greater in the set of patients who have stopped taking their

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antihypertensive medication, are relatively young or are smokers. ICH accounts for approximately 10-20% of all strokes

Iron has been involved in cerebral injury after the occurrence of intracerebral hemorrhage. Free iron released from the lysis of red blood cells plays a role in injury. Iron toxicity is generally thought to result from the generation of free radicals via the Fenton reaction⁴. In that reaction, ferrous iron reacts with hydrogen peroxide to form radical oxygen. The resulting ferric iron can be reduced back to Fe²⁺ by a variety of reducing agents and thereby regenerate the starting reagents. In this way, the radical reaction cycle can begin again. Some cellular antioxidants like GSH and superoxide dismutase work to limit this damage, but these antioxidants have limited efficacy to combat the amount of oxidative stress during ICH.⁵

Free iron is considered toxic to cells and the body has established an elaborate set of protective mechanisms to bind iron in various tissue compartments. Within tissues the iron is stored complexed to protein as ferritin or hemosiderin. Stored iron in the form of ferritin is not essential for sustaining life or for preventing anemia, but when liberated, it can promote tissue injury by provoking iron mediated Fenton reaction⁵

Materials And Methods:-

A Hospital based observational study conducted in Jorhat Medical College & Hospital, Department of Medicine, Jorhat for a duration of 1 year from 1st July 2020- 31st June 2021 upon a total number of 90 patients. The patients attending the hospital with the diagnosis of acute hemorrhagic stroke and willing to participate were enrolled in the study

Inclusion Criteria:

1. Patients equal to or above 18 years of age with acute hemorrhagic stroke
2. Patients/ their attendants giving informed consent for the study

Exclusion criteria:

1. Ischemic stroke
2. Anemia
3. Chronic liver disease
4. Chronic kidney disease
5. Hematological malignancy

90 Age and Sex matched healthy individuals were included in the study as control group

Patients diagnosed clinically and radiologically as acute hemorrhagic stroke were included in the study following informed consent either from them or their relatives. All patients were then subjected to non-contrast CT scan of brain. Important findings such as site, size, intraventricular extensions, midline shifts if any were noted. Clinical examination involved recording of vitals, GCS (Glasgow Coma Scale), MRS (Modified Rankin Scale) on admission, neurological examination. All data were then analyzed using the IBM SPSS 23. Chi square test was done to establish the association. A p value of <0.05 considered to be statistically significant.

Result:-

Table 1:- Serum Ferritin level in stroke patients and in control group .

Group	Sex	N	Serum Ferritin ng/ml (Mean ± SD)	P value
Haemorrhagic Stroke	Male	57	327.02± 88.9	<.001
	Female	33	300.55± 97.7	
	Total	90	333.44± 92.12	
Control	Male	57	126.72±41.06	
	Female	33	94.53±18.767	
	Total	90	115.28± 37.65	

Table 2:- Serum Ferritin and GCS score in patients with Hemorrhagic Stroke.

GCS	Serum Ferritin (Mean ±SD) ng/dl	p value
3-8	444.00±87.59	

9-12	272.22± 75.70	<.001
13-15	258.65± 62.25	

Table 3:- Serum Ferritin level in different size of Hemorrhage and across various MRS groups.

MRS (Modified Rankin Scale)	Serum Ferritin (ng/dl) Mean± SD	Hematoma volume (ml) (Mean± SD)	P value
≤ 2	265.54±75.51	18.48± 11.03	< .001
3-6	445.29±97.70	36.76±18.04	

Table 4:- Serum Ferritin values in fatal and Non-Fatal group.

In Hospital Mortality	Number	Serum Ferritin(Mean ± SD) ng/dl	P Value
Fatal	24	487.08±95.7	<.001
Non-Fatal	66	277.58± 75.2	

We observed that the mean age of the patient was 63.3±7.2 years. The mean value of serum Ferritin in the patients with acute hemorrhagic stroke was 333.44± 92.12 ng/dl ng/ml and the value of serum Ferritin in the control group was 115.28± 37.65 ng/dl. The difference is statistically significant (p value < .001). The mean serum ferritin in the male patients was 327.02±88.9 ng/dl and the mean value in male control group is 126.72±41.06 ng/dl . The mean value of serum ferritin in the female cases was 300.55 ±97.7 ng/dl and the mean ferritin value in the control group is 94.53±18.767ng/dl. The difference is found to be statistically significant. The mean serum Ferritin in patients with MRS score ≤ 2 is 265.54±75.51 ng/ml, whereas the mean serum Ferritin in patients with MRS score 3-6 is 445.29±97.70 ng/ml. The difference is found to be statistically significant. The mean serum ferritin values in the patients with GCS score between 3- 8 was 444.00±87.59ng/dl as compared to patients having GCS score 9-12 and 13-15 whose respective Ferritin values are 272.22 ±75.70ng/dl and 258.65± 62.25ng/dl, that in patients with MRS score≤ 2, the mean serum Ferritin value is 265.54±75.51ng/ml and the mean volume of hematoma is 18.48± 11.03 ml . In patients with MRS scores 3-6, the mean serum Ferritin value is 445.29±97.70ng/ml and the mean volume of the hematoma is 36.76±18.04ml. The inpatient mortality of the patients was 26.6%

Discussion:-

In the present study we found that the mean value of serum Ferritin in the patients with acute hemorrhagic stroke was 333.44± 92.12ng/ml and the value of serum Ferritin in the control group was 115.28± 37.6ng/dl. The findings are consistent with the studies conducted by Pankaj P etal. who found the serum ferritin values in the patients with hemorrhagic stroke which deteriorated were 463.91±181.2 ng/dl.⁷ Similar results were found in the study conducted by Hemant Mahur etal⁶. In hemorrhagic group the mean serum ferritin level was 355.759 in those deteriorated. They concluded that the patients with stroke with increased serum ferritin concentrations have a higher risk of poorer outcome, hemorrhagic transformation, and cerebral edema than patients with low ferritin values.⁶ Pankaj P etal. conducted a study on the patient of acute stroke where they found out that level of serum ferritin had direct correlation with poorer prognosis in patients of stroke. The mean level of serum ferritin was found to be 463.91ng/dl in deteriorated group of patients.⁷ These findings are consistent with the findings of study conducted by Dr Manish Narayanetal. (2018) where they found the mean serum ferritin in hemorrhagic stroke patients in the to be 463.91ng/ml. The difference was statistically significant, elevated ferritin levels were seen in patients with poor clinical outcome⁸

The present study found that the mean value of serum ferritin in the patients which improved , MRS ≤ 2 was 265.5± 75.51 ng/ml whereas the mean value of serum ferritin in the patients which deteriorated, MRS 3-6 was relatively higher that is 445.29±97.70ng/ml. The difference was found to be statistically significant as reflected by p values < .001.

Similar results were observed in the study conducted by Hemant Mahur etal. conducted a study on a total of 100 patients of stroke who presented to the hospital . In hemorrhagic group the mean serum ferritin level was 86.838ng/ml in clinically improvement patients and 355.759ng/ml in those deteriorated. They concluded that, the patients with stroke with increased serum ferritin concentrations have a higher risk of poorer outcome, hemorrhagic transformation, and cerebral edema than patients with low ferritin values⁶

The findings are consistent with the studies conducted by Pankaj P et al. who conducted a study on the patient of acute stroke where they found out that level of serum ferritin had direct correlation with poorer prognosis in patients of stroke. The mean level of serum ferritin in the group of clinically improved was 87.01ng/ml was much lesser compared to the group clinically deteriorated or died 458.7 ng/ml among patients of ischemic stroke. Similarly in patients of hemorrhagic stroke it was 96.4ng/ml in improved group compared to 463.91ng/ml in deteriorated. The differences were statistically significant⁷

Similar results were observed in the study conducted by Rajendran S R et al. c where they concluded that elevated levels of serum ferritin were seen in patients of haemorrhagic stroke and those elevated levels were associated with poor outcome of the patients¹⁰

Conclusion:-

Hemorrhagic Strokes are common in Males as compared to Females. It is more common in age group of 60 years and above. Mean Serum Ferritin level was higher in the patients with HemorrhagicStroke. The Patients with higher MRS scores and lower GCS scores had higher serum Ferritin levels. The larger size of hemorrhage was associated with higher levels of serum Ferritin. In patients with Hemorrhagicstroke, higher Ferritin level was associated with higher rates of in hospital mortality.

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