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A STUDY OF SERUM FERRITIN LEVEL IN PATIENTS OF STROKE AS A PROGNOSTIC MARKER

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Abstract

Background: Stroke/cerebrovascular accident (CVA) is the second most common cause of mortality after coronary artery disease (CAD). Amongst all neurological diseases, stroke ranks first in frequency and importance. In India, the scenario is no different, its incidence and prevalence are on a steady rise. To evaluate the concentration of serum ferritin in patients of acute stroke as a prognostic marker.

Methods: This was a hospital based observational and cross sectional study conducted on 60 cases of acute stroke as per seed article having minimum difference of mean (f ferritin level) 365 and 145.43 for 80% power and 0.05 alpha error.

Results: Out of 34 cases of haemorrhagic cases 13 cases mortality was observed while 14 cases had deteriorated outcome and 15 cases improved. Mean serum ferritin of dead, deteriorate and improved haemorrhagic cases was 1169±114.28, 723.07±88.07 and 107.43±26.80. Serum ferritin level was abnormal [raised] in all 22[36%] death cases and 24[40%] cases who had deteriorate.

Conclusion: Elevated serum ferritin is strongly associated with early neurological deterioration in patients of stroke and is a definite poor prognostic marker of acute stroke [ischemic or haemorrhagic] an elevated serum ferritin (A marker of iron stores) herald more intensive management protocols and care for the patient as it can predict early neurological deterioration. Iron chelation therapy in acute stroke seems to be a strong theoretical possibility and further studies are required to investigate its role in treatment of stroke.

Keywords: Stroke, Prognostic Marker, Elevated serum ferritin

Introduction

Stroke/cerebrovascular accident (CVA) is the second most common cause of mortality after coronary artery disease (CAD). Amongst all neurological diseases, stroke ranks first in frequency and importance[1].

In India, the scenario is no different, its incidence and prevalence are on a steady rise. The first community based study of stroke was carried out in and around the town of Vellore, Tamilnadu, South India, between 1968 and 1969[2]. The second one was conducted in Rohtak, Haryana, North India, during 1971-1974[3]. The very low prevalence rates of stroke in these studies led to the belief that stroke was less frequent in India than in the Western countries. However, during the 1980s and 1990s, a battery of surveys was conducted in various parts of the country in both urban and rural communities, and it was found that the prevalence had almost doubled in a span of ten years. Over the last two decades the crude stroke prevalence in different parts of India ranges from 44.29 to 559/1,00,000 persons which is significantly higher as compared to the western data[4].

A stroke/CVA is defined as the abrupt onset of a neurologic deficit that is attributable to a focal vascular cause[5]. Indian Collaborative Acute Stroke Study (ICASS); a multi-centric study conducted among 2,162 admitted stroke patients across southern, northern, and western India observed ischemic stroke in 77%, haemorrhagic stroke in 22%, and unspecified stroke in 1% cases; a statistics similar to the global trend[7]

Diagnosis is typically based by physical exam and CT Scan or MRI scan. ICH is diagnosed by CT scan and, ischemic strokes is early diagnosed by MRI [DWI]. Other tests such CT-ANGIOGRAPHY, MRI ANGIOGRAM, DSA, ECG, ECHO and blood tests are done to determine risk factors and rule out other possible causes.

Ferritin is the cellular storage protein for iron. Ferritin is essentially located within cells and constitutes the main intracellular iron storage protein. The principal factor that controls cellular ferritin content is the intracellular level of free iron. Ferritin 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 Ferritin is still unknown. However, serum Ferritin has been used widely in clinical medicine chiefly as an indicator of body iron stores[7]. It is an acute-phase reactant involved in cellular defence against oxidative stress and inflammation along withtransferrin[8].

Material and Methods

Study Design: Hospital based observational and cross-section analysis.

Study area- The present study was conducted in the Department of General Medicine, S.M.S Hospital & Attached Group of Hospitals, Jaipur.

Study Period- After approval of the research review board, this study was carried out up-to sample size completed.

Sample Size- Sample size is calculated 60 cases of acute stroke as per seed article having minimum difference of mean (ferritin level) 365 and 145.43 for 80% power and 0.05 alpha error.

Inclusion criteria

1. Age of patients is above 18 years.
2. Diagnosis of stroke is confirmed by CT scan/MRI.
3. Patient presents within 48 hrs of onset of symptoms.

Exclusion criteria

1. Patient not fulfilling inclusion criteria.
2. Patient with associated infection or inflammation.
3. Patient with history of malignancy.
4. Patient with anaemia of chronic disease.
5. Secondary iron overload conditions (History of blood transfusion and haemolysis).
6. Patient with known case of Haemochromatosis.
7. Patient with known case of Hepatocellular carcinoma.
8. Patient with known case of Still's disease.
9. Patient with known case of Gaucher's disease.
10. Patient with known case of Hyperthyroidism.

Methodology

Patients of stroke presenting within 48hrs of symptom onset were included in the study and diagnosis of stroke was confirmed by CT scan/MRI.

Neurological assessment was done by CANADIAN STROKE SCALE. Serum ferritin levels were 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 three categories namely clinical improvement, deterioration and death.

Statistical analysis

Significance of difference in proportion was inferred by chi-squire test. Significance of difference in means' were inferred by unpaired 't' test on the basis of various independent predictor. The level of significance was kept at 95% for all statistical analysis.

Results

Table 1: Distribution of cases according to clinical examination of respiratory system in relation to serum ferritin

Respiratory System	Serum Ferritin				Total	
	Normal		Abnormal [raised]			
	No.	%	No.	%	No.	%
NVBS+ B/L Crepitation	3	13.6	21	55.3	24	40.0
NVBS + No Added Sound	19	86.4	17	44.7	36	60.0
Total	22		38		60	
χ^2	10.060					
P	0.002					

Table 2: Distribution of cases according to cardiovascular system in relation to serum ferritin

Cardiovascular System	Serum Ferritin				Total	
	Normal		Abnormal [raised]			
	No.	%	No.	%	No.	%
Mild Diastolic Murmur	8	36.4	5	13.2	13	21.7
S1&S2 Heart, No Murmur	14	63.6	33	86.8	47	78.3
Total	22		38		60	
χ^2	4.421					
P	0.036					

Table 3: Distribution of cases according to ECG Findings in relation to serum ferritin

ECG Findings	Serum Ferritin				Total	
	Normal		Abnormal[raised]			
	No.	%	No.	%	No.	%
LVH	8	36.4	33	86.8	41	68.3
TWNL	14	63.6	5	13.2	19	31.7
Total	22		38		60	
χ^2	16.407					
P	<0.001					

Table 4: Distribution of cases according to serum ferritin level in relation to outcome

Serum Ferritin Level	Outcome						Total	
	Death		Deteriorate		Improved			
	No.	%	No.	%	No.	%	No.	%
Normal	0	-	0	-	22	100.0	22	36.7
Abnormal(raised)	14	100	24	100	0	-	38	63.3
Total	14		24		22		60	
Mean ferritin	1157.64		687.54		91.32			
SD	119.03		105.03		29.84			
F	636.823							
P	<0.001							

Table 5: Distribution of cases according CT-Scan/MRI Findings in relation to outcome

CT-Scan/MRI Findings	Outcome						Total	
	Death		Deteriorate		Improved			
	No.	%	No.	%	No.	%	No.	%
Haemorrhagic	13	92.9	14	58.3	7	31.8	34	567
Ischaemic	1	7.1	10	41.7	15	68.2	26	43.3
Total	14		24		22		60	
χ^2	13026							
P	<0.001							

Table 6: Distribution of cases according to CT Scan/MRI Findings in relation to serum ferritin

Serum Ferritin Level	CT Scan/MRI Finding				Total	
	Haemorrhagic		Ischemic			
	No.	%	No.	%	No.	%
Normal	7	20.6	15	57.7	22	36.7
Abnormal [raised]	27	79.4	11	42.3	38	63.3
Total	34		26		60	
Mean Ferritin Level	767.18		332.04			
SD	406.19		311.44			
T	4.534					
P	<0.001					

Discussion

A Stroke is defined as an abrupt onset neurological deficit attributable to a focal vascular cause. There are two main types of stroke: ischemic due to lack of blood flow, and haemorrhagic due to bleeding. Patients of stroke presenting within 48hrs of symptom onset were included in the study and diagnosis of stroke was confirmed by CT scan/MRI scan.

Neurological assessment was done by CANADIAN STROKE SCALE at the time admission. Serum ferritin level 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 three categories namely clinical improvement, deterioration and death on basic CANADIAN STROKE SCLAE score.

In our study, distribution of cases according to respiratory infection in relation to serum ferritin, NVBS+B/L Crepitation [aspiration pneumonitis] was present in 24 cases and out of them 21 had abnormal [raised] serum ferritin level. Aspiration pneumonitis was presented in 40 % of total cases while NVBS+No added sound [normal respiratory finding] was present in 36 cases[60%] and this difference was also found statistically significant ($p<0.01$).

This observation was similar with the study of Armstrong and Mosher9 chest infection may affect up to as many as one-third (33%) of stroke patients who have raised serum ferritin. They increased the morbidity and mortality. Aspirated Pneumonitis with raised serum ferritin causes the highest attributable mortality of all medical complications following stroke.

In our study, mild diastolic murmur was presented in 13 cases [21% of total stroke cases] which are associated with cardio-embolic stroke. Normal heart sound was presented in 47 cases [79%]. On applying chi square test, the difference was found statistically significant ($p<0.05$).

This observation was similar with the study of Schneck and Lutsep10. This study shows that Cardio-embolic strokes accounts for approximately 20% of total stroke patients.

In our study, total number of cases was 60 out of them. 48cases had moderate to severe anaemia. Out of 48 cases 32 have raised serum ferritin and those who were raised serum ferritin had poor clinical out -come .In cases of strokes who have raised serum ferritin and anaemia [moderate and sever] had associated with poor prognostic outcome [in form of clinical deterioration and death] .

This observation was similar with the study of Khan et al11. Their study showed that anaemia is a frequent finding in patients with acute stroke. Moderate to severe anaemia with raised serum ferritin had associated with poor prognosis in acute stroke patients.

In our study total number of cases was 60, out of them 14 mortality was observed while 24 cases had deteriorated outcome and 22 cases were improved. Serum ferritin level was abnormal [raised] in all 14 death cases, while all 24 cases who had deteriorated also have abnormal [raised] serum ferritin level and this difference was found statistically highly significant ($p<0.001$). In our study mean serum ferritin in dead patients was 1157.64 ± 119.03, in deteriorated cases mean serum ferritin was 687.54 ± 105.93 and in improved cases, mean serum ferritin level was 91.32 ± 29.84. On applying ANOVA test, the difference was found statistically highly significant ($p<0.001$).

This observation was similar with study of Narayan and Singh12. Their study shows that mean serum ferritin level was 96.44 in those cases who were improved and those cases who were deteriorated mean serum ferritin was 463.91. Mean serum ferritin in deteriorated patients is significantly higher than those who improved.

Conclusion

Elevated serum ferritin is strongly associated with early neurological deterioration in patients of stroke and is a definite poor prognostic marker of acute stroke [ischemic or haemorrhagic] an elevated serum ferritin (A marker of iron stores) herald more intensive management protocols and care for the patient as it can predict early neurological deterioration. Iron chelation therapy in acute stroke seems to be a strong theoretical possibility and further studies are required to investigate its role in treatment of stroke.

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