Biomarkers of hemorrhagic transformation of acute ischemic stroke – A cross-sectional study

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Biomarkers of hemorrhagic transformation of acute ischemic stroke – A cross-sectional study

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ABSTRACT

Background. Hemorrhagic transformation (HT) is a serious complication that can arise in individuals experiencing acute ischemic stroke (AIS), whether it occurs spontaneously or following thrombolytic therapy, resulting in considerable morbidity and mortality. Hemorrhagic changes are associated with several risk factors, including excessive blood sugar levels, hypertension, the severity of a stroke, and reperfusion.

Aim. To assess the commonly available blood parameters such as lipid profile, serum magnesium, and serum ferritin as tools to identify patients who are at risk of hemorrhagic transformation after an acute ischemic stroke.

Materials and methods. The study was conducted at the Saveetha Medical College, Chennai, Tamil Nadu in India as a cross-sectional study, and a total of 142 patients diagnosed with acute ischemic stroke were enrolled for this study from January 2023 to January 2024.

Results. Among the 32 patients who had a hemorrhagic transformation, all 32 (100%) patients had elevated serum ferritin levels and the remaining 110 patients who had no hemorrhagic transformation were found to have normal serum ferritin levels and the difference was statically significant ($p < 0.001$). Total Cholesterol, Serum LDL, Serum HDL, and Serum Triglycerides had no statistically significant association with hemorrhagic transformation among the patients.

Conclusion. The present study concludes that people with lower Serum Magnesium on admission and higher Serum Ferritin were found to be at risk. Serum lipid profile had no statistically significant association with hemorrhagic transformation among the patients.

Keywords: hemorrhagic transformation, acute ischemic stroke

BACKGROUND

Acute cerebrovascular accident remains a significant global and Indian health concern [1]. Thrombolytic treatments have advanced acute ischemic stroke management significantly. However, hemorrhagic transformation poses a frightening risk associated with various factors such as high blood sugar, hypertension, stroke severity, and reperfusion. Certain radiological findings and high NIHSS scores predict the risk of hemorrhagic transformation [2].

Although strokes in individuals under 45 are rare, they still account for 0% to 15% of all cases [3]. Despite advancements in prevention, diagnostics, and therapy, stroke continues to rank high among causes of mortality and disability.

By 2030, it's projected to be equal to other leading causes of death. Stroke, especially in young adults, contributes significantly to healthcare costs and lost productivity [4]. High NIHSS scores have also been linked to a higher likelihood of hemorrhagic transformation in studies [5].

Therefore, healthcare planning must prioritize stroke prevention due to its cost-effectiveness in mitigating both treatment expenses and economic impacts [6].

The study aimed to assess the commonly available blood parameters such as lipid profile, serum magnesium and serum ferritin as tools to identify patients who are at a risk of hemorrhagic transformation after an acute ischemic stroke. The primary objective was to find whether a significant association exists between the occurrence of hemorrhagic transformation after an acute ischemic stroke and low lipid profile, low magnesium and high ferritin.

MATERIALS AND METHODS

Study design and setting: This cross-sectional study was carried out at the Outpatient Department of Saveetha Medical College situated in Chennai, Tamil Nadu, spanning six months from January 2023 to January 2024. Saveetha Medical College is a large multi-specialty hospital with 1600 beds, situated in Kuthambakkam, southwest of Chennai.

Study population: The study included patients admitted with acute ischemic stroke to the Department of General Medicine

Sample size calculation: The sample size calculation, using the prevalence formula to calculate the sample size, using p of 49.7, a confidence interval of 95% and a margin of error of 10% came out to be 142. Therefore, 142 cases admitted to the medical wards of Saveetha

Medical College, who provided consent and met the inclusion criteria, were incorporated into the study.

Inclusion and exclusion criteria: Inclusion criteria comprised patients above 18 years with acute ischemic stroke who provided informed consent. Patients with acute hemorrhagic stroke, prior history of acute cerebrovascular accidents, trauma, those thrombolyzed for acute cerebrovascular accident, presence of other brain mass lesions or vascular malformations, and cerebral venous thrombosis were excluded.

Method of data collection: After obtaining informed consent, blood samples were collected from acute ischemic stroke patients within 24 hours of admission. The following parameters were assessed: i) Lipid profile (total cholesterol, HDL cholesterol, triglycerides, LDL cholesterol) ii) Serum magnesium iii) Serum ferritin Patients were followed up for one week, and those with declining Glasgow Coma Scale (GCS) underwent repeat CT scans. If hemorrhagic transformation was detected, initial blood parameters were correlated and reassessed.

Ethical considerations: Prior to the study's initiation, ethical clearance (SAV/AP/22/89) was obtained from the Committee on Human Research Publication and Ethics of Saveetha Medical College, Chennai. Written informed consent was obtained from each participant before administering the standard structured questionnaire and collecting blood samples. Eligible participants were required to sign or thumbprint a consent form before enrollment, ensuring participant confidentiality and anonymizing all data collected.

All study participants received standard treatment according to our routine protocol, with no expenses incurred by either the participants or the hospital for the study's completion. Additionally, there were no personal or professional gains received directly or indirectly from any commercial entity by the study participants.

Data collection: All participants underwent interviews utilizing a pre-tested structured questionnaire to collect demographic information and relevant data. Anthropometric measurements including weight and height were conducted using standard equipment, and Body Mass Index (BMI) was subsequently calculated. Fasting and postprandial blood glucose levels were determined using the Glucose oxidase/Peroxidase method, while blood urea and serum creatinine levels were assessed through the Urease method and Jaffe's method, respectively. The following parameters were assessed: i) Lipid profile (total cholesterol, HDL

cholesterol, triglycerides, LDL cholesterol) ii) Serum magnesium iii) Serum ferritin Patients were followed up for one week, and those with declining Glasgow Coma Scale (GCS) underwent repeat CT scans. If hemorrhagic transformation was detected, initial blood parameters were correlated and reassessed.

Statistical analysis: Statistical analysis was conducted using SPSS Version 27. Continuous variables were presented as mean (standard deviation), while discrete variables were expressed as number (percentages). Descriptive statistics such as frequency, percentages, and graphs were utilized to address the first objective, while the association between variables and healthcare seeking behavior was examined using the Chi-square test for proportions, with Fisher's exact test applied where applicable. A significance level of $p < 0.05$ was chosen to determine the strength and significance of associations. Level of Significance (Alpha level): The alpha level, set at 0.05, defines the boundaries between high and low probability samples, separating the most unlikely 5% from the most likely 95%. P-value: A p-value less than 0.05 indicates statistical significance, representing the probability of obtaining the result if the null hypothesis were true, thereby indicating a Type I error. Chi-square Test: A non-parametric test used to evaluate hypotheses about proportions and study population relationships, including testing goodness of fit to theoretical expectations.

RESULTS

The majority of our study participants fell within the age range of 31-40 years (24.6%), with males comprising 76.8% of the total participants. Table 1 shows the distribution of clinical profile of the patients. Among the 142 patients, 41.5% had FP Hemi-motor type, 26.8% had hemi-motor, sensory type, 9.9% had hemimotor, aphasia, 5.6% had monoplegia, 4.9% had only aphasia, 3.5% had only cerebellar type and 3.5% had Hemimotor, FP, HH aphasia. Table 2 shows the distribution of hemorrhagic transformation of the patients. Among the 142 patients, 32 (22.5%) had hemorrhagic transformation.

Table 2 outlines the distribution of comorbidities among the study participants. The most prevalent comorbidities were diabetes mellitus (45.8%) and hypertension (23.2%). Table 3 shows the distribution of blood parameters among the patients. 40.1% of the patients had elevated total cholesterol, 53.5% had elevated serum LDL, 95.8% had abnormal HDL level and 14.8% had elevated serum triglycerides.

Table 4 shows the association between hemorrhagic transformation of the patients and lipid profile. Total Cholesterol, Serum LDL, Serum HDL and Serum Triglycerides had no statistically significant association with hemorrhagic transformation among the patients.

Table 5 shows the association between hemorrhagic transformation of the patients and Serum Ferritin. Among the 32 patients who had hemorrhagic transformation, all 32 (100%) patients had elevated serum ferritin level and the remaining 110 patients who had no hemorrhagic transformation were found to have normal serum ferritin level and the difference was statically significant ($p < 0.001$).

Tables 6 shows the association between hemorrhagic transformation of the patients and Serum Magnesium. Among the 32 patients who had hemorrhagic transformation, all 32 (100%) patients had abnormal serum magnesium level and the remaining 110 patients who had no hemorrhagic transformation, 10.9% had abnormal serum magnesium level and the difference was statically significant ($p < 0.001$).

Table 1: Distribution of Study Participants based on Clinical Profile

S.No.	Variables	Frequency (n)	Percentage (%)
1.	Aphasia	7	4.9
2.	Cerebellar	5	3.5
3.	FP motor, sensory	2	1.4
4.	FP Hemi-motor	59	41.5
5.	Hemi-motor, sensory	38	26.8
6.	Hemi-motor, Aphasia	14	9.9
7.	Hemi-motor, FP, HH, aphasia	5	3.5
8.	Hemianopia, motor, aphasia	2	1.4
9.	Monoplegia	8	5.6
10.	Motor, Sensory Aphasia	2	1.4

Table 2: Distribution of Study Participants based on Hemorrhagic transformation

S.No.	Hemorrhagic transformation	Frequency (n)	Percentage (%)
1.	Yes	32	22.5
2.	No	110	77.5

Table 3: Distribution of Study Participants based on Lipid profile

S.No.	Blood Parameters	Normal (%)	Abnormal (%)
1.	Total Cholesterol	85 (59.9)	57 (40.1)
2.	Serum LDL	66 (46.5)	76 (53.5)
3.	Serum HDL	6 (4.2)	136 (95.8)
4.	Serum Triglyceride	121 (85.2)	21 (14.8)

Table 4: Association between Hemorrhagic transformation and Lipid profile

S.No.	Variables	Hemorrhagic transformation		p-value
		Yes	No	
1	**Total Cholesterol**			
	Normal	21 (65.6)	64 (58.2)	0.293
	Elevated	11 (34.4)	46 (41.8)	
2	**Serum LDL**			0.559
	Normal	15 (46.9)	51 (46.4)	
	Elevated	17 (53.1)	59 (53.6)	
3	**Serum HDL**			0.592
	Normal	1 (3.1)	5 (4.5)	
	Elevated	5 (96.9)	105 (95.5)	
4	**Serum Triglycerides**			0.322
	Normal	26 (81.3)	95 (86.4)	
	Elevated	6 (18.8)	15 (13.6)	

Table 5: Association between Hemorrhagic transformation and Serum Ferritin

S.No.	Serum Ferritin	Hemorrhagic transformation		p-value
		Yes	No	
1.	Normal	0 (0%)	110 (100%)	< 0.001
	Elevated	32 (100%)	0 (0%)	

Table 6: Association between Hemorrhagic transformation and Serum Magnesium

S.No.	Serum Magnesium	Hemorrhagic transformation		p-value
		Yes	No	
1.	Normal	0 (0%)	98 (89.1%)	< 0.001
	Elevated	32 (100%)	12 (10.9%)	

DISCUSSION

The study included 142 patients who suffered from Acute Ischemic Stroke, between the ages of 18 and 60, who presented at the Outpatient department in the Department of General Medicine at Saveetha Medical College, Chennai

The study examined various demographic and clinical factors in patients with acute ischemic stroke. Among the patients assessed, a notable distribution across different age groups was observed. Specifically, 24.6% of patients fell within the 31-40 age range, with 19% aged 61-70, and 18.3% aged 41-50. Gender distribution revealed a clear majority of male patients, constituting 77% of the total participants, while females accounted for 23%.

Comorbidities were prevalent among the patient population, with 86.6% of individuals presenting with one or more additional health conditions. Diabetes was the most common comorbidity, affecting 45.2% of patients, followed by hypertension at 23.2%, coronary heart disease at 8.5%, and chronic kidney disease at 7.7%. The clinical profile of patients highlighted various presentations, with the most common being FP Hemi-motor type (41.5%), followed by hemi-motor, sensory type (26.8%).

Hemorrhagic transformation, a significant complication, occurred in 22.5% of patients. In terms of lipid profile, a considerable proportion of patients exhibited abnormalities, with 40.1% showing elevated total cholesterol, 53.5% elevated serum LDL, and 14.8% elevated serum

triglycerides. Additionally, 95.8% had abnormal HDL levels. Analysis of serum ferritin and magnesium levels revealed intriguing associations with hemorrhagic transformation. All patients experiencing hemorrhagic transformation had elevated serum ferritin (100%) and abnormal serum magnesium (100%), with statistically significant differences compared to non-transformed patients ($p < 0.001$).

However, no statistically significant associations were found between hemorrhagic transformation and age or gender, nor with common comorbidities such as diabetes, hypertension, coronary artery disease, chronic kidney disease, or bronchial asthma. Similarly, there were no significant associations observed between hemorrhagic transformation and lipid profile parameters, including total cholesterol, serum LDL, serum HDL, and serum triglycerides.

CONCLUSION

This study has shown people with lower Serum Magnesium on admission and higher Serum Ferritin were found to be at risk. Serum lipid profile had no statistically significant association with hemorrhagic transformation among the patients. Hence identifying such patients might be useful in anticipating further complications with careful monitoring and hence timely management can be done.

Conflict of interest: none to declare. Subashini.K and Devipriya Surapaneni contributed equally to the study.

References

1. *Chandra, Ankush, et al. "The Cerebral Circulation and Cerebrovascular Disease I: Anatomy." Brain Circulation, vol. 3, no. 2, 2017, pp. 45–56. PubMed Central, https://doi.org/10.4103/bc.bc_10_17.*

2. *Elsaid, Nada, et al. "Radiological Predictors of Hemorrhagic Transformation after Acute Ischemic Stroke: An Evidence-Based Analysis." The Neuroradiology Journal, vol. 33, no. 2, Apr. 2020, pp. 118 – 33. PubMed https://doi.org/10.1177/1971400919900275.*

3. *Ntaios G. Embolic Stroke of Undetermined Source: JACC ReviewTopic of the Week. J Am Coll Cardiol. 2020 Jan 28;75(3):333-340. [PubMed]*

4. *Mozaffarian D, Benjamin EJ, Go AS, Arnett Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB., American HeartAssociation Statistics Committee. Stroke Statistics Subcommittee. Executive Summary: Heart Disease and Stroke Statistics—2016 Update: A Report From the American Heart Association. Circulation. 2016 Jan 26;133(4):447-54. [PubMed]*

5. *Wen, Lihong, et al. "Risk Factors of Haemorrhagic Transformation for Acute Ischaemic Stroke in Chinese Patients Receiving Intravenous Thrombolysis." Medicine, vol. 99, no. 7, Feb. 2020, p. e18995. PubMed Central, https://doi.org/10.1097/MD.0000000000018995.*

6. *Chen S, Zeng L, Hu Z. Progressing haemorrhagic stroke: categories, causes, mechanisms and managements. J Neurol. 2014 Nov;261(11):2061-78. [PMC free article] [PubMed]*