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Original Research Article

FREQUENCY AND FACTORS OF HEMORRHAGIC TRANSFORMATION IN PATIENTS WITH ISCHEMIC STROKE

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ABSTRACT

Background: *Hemorrhagic transformation (HT) is a serious complication of ischemic stroke that can significantly impact clinical outcomes. Identifying its frequency and associated risk factors is crucial for improving patient management and reducing morbidity and mortality. Understanding these risk factors may help in developing targeted preventive strategies and optimising stroke treatment protocols.* ***Objective:*** *To determine the frequency of hemorrhagic transformation in ischemic stroke patients and to identify the associated risk factors contributing to its occurrence.* ***Study Design:*** *Descriptive study.* ***Setting:*** *The study was conducted in the Department of Neurology at Fauji Foundation Hospital in Rawalpindi.* ***Duration of Study:*** *This study was carried out from 11 July 2024 to 11 January 2025.* ***Methods:*** *A total of 180 ischemic stroke patients were enrolled in the study. Demographic data, medical history, and risk factors—including hypertension, diabetes, hyperlipidemia, ischemic heart disease, and smoking—were recorded. The frequency of HT was assessed using imaging modalities. Patient characteristics such as age, gender, and ICU admission were also analysed. Statistical analyses, including chi-square and logistic regression, were performed to determine significant risk factors for HT, with a significance level set at $p \leq 0.05$.* ***Results:*** *Among the 180 ischemic stroke patients, 17 (9.4%) developed HT. The most prevalent risk factors in the HT group were hypertension (70.6%), diabetes (58.8%), hyperlipidemia (41.2%), ischemic heart disease (23.5%), and smoking (41.2%). An age-related trend was observed, with the highest incidence of HT occurring in the 61–80 years age group (58.8%). Additionally, patients with HT had a higher ICU admission rate (35.3%) compared to those without HT (8.0%).* ***Conclusion:*** *This study highlights a significant association between hypertension, diabetes, hyperlipidemia, ischemic heart disease, and smoking with the development of hemorrhagic transformation in ischemic stroke patients. Early detection and management of these risk factors are essential in mitigating HT risk and improving patient outcomes. Close monitoring and individualised treatment strategies should be prioritised, particularly for high-risk patients, to reduce the likelihood of severe HT complications.*

Keywords: Hemorrhagic Transformation, Ischemic Stroke, Hypertension, Diabetes, Hyperlipidemia, Risk Factors, Intensive Care Unit, Parenchymal Hematoma

INTRODUCTION

Stroke ranks as the second leading cause of fatalities worldwide, following ischemic heart disease. The World Stroke Organization reports that over 13.7 million stroke incidents occur every year, with 60% of those cases involving individuals below the age of 70. The probability of suffering from a stroke for individuals 25 and above is 24.9%. Annually, over 2.7 million individuals give in to ischaemic stroke attacks. Brain damage can occur due to a blockage in a cerebral artery, known as ischaemic stroke, or by a rupture of a cerebral artery, referred to as hemorrhagic stroke. Acute stroke with ischaemic symptoms represents the dominant type, constituting around 85% of instances. Thromboembolism linked to extensive artery atherosclerosis, as well as cardiac conditions like atrial fibrillation, represents the most prevalent causes (1, 2).

Hemorrhagic transformation (HT) adhering to cerebral infarction has been reported to occur in a range of 3.2 to 43.3% of cases of stroke, often leading to a less favorable prognosis. Prior investigations have recognised numerous risk factors for HT, including atrial fibrillation, elevated baseline NIHSS score, older age, and extended duration from stroke onset to treatment (3-6). While numerous risk factors for HT have been documented, the results frequently present inconsistencies. The number of stent retrievers at EVT has been noted with variability in its ability to anticipate HT in similar single-center cohorts (7-9), underscoring the heterogeneity present in the evidence base. Intravenous tissue plasminogen activator boosts outcomes in cases of ischaemic stroke when given to suitably specified patients within 9 hours of symptom onset (10-12). Endovascular thrombectomy, which may be utilised either alone or alongside IVT, has demonstrated significant advantages for patients experiencing large vessel occlusion (13, 14). Recent findings indicate that the risk factors associated with HT differ substantially based on the type of reperfusion treatment used. A study suggested that the frequency of HT in patients with ischemic stroke was 8%. The identified risk factors included Hypertension at 73.7%, Diabetes at 65.8%, Hyperlipidemia at 63.2%, Ischemic Heart disease at 60.5%, and smoking at 31.6% (15).

Ischemic stroke plays a crucial role in the rates of illness and death worldwide. HT, a complication arising from ischemic stroke, exacerbates the severity and intricacy of the condition. Based on the existing information, there is limited data on this topic with varying outcomes. The objective of this study is to assess the frequency and factors associated with hemorrhagic transformation in patients experiencing ischemic stroke within our medical facility. Acquiring an in-depth understanding of the essential mechanisms that lead to hemorrhagic change is vital for improving risk assessment, guiding treatment decisions, and ultimately elevating the overall quality of life for these patients. This study's findings will fill a significant gap in understanding and lay the groundwork for improved management strategies in clinical practice.

METHODOLOGY

This descriptive research was conducted in the Department of Neurology at Fauji Foundation Hospital in Rawalpindi from [11 July 2024—11 January 2025]. To determine the number of participants needed, the WHO sample size calculator was used. Based on previous

studies, the frequency of hemorrhagic transformation was estimated to be around 8% (15), and with a margin of error set at 4% and a confidence level of 95%, the required sample size was calculated to be 180 patients. Participants were selected using a consecutive non-probability sampling method, meaning every eligible patient who met the criteria was included until the target number was reached.

The study focused on individuals aged between 25 and 80 years, regardless of gender, who had been diagnosed with ischemic stroke. Patients with hemorrhagic stroke, neurodegenerative conditions, liver cirrhosis, and severe cognitive impairment were excluded from the study.

Before beginning the research, ethical approval was obtained from the hospital's ethical review board. Patients who met the inclusion criteria were approached, and the purpose and benefits of the study were explained to them in detail. Written consent was obtained from each participant, and they were assured that their participation posed no additional risks. Basic demographic information was collected for each participant. Patients diagnosed with ischemic stroke were then assessed for the presence of hemorrhagic transformation and evaluated for potential risk factors, including hypertension, diabetes, hyperlipidemia, ischemic heart disease, and smoking. These assessments were conducted under the guidance of an experienced consultant with at least five years of post-fellowship experience. A structured proforma was used to record all relevant patient details systematically.

For data analysis, SPSS version 21 was utilised. Numerical data, such as age and duration of hospitalisation, were presented by mean and standard deviation or median (IQR), depending on whether the data followed a normal distribution, which was checked using the Shapiro-Wilk test. Categorical variables, such as gender, presence of hemorrhagic transformation, risk factors, ICU admission, employment status, and place of residence, were presented as frequencies and percentages. To account for potential influencing factors like age, gender, ICU admission, employment status, and place of residence, the data was stratified. After stratification, statistical tests such as chi-square or Fisher's exact test were used, with results considered significant if the p-value was less than 0.05.

RESULTS

The study included 180 patients with ischemic stroke, with a mean age of 51.74 ±16.13 years and a median stroke duration of 7.32 ±3.16 hours from onset. The cohort comprised 102 males (56.7%) and 78 females (43.3%), with nearly half employed (87, 48.3%) and a slight majority residing in urban areas (95, 52.8%) (Table 1). Hemorrhagic transformation (HT) occurred in 17 patients (9.4%), while the majority (163, 90.6%) did not develop this complication (Table 2).

Among risk factors, hypertension was more prevalent in the HT group (12, 70.6%) compared to non-HT patients (46, 28.2%; p=0.0001). Similarly, diabetes was observed in 10 HT cases (58.8%) versus 25 non-HT cases (15.3%; p=0.0001). Hyperlipidemia (7, 41.2% vs. 19, 11.7%; p=0.001), ischemic heart disease (4, 23.5% vs. 10, 6.1%; p=0.01), and smoking (7, 41.2% vs. 20, 12.3%; p=0.001) also showed notable associations with HT (Table 3). Age distribution revealed a higher incidence of HT in older patients aged 61–80 years (10, 58.8%) compared to younger cohorts (p=0.05). ICU admission was required for 19 patients (10.6%), with a markedly higher proportion in the HT group (6, 35.3%) than in non-HT cases (13, 8.0%; p=0.0001) (Table 4). We could not find any notable association of HT with gender, employment status, and residence. We also could not find an association of risk factors with age, gender, ICU admission, employment status, and residence.

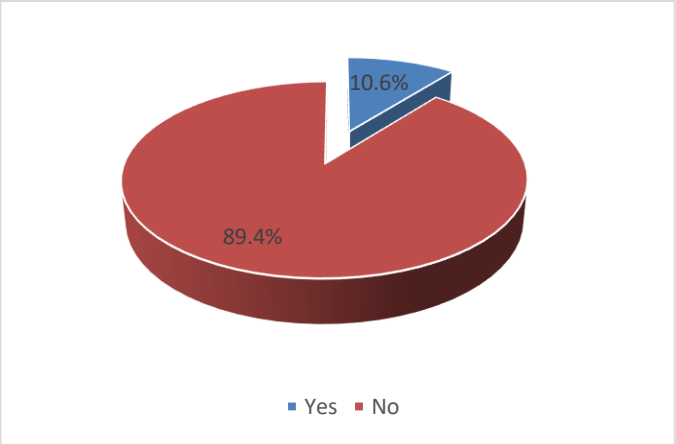

Figure 1: ICU admission

Table 1: Demographics

Demographics		N	%
Gender	Male	102	56.7%
	Female	78	43.3%
Employment status	Employed	87	48.3%
	Unemployed	93	51.7%
Place of living	Urban	95	52.8%
	Rural	85	47.2%

Table 2: Frequency of Hemorrhagic transformation

Hemorrhagic transformation	N	%
Yes	17	9.4%
No	163	90.6%
Total	180	100%

Table 3: Risk factors of Hemorrhagic transformation

Risk factors		Hemorrhagic transformation				P value
		Yes		No		
		N	%	N	%	
Hypertension	Yes	12	70.6%	46	28.2%	0.0001
	No	5	29.4%	117	71.8%	
Diabetes	Yes	10	58.8%	25	15.3%	0.0001
	No	7	41.2%	138	84.7%	
Hyperlipidemia	Yes	7	41.2%	19	11.7%	0.001
	No	10	58.8%	144	88.3%	
Ischemic Heart disease	Yes	4	23.5%	10	6.1%	0.01
	No	13	76.5%	153	93.9%	
Smoking	Yes	7	41.2%	20	12.3%	0.001
	No	10	58.8%	143	87.7%	

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Table 4: Association of Hemorrhagic transformation with various parameters

Parameters		Hemorrhagic transformation				P value
		Yes		No		
		N	%	N	%	
Age distribution (Years)	25 to 45	2	11.8%	51	31.3%	0.05
	46 to 60	5	29.4%	62	38.0%	
	61 to 80	10	58.8%	50	30.7%	
ICU admission	Yes	6	35.3%	13	8.0%	0.0001
	No	11	64.7%	150	92.0%	

DISCUSSION

Our study aimed to explore the frequency and risk factors linked to hemorrhagic transformation (HT) in ischemic stroke (IS) patients. We identified 180 participants with an HT occurrence rate of 9.4%. After analysing demographic and comorbid factors, we found that hypertension, diabetes, hyperlipidemia, ischemic heart disease (IHD), and smoking were notably associated with the development of HT. These findings are consistent with previous research, though some differences were observed when compared to existing studies.

Hypertension, the most common comorbidity in patients with HT (70.6%), was notably higher in HT patients compared to those without HT (28.2%). This result supports the findings of Larrue et al. (16), who recognised hypertension as a significant risk factor for HT in ischemic stroke patients, especially those treated with thrombolytic therapy (rtPA). The elevated blood pressure puts extra strain on the delicate cerebral vessels, increasing the likelihood of hemorrhagic transformation following ischemia. Levent et al.. have similarly highlighted hypertension as a decisive risk factor for HT. This association is likely due to the compromised vascular integrity in hypertensive patients, making their cerebral vessels more prone to rupture during ischemic events (17).

Similarly, diabetes was linked to HT in our cohort, where 58.8% of HT patients had diabetes, compared to just 15.3% of non-HT patients. Diabetic patients often experience endothelial dysfunction, hyperglycemia, and increased atherosclerosis, all of which can worsen ischemic damage and raise the risk of hemorrhage. The combination of metabolic and vascular changes in diabetic patients makes them more susceptible to cerebrovascular complications, including HT. Aljundi et al.. also mentioned diabetes as a risk factor for HT in their cohort (15).

Our study also found a significant association between hyperlipidemia and HT. Forty-one percent of HT patients had high cholesterol, a much higher percentage than the 11.7% seen in non-HT patients. While Levent et al.. observed an association between hyperlipidemia and HT, they did not emphasise it as the primary factor (16). Hyperlipidemia is a significant risk factor but is often seen as one of several contributing factors to vascular injury and atherosclerosis. These conditions can reduce cerebral blood flow and increase the risk of hemorrhage after ischemic events. This finding is consistent with existing literature but suggests that hyperlipidemia plays a secondary role compared to hypertension or diabetes in the development of HT.

Ischemic heart disease (IHD) was another risk factor for HT in our study. Twenty-three % of HT patients had IHD, compared to just 6.1% of non-HT patients, which resonates with Aljundi et al. 's study, which also reported IHD as a factor for HT (15).

Our study identified smoking as a notable risk factor for HT, aligning with the findings of Aljundi et al., which also acknowledged smoking as a contributing factor to the development of hemorrhagic complications in ischemic stroke (15). Our study highlights the importance of considering smoking as a modifiable risk factor for HT in ischemic stroke patients, given its well-established role in vascular disease.

In terms of age, we found that patients aged 61-80 years had a higher incidence of HT, with 58.8% of HT patients falling into this age group. Both Larrue et al.. and Lindley et al.. found that older age is a significant risk factor for HT, which aligns with our results.16,18 Aging is associated with vascular changes such as increased arterial stiffness, reduced cerebral blood flow, and a higher incidence of comorbidities like hypertension and diabetes, all of which increase the risk of hemorrhagic complications following ischemic stroke.

Our study also noted that a higher proportion of HT patients (35.3%) required ICU admission compared to non-HT patients (8.0%). This finding is consistent with Larrue et al., who note that patients with symptomatic intracerebral hemorrhage (SICH) often require intensive care due to the severity of the condition. Severe hemorrhagic transformation (HT), particularly in the form of parenchymal hematoma, is associated with rapid neurological deterioration. This necessitates close monitoring and aggressive management to prevent further complications or death (16).

CONCLUSION

In summary, our study reported a 9.4% rate of hemorrhagic transformation (HT) in ischemic stroke patients, with notable associations with several key risk factors, including hypertension, diabetes, hyperlipidemia, ischemic heart disease, and smoking. These findings align with previous research, which suggests that HT is a multifactorial condition. Comorbidities play a crucial role in increasing the risk of hemorrhagic complications after an ischemic event.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (834/RC/FFH/RWP)

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declared the absence of a conflict of interest.

AUTHOR CONTRIBUTION

ZAHOOR AHMAD (Resident Neurology)

Conception of Study, Data Collection, Development of Research Methodology Design, Study Design, Review of manuscript, and final approval of manuscript.

HUSNAIN HASHIM (Assistant Professor & Head of Department of Neurology)

Study Design, Review of Literature, Critical Input, and final approval of manuscript

LAIBA AFREEN (Resident Neurophysiotherapy)

Literature Search
MURAD KHAN(Resident Neurology)
Review of manuscript

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