Trigger Factors and Their Relation to Spontaneous Intracerebral Haemorrhage

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Abstract

Background: Spontaneous intracerebral hemorrhage is a leading cause of stroke-related mortality, with a 30-day fatality rate of approximately 40%. Acute blood pressure surges, potentially triggered by physiological and environmental factors such as Valsalva maneuvers, infections, and emotional stress, have been hypothesized as precipitating events. Identifying these triggers is crucial for developing targeted prevention strategies.

Objective: To identify types of potential trigger factors in patients with sICH and to study their association with demographic and clinical characteristics.

Patients and Methods: A retrospective cross-sectional study was conducted at Baghdad Teaching Hospital and Alyarmook Teaching Hospital from March to November 2023. Data from 50 patients diagnosed with sICH were collected, including demographics, medical history, and exposure to potential triggers. Statistical analyses, including chi-square tests and odds ratio calculations, were performed using SPSS version 23.

Results: The mean patient age was 59 ± 11.27 years, with a male predominance (2:1). Hypertension was the most prevalent comorbidity (80%), followed by diabetes (36%). Potential triggers were identified in 48% of patients, with Valsalva maneuvers (18%), flu-like illnesses (14%), emotional stress (10%), and sexual activity (6%) being the most common. A significant association was found between hypertension and the presence of triggers (p=0.041). Deep intracerebral hemorrhage was the most frequent type (60%).

Conclusion: Nearly half of sICH cases were associated with identifiable triggers, with Valsalva maneuvers being the most common. The significant association with hypertension underscores the importance of blood pressure management in reducing sICH risk in high-risk individuals.

Key words: Spontaneous intracerebral hemorrhage, Trigger factors, Hypertension, Valsalva maneuvers

Introduction

Spontaneous intracerebral hemorrhage (sICH) is a severe form of stroke, accounting for 10–15% of cases worldwide and associated with a high 30-day mortality rate of approximately 40%.[1,2] Despite its lower incidence compared to ischemic stroke, sICH poses a substantial burden due to its high fatality and disability rates.[3, 4]

The condition arises from the rupture of cerebral blood vessels, often complicated by ventricular involvement, leading to increased intracranial pressure and secondary brain injury. Hypertension remains the most significant modifiable risk factor, contributing to chronic vascular damage and increasing the likelihood of vessel rupture during acute blood pressure surges.[5, 6]

Various acute physiological and environmental stressors, termed "trigger factors," are hypothesized to precipitate sICH by causing sudden elevations in blood pressure or intracranial pressure. These include Valsalva maneuvers, flu-like illnesses, emotional stress, and sexual activity. While extensive research has identified hypertension as a key driver of sICH, limited data exist on the role of acute triggers in its onset, particularly in Middle Eastern populations. Studies from neighboring countries indicate a high prevalence of hypertension-related sICH, but population-specific data on trigger factors remain scarce.[7, 8]

In Iraq, where hypertension is a growing public health concern, understanding these triggers is critical for identifying high-risk individuals and developing targeted prevention strategies.[9] This study aims to assess the prevalence and types of trigger factors among patients with sICH and explore their association with clinical and demographic characteristics, thereby addressing a critical gap in regional stroke research.

Patients and Methods

Study Design and Setting

This retrospective cross-sectional study was conducted to investigate potential trigger factors associated with spontaneous intracerebral hemorrhage (sICH) among patients admitted to Baghdad Teaching Hospital and Alyarmook Teaching Hospital between March 2023 and November 2023. These tertiary care centers were selected due to their high patient volumes, specialized neurological services, and comprehensive stroke management programs, ensuring a diverse representation of sICH cases. Given the scarcity of national data on sICH triggers, studying patients from these hospitals provides insights that may be generalizable to broader Iraqi populations.

Study Population and Eligibility Criteria

The study included a convenient sample of patients aged ≥18 years with a confirmed diagnosis of sICH based on clinical presentation and neuroimaging findings. Inclusion criteria required that patients had accessible medical records and could provide relevant clinical history either directly or through caregivers. Patients were excluded if they had secondary intracerebral hemorrhage due to trauma, metastasis, vascular malformations, or anticoagulant use.

Additionally, those with altered consciousness, aphasia, or cognitive deficits were excluded to minimize recall bias and ensure reliable reporting of trigger events. While this exclusion may limit generalizability to more severe cases, it enhances data accuracy by focusing on patients capable of providing detailed event histories.

Data Collection Process

Patient data were obtained through structured interviews and medical record reviews. Demographic and clinical variables collected included age, sex, hypertension, diabetes, cardiac conditions, smoking history, and medication use. Potential trigger factors were assessed using a predefined checklist, categorizing exposures such as:

- **Valsalva maneuvers** (coughing, sneezing, heavy lifting, straining during defecation)
- **Flu-like illnesses** (documented fever, myalgia, upper respiratory symptoms within one week of onset)
- **Emotional stress** (acute distressful events, validated using the Perceived Stress Scale [PSS-10]).[11]
- **Recent sexual activity** (self-reported intercourse within 24 hours before symptom onset)

To mitigate recall bias, patients and caregivers were encouraged to recount events chronologically. Additionally, clinical documentation was reviewed to corroborate flu-like symptoms and emotional distress when available.

Neuroimaging and Hemorrhage Classification

Computed tomography (CT) scans were performed using the Siemens SOMATOM Definition Edge system (Siemens Healthcare, Erlangen, Germany) to confirm diagnoses and classify hemorrhage locations. Hemorrhages were categorized as deep (e.g., basal ganglia, thalamus), lobar (cortical and subcortical), cerebellar, or intraventricular. Two independent radiologists and one neurologist reviewed imaging findings. To ensure classification consistency, inter-rater reliability was assessed using Cohen's kappa coefficient. Discrepancies were resolved through consensus discussions.

Ethical Considerations

The study adhered to ethical standards, and approval was obtained from the Ethical Review Board of the Iraqi Committee for Medical. Verbal consent was obtained from all patients or their legal guardians before their inclusion in the study, following the principles outlined in the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was carried out using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and clinical data, with means and standard deviations calculated for continuous variables, and frequencies and percentages for categorical variables. Chi-square tests were used to assess the association between categorical variables, while odds ratios (OR) with 95% confidence intervals (CI) were computed to quantify the strength of associations between trigger factors and clinical characteristics. A p-value of less than 0.05 was considered statistically significant.

Results

Fifty patients with sICH have been included in this study.

Demographic data

The mean age of patients was 59 ± 11.27 years (Range 38 – 93 years). Males were representing with male: female ratio of 2:1. For the past medical history, hypertension was the most frequent disease presented (80%) followed by diabetes (36%). The use of anticoagulant was observed among 2 patients only. There were 19 (38%) of patients either currently or on past they were smokers with only 4 patients are alcoholic (Table 1).

Table 1: Demographic characteristics of patients (N=50)

Variable	Data
Age, yeas	
Mean ± SD	59 ± 11.27
Range	38 – 93
< 60 years	22 (44%)
≥ 60 years	28(56%)
Sex	
Male	31 (62%)
Female	19 (38%)
Past medical history	
Hypertension	40 (80%)
Hypercholesterolemia	7 (14%)
Previous ICH	0
Diabetes	18 (36%)
Cardiac diseases	6 (12%)
Atrial fibrillation	1 (2%)
Anticoagulation use	
AOAC	2 (4%)
Cigarette smoking	
Never	31 (62%)
Past	9 (18%)
Current	10 (20%)
Alcohol	
Yes	4 (8%)

Site intracerebral haemorrhage

For the site of intracerebral haemorrhage, the majority of patients (60%) presented with deep intracerebral haemorrhage, followed by lobar and intraventricular intracerebral haemorrhage (Figure 1).

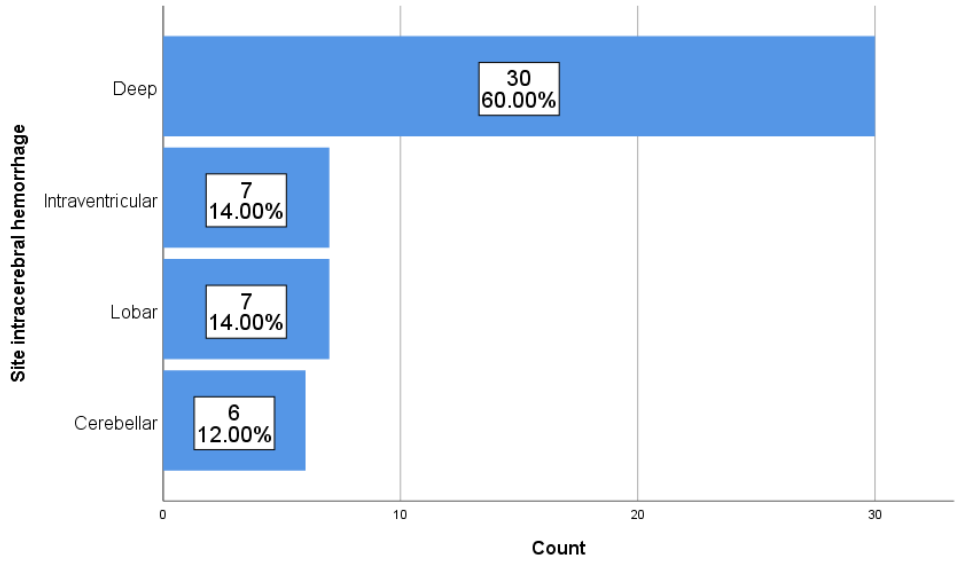

Figure 1: Distribution of the sample based on site of intracerebral haemorrhage (N=50)

Trigger Factors

The incidence of trigger factors was (48%), in which the trigger factors was presented among 24 (48%) patients (Figure 2).

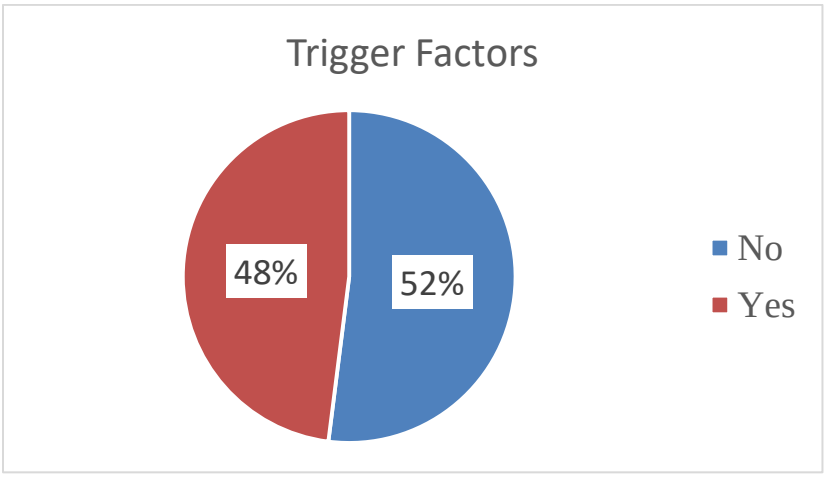

Figure2: Presence of trigger factors among studied patients (N=50)

The most frequent trigger factor presented among studied patients was Valsalva maneuvers in which it was presented among 9 (18%) of patients. Flu-like disease or fever was presented as trigger factor among 7 (14%) patients. The sICH was triggered by strong emotions among 5 (10%) patients and by sexual activity among 3 (6%) patients (Table 2).

Table 2: Trigger Factors for ICH (N=50)

Trigger factor	Count (%)
Strong emotions	5 (10%)
Sexual activity	3 (6%)
Flu-like disease or fever	7 (14%)
Valsalva maneuvers	9 (18%)
Coughing	4 (8%)
Lifting > 25 Kg	1 (2%)
Straining for defecation	4 (8%)
No	26 (52%)

Factors associated with Trigger factors

The assessment of trigger factors showed that only hypertension was associated significantly with trigger factors in which presence of hypertension may aggravate the IHC in presence of trigger factors (p=0.041) (Table 3).

Table 3: Factors associated with Trigger factors

		Trigger Factors				
		No (N=26)		Yes (N=24)		
		Count	%	Count	%	P value
Age	< 60 years	11	42.3%	11	45.8%	0.8
	≥ 60 years	15	57.7%	13	54.2%	
gender	Female	12	46.2%	7	29.2%	0.21
	Male	14	53.8%	17	70.8%	
Site intracerebral hemorrhage	Cerebellar	5	19.2%	1	4.2%	0.25
	Deep	15	57.7%	15	62.5%	
	Intravent.	4	15.4%	3	12.5%	
	Lobar	2	7.7%	5	20.8%	
Hypertension	No	8	30.8%	2	8.3%	**0.041**
	Yes	18	69.2%	22	91.7%	
Hypercholesterolemia	No	24	92.3%	19	79.2%	0.18
	Yes	2	7.7%	5	20.8%	
Diabetes	No	19	73.1%	13	54.2%	0.16
	Yes	7	26.9%	11	45.8%	
Cardiac disease	No	22	84.6%	22	91.7%	0.44
	Yes	4	15.4%	2	8.3%	
Atrial fibrillation	No	26	100.0%	23	95.8%	0.29
	Yes	0	0.0%	1	4.2%	
Anticoagulation use	No	24	92.3%	24	100.0 %	0.16
	NOAC	2	7.7%	0	0.0%	
Cigarette smoking	Current	4	15.4%	6	25.0%	0.23
	Never	19	73.1%	12	50.0%	
	Past	3	11.5%	6	25.0%	
Alcohol	No	24	92.3%	22	91.7%	0.93
	Yes	2	7.7%	2	8.3%	

Discussion

In this study, the average age of individuals experiencing sICH was 59 years, closely aligning with findings from a 2017 Iraqi study by Salman BH et al., which reported a mean age of 60 years.[11] Notably, 60% of patients in Salman BH et al.'s study experienced sICH before the age of 55.[11] This consistency in average age highlights the reliability and comparability of findings between the current research and prior Iraqi studies. Similarly, Van Etten et al. documented a mean age of 64 years among sICH patients, further aligning with the demographic trends observed in this study.[12] The agreement across these studies underscores the generalizability and consistency of age-related findings in sICH research across diverse populations.

The sex distribution in this study, with 60% of patients being male, mirrors the findings of both Salman BH et al. and Van Etten et al., which also reported a male predominance in sICH cases.[10,11] In this study, hypertension was identified in 80% of the examined sample, aligning with findings from Bahrami M et al., who reported hypertension in 60% of their participants.[13] Their study also concluded that hypertension was the most prevalent medical condition significantly associated with hemorrhage. This consistent prevalence across studies highlights the critical role of hypertension as a major risk factor for intracerebral hemorrhage.[13]

Epidemiological studies in the United States have reported a spontaneous intracerebral hemorrhage prevalence of approximately 9 per 100,000 people per year.[14] Notably, 70% to 90% of individuals with sICH have a history of hypertension.[15]

In this study, the majority of intracerebral hemorrhage cases (60%) were located in deep brain regions, followed by lobar and intraventricular ICH. This pattern contrasts with findings by Van Etten et al., who reported a higher prevalence of lobar ICH (45%), with 40% deep ICH, 13% cerebellar ICH, and 2% intraventricular hemorrhage.[12] The observed discrepancy in the distribution of ICH locations highlights the variability in the anatomical presentation of the condition across different populations and studies. The predominance of deep ICH in the current study may reflect demographic and clinical differences, such as a higher prevalence of hypertension in the studied population. Hypertensive small vessel disease, a common underlying pathology in deep ICH, is strongly associated with chronic hypertension, which was prevalent in 80% of the current cohort. In contrast, the higher occurrence of lobar ICH reported by Van Etten et al. may be linked to a greater incidence of cerebral amyloid angiopathy or other vascular pathologies in their population.[12]

The incidence of trigger factors contributing to sICH among patients in this study was 48%, closely aligning with findings by Van Etten et al., who reported trigger factors in approximately 42% of their cohort.[12] Similarly, a study by Vlak MH et al. identified trigger factors in 30% of patients with ruptured intracranial aneurysms, highlighting their significant role in cerebrovascular events.[16] In contrast, Na JH et al. observed a much lower prevalence of trigger factors, with only 6.6% of patients experiencing such events at the onset of hemorrhage.[17]

In this study, the most frequently identified trigger factor for spontaneous intracerebral hemorrhage was the Valsalva maneuver, reported in 9 individuals (18%). Flu-like illness or fever was identified in 7 patients (14%), while strong emotions and sexual activity were associated with sICH in 5 (10%) and 3 (6%) patients, respectively.

The prevalence of Valsalva maneuvers as a trigger in this study aligns with findings by Vlak MH et al.,[16] who identified similar triggers in approximately 15–20% of their cohort experiencing cerebrovascular events, particularly intracranial aneurysm rupture illness or fever, reported in 14% of patients here, is consistent with the systemic inflammatory conditions discussed by Feigin VL et al., which were shown to exacerbate vascular fragility and increase the risk of hemorrhage.[18] Emotion and physical exertion, including sexual activity, have also been recognized as notable triggers. For example, Passero S et al. reported emotional stress as a factor in 10–15% of cases, closely matching the findings of this study.[19]

The variability trigger factors across studies can be attributed to differences in study populations, methodologies, and regional or cultural influences. For instance, Na JH et al. identified a significantly lower prevalence of trigger factors (6.6%), likely due to recall bias, as their study spanned a nine-year period, leading to potential inaccuracies in event recollection.[17] In contrast, the short time frame in the present study enhances the accuracy of reporting, minimizing recall bias and providing a clearer representation of acute triggers.

In the assessment of trigger factors for spontaneous intracerebral hemorrhage, this study found that hypertension was the only factor significantly associated with triggering events. This finding suggests that hypertension may exacerbate the risk of intracerebral hemorrhage in the presence of specific triggers. This result aligns with the study by Na JH et al., which similarly reported no significant associations between other known risk factors for intracranial hemorrhage and triggering events.[17] Additionally, Nguyen B et al. found no notable association between physical activity at work and sICH, further supporting the complexity of identifying direct links between trigger factors and hemorrhagic events.[20]

Interestingly, Passero et al. analyzed 848 patients with intracerebral hemorrhage and identified a significant association between hypertensive intracerebral hemorrhage and moderate or heavy physical exertion.[19] This finding is consistent with the current study and highlights that, in specific instances, exertion may act as a trigger for intracerebral hemorrhage, particularly when hypertension is present.

Conclusion

This study highlights that nearly half of spontaneous intracerebral hemorrhage (sICH) cases were associated with identifiable triggers, with Valsalva maneuvers being the most common. Hypertension emerged as the strongest risk factor, significantly linked to trigger-induced sICH and deep hemorrhages, emphasizing its role in disease pathogenesis.

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Author contributions: Both authors contributed to this study.

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