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Association of Seizure in Functional Outcome of Spontaneous Intracerebral Haemorrhage

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ABSTRACT

Background: Spontaneous intracerebral hemorrhage (sICH) is a severe and life-threatening condition, characterized by bigh mortality and morbidity rates. Seizures often complicate the acute phase of sICH, and understanding the impact of seizures on outcomes is limited. Appropriate addressing seizures in sICH improve functional outcomes.

Objectives of the study: To see association of seizure in functional outcome of spontaneous intracerebral haemorrhage.

Materials and Methods: A prospective longitudinal study was conducted at the Stroke Clinic, Stroke Centre, Indoor, EEG Lab of the Department of Neurology and Indoor, Emergency of the Department of Neurosurgery at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The study included 66 patients with spontaneous intracerebral hemorrhage (sICH) aged 18 years or older who were consecutively recruited during the study period. Data was analyzed using SPSS version 21, with statistical tests including chi-square and t-tests as appropriate.

Result: The study result reveals that slCH with seizure associated with poor outcome. Disorientation (15.6% vs. 93.8%, p<0.001), hyponatremia (15.6% vs. 37.5%, p <0.048), pneumonia (25.0% vs. 6.3%, p=0.039) were more common in patients of sICH with seizure than witout seizure and has impact on functional outcome. According to a multivariate logistic regression analysis, seizures, disorientation, hypertension, high NIHSS score, hyponatremia, and intraventricular extension were significant predictors of poor outcome in patients with spontaneous intracerebral hemorrhage with seizure.

Conclusion: Patients of spontaneous intracerebral hemorrhage with seizures exhibited more severe neurological impairments and poorer outcomes compared to those without seizures.

Keywords: *Spontaneous intracerebral hemorrhage (sICH), seizure, outcome, risk factors, modified rankin scale (mRS)*

1. INTRODUCTION

Spontaneous intracerebral haemorrhage (sICH) is a stroke subtype associated with poor prognosis and high mortality. Seizure is a significant complication of ICH [1]. Post-stroke seizure is more often observed in patients with intracerebral haemorrhage (sICH) than with ischemic stroke and early post-ICH seizures were associated with greater stroke severity, larger brain lesions and more lobar haemorrhage [2,3]. Worldwide stroke is the second leading cause of death and the most common cause of severe disability [4] (Johnson et al. 2016). World Health Organization fact sheet revealed that, worldwide more than 5 million deaths occurred due to stroke [5] (World Health Organization, 2019). Over the last four decades, the incidence of stroke in low- and middle-income countries has become more than double [6]. In Bangladesh the high number of disabilities adjusted life-years lost due to stroke shows that stroke severely impacts on our economy [7]. Stroke is classified broadly into two categories; ischemic stroke and haemorrhagic stroke. Haemorrhagic stroke occurs due to rupture of blood vessel leading spillage of blood in the intracranial cavity. Depending on the site of blood spillage the haemorrhagic stroke can be classified as intracerebral haemorrhage (ICH) and subarachnoid haemorrhage [8]. Intracerebral haemorrhage (ICH) accounts for 10-15% of all strokes and results in death or severe disability in more than 60% of patients [9]. (poon et al.,2013). The acute phase of spontaneous intracerebral haemorrhage (sICH) is often complicated by seizures, likely reflecting the disruptive effect on neuronal networks of the haematoma and surrounding edema [10]. Seizures occur in approximately 4 to 14% of patients with acute spontaneous intracerebral haemorrhage (sICH) [11]. The incidence of seizure is approximately 30% when subclinical or non-convulsive seizures are diagnosed by continuous electroencephalogram (EEG) [12]. Younger age, lobar haematoma, stroke severity and haematoma expansion have been identified as risk factors for early seizures after sICH [13]. In patients with early seizures, larger haematoma and intraventricular haemorrhage volume, lobar location and lower Glasgow Coma Scale increase the risk of recurrent seizures beyond 7 days [14]. Similarly, cortical involvement, younger age and larger haematoma volume increase the risk of late-onset seizures [15]. Some previous reports have demonstrated the effect of seizures on the outcome with small patient populations [16,17,18] but the significance of seizures for the outcome, their prevention and their association with other complications were matters that remained unclear. The impact of early seizures on outcomes in sICH is debatable. Several studies reported an increased in-patient and 30-day mortality rate, two to three-fold higher in patients with seizures compared to those with no seizures [19]. Early seizure is associated with a worse clinical outcome. Future research on prevention and treatment of early seizure after sICH should consider focus on patients with lobar sICH. We aimed to find out the effect of post-sICH seizure on clinical outcomes.

Methodology

Study setting and population

This study was designed as a prospective longituidinal study. This study was carried out from May 2023 to September 2024. The Study was conducted in the Stroke clinic, Stroke centre and emergency, Indoor, EEG lab of Department of Neurology and Indoor and Emergency of Department of Neurosurgery, BSMMU. All the patients diagnosed with spontaneous ICH aged more than 18 years of both sexes were the study popularion. Subject are selected by non randomized sampling method.

Study Procedure

Patients with spontaneous intracerebral haemorrhage (ICH) were recruited based on predetermined inclusion and exclusion criteria following ethical clearance from the Institutional Review Board (IRB). Every patient ce their authorised representative provided written informed consent. With the aid of a standardised checklist that asked questions about focal, generalised, and other types of seizures, patient histories involving seizures were gathered. Seizures were diagnosed based on video evidence, family members or emergency personnel's credible testimonies, or direct observation by a doctor during hospitalisation.

An electroencephalogram (EEG) was carried out when practical in a few chosen instances after admission, albeit it was not required for study inclusion. Following a thorough physical and neurological assessment of each participant, patients were divided into two groups those with seizure and without seizure

Data Collection

A semi-structured data collection sheet was developed to align with the study's objectives, undergoing modifications before finalization. Participants received a detailed explanation of the study and provided informed written consent prior to data collection. The collected data encompassed demographic details, medical histories, examination findings, and relevant laboratory, radiological, and electrographic records. This data was documented on the collection sheet, with preserved copies

maintained. Face-to-face interviews were conducted to gather focused histories and complete clinical examinations. The modified Rankin Scale (mRS) scores were recorded at 7 and 90 days post-sICH, obtained through either in-person or telephone interviews. To maintain data reliability, a single interviewer completed all questionnaires.

Data Processing and Data Analysis

All the data were checked and edited after collection. Patients was divided into two groups, one is sICH with seizure and another is sICH without seizure. Two groups was compared by means of outcome. Continuous variables were expressed as Mean ± SD. Categorical variable were presented by frequency, percentage and graph. Qualitative data (NIHSS, mRS, Functional outcome) was analyzed by chi square test. Quantitative data (Age, Blood pressure) and comparartive analysis was by t test. The cut off for statistical significance was set at $p<0.05$ for all of the data analysis. Statistical analysis was done using SPSS (Statistical package for social sciences) win version 21.

Ethical Consideration

The study protocol involving human subjects received approval from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), resulting in a certificate of ethical clearance. Participants were informed about the study's aims, objectives, procedures, risks, and benefits in clear, local language. Informed written consent was secured from all respondents, ensuring the confidentiality of their information and records.

2. RESULT AND OBSERVATION

This was a hospital-based prospective longituidinal study conducted at Department of Neurology. Bangabandhu Sheikh Mujib Medical University Dhaka. After careful history taking, examination and appropriate investigations fulfilling inclusion and exclusion criteria, a total of 64 patients diagnosed as spontaneous intracerebral hemorrhage (sICH) were enrolled in the study. The aim of study was comparison of functional outcome of spontaneous intracerebral haemorrhage with and without seizure.

Table-1: Demographic characteristics and clinical profile of the study subjects (N=64)

Variables	sICH without Seizure (n=32)		sICH with Seizure (n=32)		p-value
	n	(%)	n	(%)	
Age group (year)					
≤30	0	0.0%	2	6.3%	
31-40	2	6.3%	2	6.3%	
41-50	10	31.3%	6	18.8%	
51-60	7	21.9%	4	12.5%	
≥60	9	28.1%	13	40.6%	
Mean±SD	58.2±12.4		59.5±15.3		0.708
Range (min-max)	(32-87)		(20-82)		
Sex					
Male	18	56.30%	21	65.6%	0.442
Female	14	43.80%	11	34.4%	
Clinical profile					
Hemiparesis	32	100.0%	30	93.8%	0.081
Headache	28	87.5%	22	68.8%	
Nausea and vomiting	3	9.4%	8	25.0%	
Dysphasia	2	6.3%	0	0.0%	
Disorientation	5	15.6%	30	93.8%	
Vertigo	3	9.4%	8	25.0%	
Other	0	0.0%	1	3.1%	

p-value obtained by Unpaired t-test and Chi-square test, p<0.05 was considered as a level of significant

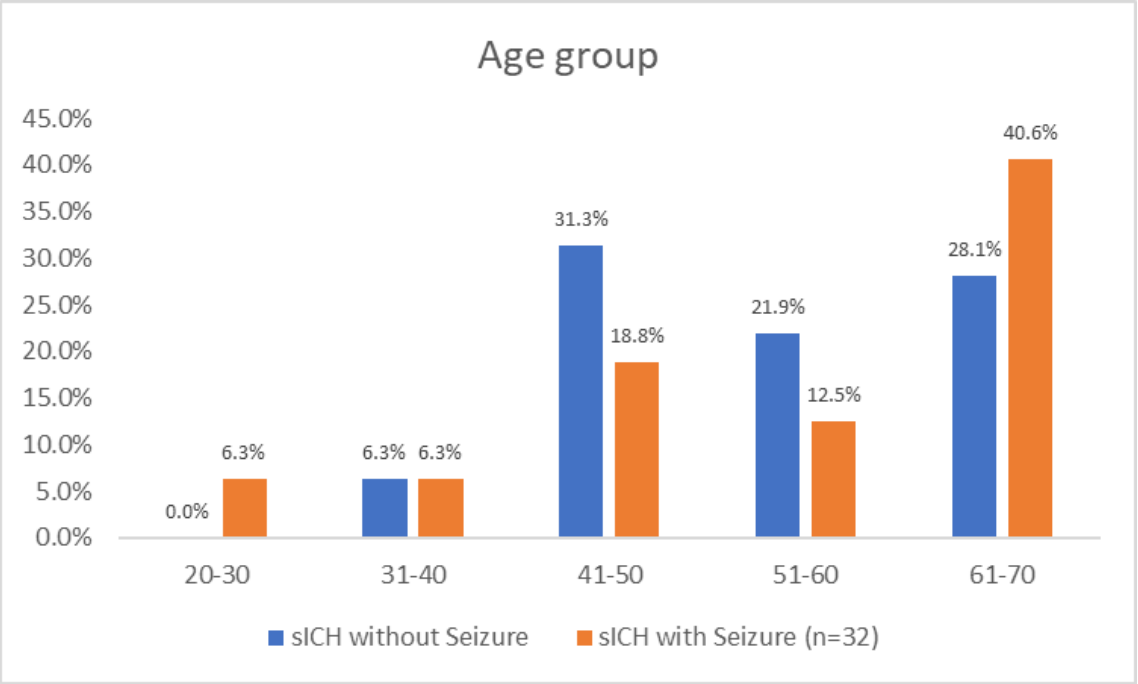

Figure-1: Age distribution of participants between two groups (N = 64)

The study examined the demographics and symptoms of participants with spontaneous intracerebral hemorrhage (sICH), comparing those with seizures to those without. No significant differences were found in age ($p = 0.708$) or sex ($p = 0.442$); however, age distribution differed significantly ($p < 0.05$) and occupation differences were nearly significant ($p = 0.081$). A greater percentage of participants aged 61 to 70 had seizures (40.6%) compared to 28.1% without seizures, and 28.1% of the seizure group were involved in agriculture versus 9.4% in the non-seizure group, indicating potential demographic disparities warranting further research.

Additionally, disorientation occurred significantly more in patients with seizures (93.8%) compared to those without (15.6%, $p < 0.001$). Other symptoms such as headache, nausea, vertigo, dysphasia, and hemiparesis showed no significant differences between groups, suggesting that while headaches and hemiparesis are more common in sICH patients without seizures, disorientation is a key feature associated with seizure activity.

Table-2: Comparison of GCS score between SICH without seizure and SICH with seizure (N=64)

GCS	sICH without Seizure		sICH with Seizure		p-value
	(n=32)		(n=32)		
	Mean±SD		Mean±SD		
	n	(%)	n	(%)	
15	27	84.4%	10	31.3%	<0.001*
12-14	5	15.6%	20	62.5%	
8-11	0	0.0%	2	6.3%	
<8	0	0.0%	0	0.0%	
Total	32	100.0%	32	100.0%	

p-value obtained by Chi-square test, p<0.05 was considered as a level of significant

A comparison of Glasgow Coma Scale (GCS) scores in patients with spontaneous intracerebral hemorrhage (sICH) shows that those with seizures exhibit significantly lower scores ($p < 0.003$). Among patients with seizures, 43.8% had GCS scores between 9 and 12, compared to only 15.6% in those without seizures. Additionally, 43.8% of seizure patients scored 13 or higher, in contrast to 84.4% of non-seizure patients. These results indicate that sICH patients experiencing seizures generally have more severe impairments in brain function and consciousness, as reflected in their lower GCS scores.

Table-3: Comparison of complications between SICH without seizure and sICH with selzure (N-64)

Complications	sICH without Seizure		sICH with Seizure		p-value
	(n=32)		(n=32)		
	Mean±SD		Mean±SD		
	n	(%)	n	(%)	
UTI	7	21.90%	11	34.4%	0.266
Pneumonia	2	6.30%	8	25.0%	0.039
Hyponatremia	5	15.60%	12	37.5%	0.048
Bed sore	5	15.60%	9	28.1%	0.266

p-value obtained by Chi-square test, $p<0.05$ was considered as a level of significant

Patients with spontaneous intracerebral hemorrhage (sICH) who had seizures exhibited a greater risk of complications than those without seizures. Specifically, hyponatremia was present in 37.5% of the seizure group compared to 15.6% in the non-seizure group ($p = 0.048$), and pneumonia was reported in 25.0% of those with seizures versus 6.3% without ($p = 0.039$). No significant differences were observed in the rates of bed sores or urinary tract infections (UTIs) between the groups. Overall, the findings suggest that respiratory and electrolyte-related complications are more prevalent among sICH patients who experience seizures.

Table-4: Characterstics of sICH patient with and without seizure [N-64].

Hematoma Location	sICH without Seizure		sICH with Seizure		p-value
	(n=32)		(n=32)		
	Mean±SD		Mean±SD		
	n	(%)	n	(%)	
Lobar	1	3.1%	17	53.1%	<0.001*
Deep	30	93.8%	14	43.8%	
Cerebellar	1	3.1%	0	0.0%	
Brainstem	0	0.0%	1	3.1%	
Hematoma volume (cm^3)	35.48±4.06		43.27±4.93		<0.001*
Intraventricular extension					
Yes	6	18.8%	9	28.1%	<0.001*
No	26	81.3%	23	71.9%	
Midline shifting					
Yes	5		15		<0.007*
no	27		17		

p-value obtained by Chi-square test, $p<0.05$ was considered as a level of significant

Significant changes in haematoma features were found in a study comparing 64 individuals with spontaneous intracerebral haemorrhage (sICH) who had seizures with those who did not. Lobar haematomas were more common in seizure patients

(53.1%) than in non-seizure patients (3.1%); deep haemorrhages were more common in non-seizure patients (93.8%) than in seizure patients (43.8%), (p <0011). Furthermore, there was a significant difference (p <.001) in the mean haematoma volume between the patients who experienced seizures (M = 43.27, SD = 4.93) and those who did not (M = 35.48, SD = 4.06). Additionally, intraventricular extension was observed in 28.1% of patients with seizures versus 18.8% of patients without seizures, (p <.001). Additionally, midline displacement was more prevalent in seizure patients (46.9%) as opposed to non-seizures (15.6%) (p <.007) which is statistically significant. These results imply that particular haematoma characteristics are associated with seizures in Individuals with sICH, indicating the necessity for customised clinical care approaches.

Table-5; Comparison of mRS score at 90 days between sICH without seizure and sICH with seizure (N=64)

mRS at day 90	sICH without Seizure (n=32)		sICH with Seizure (n=32)		p-value
	n	(%)	n	(%)	
Good outcome (mRS: 0-2)	27	90.0%	9	28.1%	<0.001
Poor outcome (mRS: 3-6)	3	10.0%	23	71.9%	

p-value obtained by Chi-square test, p<0.05 was considered as a level of significant

According to their prior seizure history, patients with spontaneous intracerebral haemorrhage (sICH) (n = 32) were evaluated using modified Rankin Scale (mRS) ratings at 90 days. The functional outcomes revealed a considerable disparity: 87.5% of patients without seizures had favourable outcomes (mRS: 0-2), while only 28.1% of patients with seizures met this criteria (chi^2(1) 24.46, p<.001). Furthermore, only 12.5% of patients without seizures experienced poor outcomes (mRS: 3-6), compared to 71.9% of seizure patients.

Discussion

This study highlights critical demographic and clinical differences between participants with Spontaneous intracerebral hemorrhage (sICH) who experience seizures and those who do not. Despite no significant differences in age and sex, a significant difference in age distribution (p <0.05) and near-significant occupational disparities (p = 0.081) suggest that certain demographic factors may influence seizure occurrence. The higher incidence of seizures in the 61 to 70 age group and among individuals engaged in agriculture warrants further exploration of lifestyle or environmental risks [20].

Clinically, disorientation emerged as significant symptom in seizure patients (93.8% vs. 15.6%, p < 0.001), while other symptoms such as headache and hemiparesis did not show significant variation across groups. This finding emphasizes the importance of disorientation as a distinguishing feature of seizure activity in SICH patients. Conversely, headaches and hemiparesis appeared more prevalent inwithout seizure patients, indicating different clinical trajectories based on seizure status [21].

The results of this study demonstrate that patients with spontaneous intracerebral hemorrhage (sICH) who experience seizures have significantly lower Glasgow Coma Scale (GCS) scores (p < 0.003). Specifically, 43.8% of seizure patients scored between 9 and 12, indicating moderate to severe impairment, while only 15.6% of non-seizure patients fell within this range. Conversely, a substantial majority of without seizure patients (84.4%) exhibited GCS scores of 13 or higher, reflecting better neurological status. These findings underscore the association between seizure activity and heightened severity of brain dysfunction in SICH patients, suggesting that seizures may further compromise consciousness and neurological outcomes [12,10].

The findings of this study indicate that patients with spontaneous intracerebral hemorrhage (sICH) who experience seizures are at a heightened risk for specific complications, particularly hyponatremia and pneumonia. The prevalence of hyponatremia was significantly higher in the seizure group (37.5%) compared to the without seizure group (15.6%, p = 0.048) as was pneumonia, affecting 25.0% of the seizure patients versus 6.3% of those without seizures (p = 0.039). These results highlight the importance of monitoring for respiratory and electrolyte disturbances in sICH patients presenting with seizures, as these complications can substantially impact patient outcomes. However, no significant differences were identified for bed sores or urinary tract infections, suggesting that further research is needed to explore all potential

complications in this population [22].

The current study reveals significant differences in hematoma characteristics between patients with spontaneous intracerebral hemorrhage (sICH) who experience seizures and those who do not. Notably, lobar hematomas were more prevalent in seizure patients (53.1%) compared to only 3.1% in non-seizure individuals, while deep hemorrhages were predominantly found in non-seizure patients (93.8% versus 43.8%, $p < 0.001$). Additionally, seizure patients exhibited a greater mean hematoma volume ($M = 43.27$, $SD = 4.93$) compared to their non-seizure counterparts ($M = 35.48$, $SD = 4.06$) highlighting the severity associated with seizures. Intraventricular extension and midline displacement were also more common in seizure patients (28.1% and 46.9% respectively) compared to those without seizures. These findings suggest specific hematoma characteristics linked to seizures in sICH, underscoring the need for tailored clinical management strategies to address the unique risks posed by these complications [23,24].

The findings of this study underscore the significant impact of seizure history on functional outcomes in patients with spontaneous intracerebral hemorrhage (sICH). A stark contrast was observed in outcomes as measured by the modified Rankin Scale (mRS): 87.5% of patients without seizures experienced favorable outcomes (mRS 0-2), compared to only 28.1% of those with seizures, reflecting a profound disparity (chi ^ 2 (1) = 24.46, $p < 0.001$). Moreover, seizure patients demonstrated a markedly higher likelihood of poor outcomes, with a multivariate logistic regression indicating they were 2.714 times more likely to have unfavorable results ($p = 0.044$). Additional risk factors, including disorientation and hypertension, further contributed to adverse outcomes. Notably, hyponatremia and intraventricular extension also showed their importance in predicting complications, with odds ratios supporting their associations. This study emphasizes the necessity for careful monitoring and tailored interventions for SICH patients, particularly those presenting with seizure activity and other identified risk factors [25].

Conclusion

The study identifies the sICH with seizure patients showed higher rates of disorientation, greater neurological impairment indicated by lower Glasgow Coma Scale scores, and an increased risk of complications like hyponatremia and pneumonia. Additionally, these patients had specific hematoma characteristics, including a higher prevalence of lobar hemorrhages and larger hematoma volumes. The findings emphasize the need to recognize seizure activity in sICH cases due to its association with worse outcomes and the need for appropriate clinical management strategies to enhance patient care.

Ethical Issue: All patients gave informed written consent and the study was approved by Institutional Review Board of Bangabandhu Sheikh Mujib Medical University.

Conflict of Interest: None

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