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Complications and Outcome of Primary Intracerebral Hemorrhage at a Tertiary Care Hospital in Bangladesh: A Follow Up Study

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Abstract

Background: Patient admitted with hemorrhagic stroke, particularly primary intracerebral hemorrhage (ICH) may develop different form of complications during their hospital stay. **Objective:** The objectives of the study were to find out the different complications of primary intracerebral hemorrhage among admitted patient and their effect on hospital stay and outcome. **Methodology:** This was a hospital based observational follow up study conducted at National Institute of Neurosciences and Hospital, Dhaka, Bangladesh in a period of 18 months (from February 2021 to August 2022). Total 570 (504 finally analyzed) primary intracerebral hemorrhage patient who admitted within 48 hours of onset of stroke were enrolled consecutively by purposive sampling method. Routine biochemical, hematological tests and computed tomography scan were done to all participants. All patients were followed up every day during hospital stay and any complication developed were noted. Patients' outcome (discharge / death) was recorded. **Results:** This study revealed that mean (SD) age of participants were 59.1 (±13.4) years with majority male 262(52.0%). Electrolyte imbalance (hyponatremia) was the commonest complication found in 212 (62.7%) of patient followed by hematoma expansion 27.8%, hydrocephalus 23.0%, aspiration pneumonia 16.5%, convulsive seizure 14.7%, urinary tract infection and pressure sore both are 5.3%. Deep vein thrombosis was found in1.7%. Hypertension was the commonest risk factor (93.0%) followed by Diabetes mellitus (28.1%). Older (>50 years) age (OR: 0.53; 95% CI: 0.36-0.80; p = 0.002), urban dwellers (OR: 1.56; 95% CI: 1.04-2.27; p =0.013) and poor (<9.0) admission Glasgow Coma Scale (GCS) were associated with higher rate of complications (p = 0.001). Presence of Hydrocephalus (OR:0.66; 95% CI: 0.48-0.90; p = 0.001), Aspiration pneumonia (OR:0.53; 95% CI:0.99-0.73; p=0.0001), and convulsive seizure (OR: 0.63; 95% CI: 0.44-0.89; p=0.015) were associated with higher mortality. During hospital stay different form of complications developed in 338(67.0%) of patients and 356(70.6%) of patient discharged to home successfully. Different form of complication leads to longer hospital stay (p = 0.001) and higher mortality rate (p = 0.001) compared to those who developed no complication. **Conclusion:** Hyponatremia is the most common complication followed by hematoma expansion and hydrocephalus. Longer hospital stays and higher incidence of mortality was observed in patients who developed in-hospital complication after the stroke event. *[Journal of National Institute of Neurosciences Bangladesh, July 2024;10(2):87-93]*

Keywords: Intracerebral hemorrhage; ICH; complications; hematoma expansion; hydrocephalus; hyponatremia

Introduction

Primary intracerebral hemorrhage (ICH) is a major cause of morbidity and mortality, accounting for 10.0% to 30.0% of first-ever strokes worldwide[1]. Spontaneous intracerebral hemorrhage (ICH) affects globally more than 5 million patients per year[2]. ICH has a 40.0% to 50.0% mortality rate within 30 days, twice that of ischemic stroke[3] with half of the deaths occur in the acute phase, especially in the first 48 hour[4]. Among all the neurologic diseases of adult life, stroke ranks first in frequency and importance. Stroke causes significant physical, emotional, and cognitive disabilities among

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survivors, accounting for 3.6% of the total disability-adjusted life years (DALYs)[5]. Only 27.0% of ICH patients become functionally independent at 90 days[6]. The incidence of ICH is higher in Asian countries compared to Western populations[7].

Complications after ICH are common during acute phase of stroke care but are potentially preventable or treatable and have a significant impact on mortality and optimal recovery. The frequency of complications ranges from 40.0% to 96.0% of stroke patients[8]. Common complications of ICH includes haematoma expansion (HE), perihaematomal oedema (PHE), intraventricular extension of haemorrhage (IVH) with hydrocephalus (HCP), seizures, venous thromboembolic events (VTE), hyperglycemia, increased blood pressure (BP), infections[1], pressure sore/skin break[5] and electrolyte imbalance[9]. Complications such as HE, IVH with obstructive hydrocephalus and hyperglycemia are major predictors of increased early mortality and adverse outcome during the hyperacute phase of ICH.

Similarly, haematoma expansion, hydrocephalus, and perihaematomal oedema have been associated with early neurological deterioration and poor outcome[10]. The complications of ischaemic stroke (IS) and their management have been studied extensively[11], but there is little advancement about the complications of ICH and their evidence-based management. Despite its seriousness, the treatment options for ICH are limited and generally supportive. Therefore, prevention of complications should be the main strategies to minimize morbidity and mortality and improve quality of life among stroke survivors. There are few studies found regarding incidence, prevalence and risk factors of stroke in Bangladesh[12,13,14]. A population-based cross-sectional study shows prevalence of stroke in Bangladesh is 11.39 per 1000 population with mean age 39.9 and higher prevalence in the elderly and male people[13]. To my knowledge there is no study in Bangladesh regarding complications of stroke patient. Therefore, the current study is intended to identify the common complications of primary intracerebral haemorrhage and their effect on outcome among hospital admitted patient.

Methodology

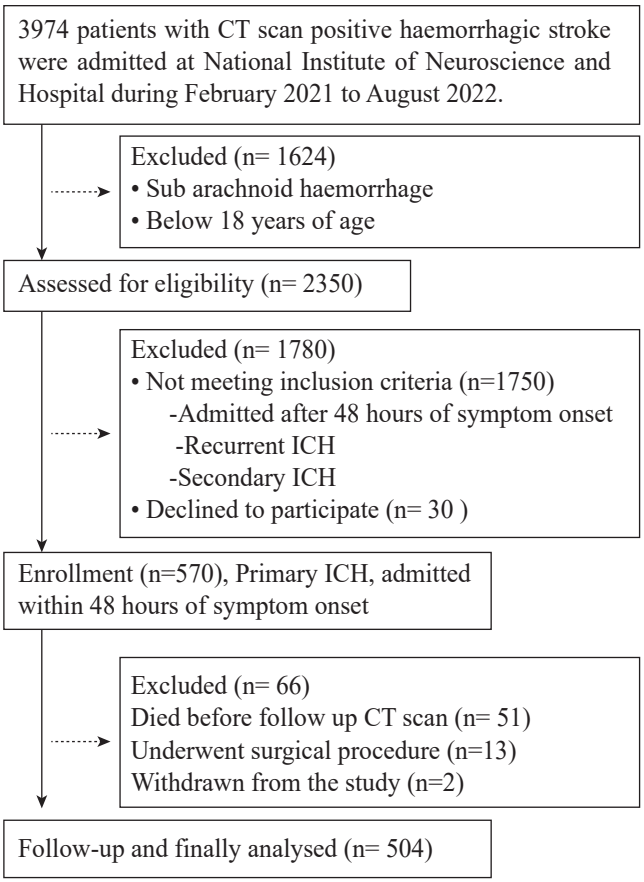
Study Population & Settings: This Prospective follow up study was conducted at National Institute of Neurosciences and Hospital, which is a tertiary care specialized neurosciences center provide care for neurology and neurosurgical cases, Dhaka, Bangladesh in a period of 18 months from February 2021 to August 2022. All patients who were diagnosed as primary intracerebral hemorrhage (ICH) based on clinical features and computed tomography (CT) scan images performed by 124 slice CT scanner made by siemens Japan, were selected for study subjects (n=2350). Among them 570 individuals of primary ICH who admitted within 48 hours of symptom onset were enrolled. Those having recurrent and/or secondary ICH like ICH due to ruptured arteriovenous malformation, bleeding diatheses or hemorrhagic transformation of infarct were excluded (n=1780).

Study Procedure: In this study Hemorrhage volume was calculated according to the ABC/2 formula, where A=longest diameter, B=diameter perpendicular to A, and C=number of slices multiplied by their thickness. Hematoma expansion was defined as an increase in volume of 33–50% or an absolute change in hematoma volume of 12.5–20 mL (on repeat CT scan)[1], Convulsive seizure as Clinical diagnosis of focal and/or generalized seizure in a previously non epileptic patient, Aspiration Pneumonia as auscultatory respiratory crackles and fever or radiographic evidence or new purulent sputum, Urinary tract infection as presence of pus cell more than 05 per high power field on urine routine test or positive urine culture, Pressure sore as any skin break or necrosis resulting from either pressure or trivial trauma[6]. Venous thrombosis was defined by clinical DVT prediction score (Wells score) combined with elevated D-dimer in a suspected case. Electrolyte imbalance was categorized as either hyponatremia (serum Na+ <135 mmol/L), or hypernatremia (serum Na+ >145 mmol/L), or hypokalemia (serum K+ <3.5 mmol/L) or hyperkalemia (serum K+>5.5 mmol/L. In noncomatous patients' hydrocephalus was considered as clinical deterioration (like deterioration from somnolence to stupor) and enlargement of temporal horns more than 2 mm and in comatose patients the enlargement of temporal horns was defined as hydrocephalus . History taking, focusing on demographic (age, gender, residence) and clinical variables and risk factors such as hypertension, diabetes, smoking, alcohol consumption and the use of anti-platelet or anticoagulant drugs were recorded by face-to-face interview and evaluating medical records. Physical examination was done as per standard protocol. Management of ICH was done on prevailing stroke guidelines in timely manner. Routine hematological and biochemical (complete blood count, Random blood glucose, serum creatinine, serum electrolytes), Electrocardiogram, Chest X-ray, Urine routine examination and CT scan of head done to all patient. Follow up CT scan and serum electrolyte were

done to every participant at 48 hours from baseline tests. Coagulation profile (such as bleeding time, clotting time, prothrombin time with international normalized ratio and activated partial thromboplastin time), Urine culture and repeat Chest X-ray were done when indicated.

Follow Up and Outcome Measures: All participants were followed up every day during hospital stay and complications if any were recorded. Those participants died before follow up CT scan and getting surgical treatment after enrollment were excluded from analysis. Patients' outcome (discharge or death) was also recorded. Variables related to hemorrhage (Hematoma expansion and Hydrocephalus) were recorded based on the initial and follow up CT scan of brain result. Two participants were withdrawn from the study and finally, 504 participants were analyzed who completed the follow up.

Figure I: CONSORT Flow Chart



Statistical Analysis: The data analysis was performed using standard statistical procedures by STATA 16. Quantitative data were expressed as mean and standard deviation while qualitative data were expressed as frequency and percentage. For continuous variables, comparison between groups was made by the students t-test. Categorical variables were analyzed by the Chi-square test. Statistical significance was accepted at $p < 0.05$.

Ethical Consideration: All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., Helsinki Declaration 2013) and also with the ethical guidelines of the Institutional research ethics. Formal ethics approval was granted by the local ethics committee. Participants in the study were informed about the procedure and purpose of the study and confidentiality of information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and were analyzed using the coding system.

Results

We enrolled 570 individuals between February 2021 and August 2022, of which 66 were excluded from this analysis (51 participants (8.9%) died before doing follow up CT scan, 13 participants (2.3%) underwent surgical procedures and 2 participants (0.35%)

Table 1: Main characteristics of 504 patient with primary intracerebral hemorrhage that were admitted in a specialized neurosciences hospital in Dhaka, Bangladesh during February 2021 to August 2022.

Characteristics	Values
Gender	
• Male	262 (52.0%)
• Female	242 (48.0%)
Age in years (mean±SD)	59.1±13.5
• ≤ 50 years	144 (28.6%)
• > 50 years	360 (71.4%)
Resident	
• Urban	292 (58.0%)
• Rural	212 (42.0%)
Risk factors	
• Hypertension	468 (93.0)
• Diabetes Mellitus	142 (28.1)
Admission GCS (mean±SD)	9.5 (2.9)
Hospital stays (mean±SD)	6.3 (3.6)
Hospital follow up	
• Complications developed	338 **(**67.0**%)**
• No complication	166 **(**33.0**%)**
Hospital Outcome	
• Discharge	356 (70.6%)
• Death	148 (29.4%)

withdrawn from the study). Mean (SD) age was 59.1 (±13.4) years. Males were more 262(52.0%) than female 242(48.0%). Maximum participants 360 (71.4%) were above 50 years of age. Majority of the study population resided in urban area 292 (58.0%). Hypertension was the commonest risk factor 468 (93.0%) followed by Diabetes mellitus 142 (28.1%). No identifiable risk factors were found in 6.0% of patients. Mean (SD) admission Glasgow coma scale was 9.5 (±2.9) (Table 1). Median (SD) hospital stay was 6.3 (±3.6) days and 356 (70.6%) of patient discharged to home successfully (Table 1).

Electrolyte imbalance was the commonest complication found in 212 (62.7%) of patient (hyponatremia is the more, 22.6% than hypokalemia, 11.5%), followed by hematoma expansion 94 (27.8%), hydrocephalus 78 (23.0%), aspiration pneumonia 56 (16.5%), convulsive seizure 50 (14.7%), urinary tract infection and pressure sore both are 18 (5.3%). Only six patient (1.7%) developed deep vein thrombosis (Table 2).

Older (>50 years) age (OR: 0.53; 95% CI: 0.36-0.80; p = 0.002), urban dwellers (OR: 1.56; 95% CI: 1.04-2.27; p =0.013) and poor (<9.0) admission Glasgow Coma Scale (GCS) were associated with higher rate of complications (p = 0.001). During hospital stay different form of complications developed in 338(67.0%) of patients which lead to longer hospital stay (p = 0.001) and higher mortality rate (p = 0.001) compared to those who developed no complication (Table 3).

Presence of Hydrocephalus (OR:0.66; 95% CI: 0.48-0.90; p = 0.001), Aspiration pneumonia (OR:0.53; 95% CI:0.99-0.73; p=0.0001), and convulsive seizure (OR: 0.63; 95% CI: 0.44-0.89; p=0.015) were associated with higher mortality. Though electrolyte imbalance was the commonest complication it was not associated with higher mortality (OR=1.15, 95% CI=0.78-1.70, p= 0.45). Other complications like Hematoma expansion (OR=0.84, p=0.17); DVT (0.88, p=0.56); and UTI (OR=0.88, p=0.44) were also not associated with higher hospital mortality (Table 4).

Table 2: Complications Developed After Admission in Hospital

Complications	Frequency	Percent
Electrolyte Imbalance		
• Hyponatremia	114	62.7
• Hypernatremia	8	1.6
• Hypokalemia	58	11.5
• Hyperkalemia	2	0.4
• Combined*	30	6.0
CT Scan findings		
• Hydrocephalus (HCP)	78	23.0
• Hematoma expansion (HE)	94	27.8
• Both HCP and HE	20	5.9
Infections		
• Aspiration pneumonia	56	16.5
• Urinary tract infection	18	5.3
Deep vein thrombosis	6	1.7
Convulsive seizure	50	14.7
Pressure sore	18	5.3

*Both hyponatremia and hypokalemia

Table 3: Baseline characteristics and complications developed during hospital stay

Characteristics	Overall	Complications N	No complications N	OR (95%CI)	P value
Age					
• <50 years	144	82(56.9%)	62(43.1%)	0.53(0.36-0.80)	0.002
• >50 years	360	256(71.1%)	104((28.9%)		
Gender					
• Male	262	172(65.6%)	90(34.4%)	0.87(0.60-1.27)	0.507
• Female	242	166(68.6%)	76(31.4%)		
Residence					
• Urban	292	208(71.2%)	84(28.8%)	1.56(1.04-2.27)	0.013
• Rural	212	130(61.3%)	82(38.7%)		
Hypertension	468	312(66.7%)	156(33.3%)	1.30(0.61-2.76)	0.314
DM	142	102(71.8%)	40(28.2%)	0.73(0.48-1.12)	0.154
Admission GCS*	9.5(2.5)	9.1(2.8)	10.3(2.9)		0.001
Hospital stays*	6.3(3.6)	7.2 (3.8)	4.7(2.3)		<0.0001

Abbreviation: DM=Diabetes Mellitus; GCS= Glasgow Coma Scale; * Mean±SD

Table 4: Secondary Complications Developed During Hospital Care After Primary Intra Cerebral Hemorrhage and Their Outcome (n=504)

Variables	Discharge	Death	OR (95% CI)	P value
Electrolyte imbalance	146(68.9%)	66(31.1%)	1.158(0.786-1.705)	0.458
Hematoma Expansion	76(66.7%)	38(33.3%)	0.846(0.624-1.147)	0.173
Hydrocephalus	46(59.0%)	32(41.0%)	0.664(0.488-0.903)	0.011
Aspiration pneumonia	28(50.0%)	28(50.0%)	0.536(0.396-0.726)	0.0001
Convulsive Seizure	28(56.0%)	22(44.0%)	0.631(0.446-0.892)	0.015
DVT*	4(66.7%)	2(33.3%)	0.880(0.281-2.749)	0.567
UTI*	12(66.7%)	6(33.3%)	0.877(0.450-1.709)	0.442

*DVT, Deep vein thrombosis; UTI, Urinary tract infection

Discussion

This observational study was conducted in the neurology department in a dedicated stroke unit of national institute of neurosciences and hospital. Five hundred and four primary intracerebral hemorrhage patients were analyzed in this study, with mean age was 59.1 years. Most of the study populations (71.4%) found above fifty years of age, which is similar in age distribution of the developed countries[18]. We know increasing age is a risk factor for developing stroke, our study support this. There were more male 262, which is comparable to study done by Jangala et al[6]. Majority of the study population resided in urban area (58.0%); this may represent that urban people are more concern about stroke care and easy access to health facilities. Poor communication system and less awareness about stroke care facilities among rural population of Bangladesh may also be a cause. The major risk factors for intracerebral hemorrhage found in this study were hypertension, diabetes mellitus, dyslipidemia and ischaemic heart disease.

Isolated hypertension was the commonest finding (93.0%) and diabetes mellitus was second most common cause (28.1%). Our observation revealed electrolyte imbalance was the commonest complication (62.7%), of which hyponatremia is commonest (22.6%). Previous study revealed electrolyte imbalance particularly hyponatremia is common in acute phase of intracerebral hemorrhage[6]. Our finding also supports this. Electrolyte disturbances may arise after brain injury due to central nervous system play a major role in controlling sodium, potassium, and water homeostasis[19]. We found hematoma expansion (HE) 94(27.8%) of participants which is a common early and severe complication of ICH. Up to 40.0% of the hematoma grows in the first few hours post ictus. The precise mechanism of early HE during the acute phase is poorly understood. It is proposed to be a heterogeneous process that includes dysregulation of hemostasis via inflammatory cascade activation and matrix metalloproteinase (MMP) overexpression, breakdown of the blood–brain barrier, a sudden increase in intracranial pressure leading to local tissue distortion and disruption, and vascular engorgement due to reduced venous outflow[1].

Other complications like hydrocephalus (23.0%), aspiration pneumonia (16.5%), convulsive seizure (14.7%), urinary tract infection and pressure sore (5.3% each) are much lower than other studies[1,5,6]. However, these findings signify better health care facilities available in our center to prevent acute complications of ICH patients, which is a dedication of our well-organized stroke care unit. Admission Glasgow coma scale (GCS) is an important contributing factor. Poor GCS on admission is a risk factor for developing complication and poor outcome, our study revealed most of the admitted patient (80%) had moderate GCS (5-12) and 16% admitted patient had good GCS (≥13). In our study most of the 356 (70.6%) admitted patient survived and discharged to home and only 148 admitted patient died during hospital care, which is comparable to other international study[1]. This high percentage of mortality of intracerebral hemorrhage is not due to stroke itself, but supposed to be mainly due to various complications of stroke. Median (±SD) hospital stays meaning duration of hospital care was found 6.3 (±3.6) days among study subject. This indicates rapid turnover of patient mainly due to high burden of stroke patient and limited number of standard stroke care facilities centers in our country.

Strength of the study is that it is done in a specialized neurosciences hospital which is the only specialized public hospital in Bangladesh where any people have access. We have some limitations also like it is a single center study and data collected by purposive sampling method.

Conclusion

We can summarize that after intracerebral hemorrhage, patients develop different types of complication which influences in hospital outcome as well as longer hospital stay and impaired quality of life who survived. By providing proper care we can reduce stroke complications, increase stroke survivors, reduce hospital stay and improve quality of life who survived.

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Conflict of interest
Other than technical and logistic support from the scientific partner the investigators did not have any conflict of interest in any means.

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Contribution to authors
Sarkar MSR, Ahmed KMA, Mamun AA conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Chowdhury MTI, Alam MB involved in the manuscript review and editing. Sarkar MSR, Ahmed KMA conceived and manuscript writing. All authors read and approved the final manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Ethical approval for the study was obtained from the Institutional Review Board. As this was a prospective study the written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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