Risk factors, Clinical Features, Severity, Hematoma Characteristics and Etiological classification of Intracerebral Hemorrhage in Young Patients (18-49 Years)

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Abstract:

Background: *Intracerebral hemorrhage (ICH) is the third common cause of all strokes but it is the deadliest subtype. ICH in younger adults is less frequent than in older people; however, it has more health and economic impact on individual, their family, and society. To ensure a favorable outcome, it is important to understand characteristics of ICH in young patients with factors contributing to its outcome. Our aim was to study the risk factors, etiologic distribution, clinical features, severity and hematoma characteristics of ICH in young patients.* ***Objective:*** *To evaluate the risk factors, etiologic distribution, clinical features, severity and hematoma characteristics of ICH in young patients.* ***Methods:*** *This cross sectional study was conducted with 100 patients of 18-49 years of CT or MRI proven ICH in Department of Neurology, Bangabandhu Sheikh Mujib Medical University and Stroke unit, National Institute of Neurosciences & Hospital, Dhaka from January 2020 to February 2022. The information about the demography, risk factors, clinical status, hematoma characteristics were noted at admission. The etiology of ICH was determined based on SMASH-U classification.* ***Results:*** *The mean age of patients was 39.54 years with 63% in 40-49 years group and 46 (46%) were female. Altered level of consciousness (61%)was the most frequent clinical presentation. Hypertension was the most common risk factor (64%). On admission, 24% patient had severe NIHSS (>20) with median NIHSS 15 and 18 %, 36%, 30%, 14%, 2% patients had ICH score 0, 1, 2, 3, 4 respectively. Thalamus and Basal Ganglia region (Deep) was the most common location of hematoma (69%). 45% patients had intraventricular hemorrhage and 24% and 29% had Midline shifting and hydrocephalus respectively. Mean hematoma volume was 17.11 ml. The etiological distribution according to SMASH-U classification showed most of the patients had hypertensive etiology (53%). Structural etiology accounts for 28% of the patients. 12% patient was of undetermined etiology. Among the structural causes 13% patients had aneurysm, 10% patients had AVM, 3% had Moyamoya disease, 1% had AVF and 1% had cavernoma.* ***Conclusion:*** *With the rising trend of hypertension in young age the etiological distribution of ICH in young is also changing, hypertension being the most frequent one. The severity of ICH in young tends to less severe.*

Key words: *Intracerebral hemorrhage, risk factors, etiology, stroke in young adults*

Introduction:

Hemorrhagic stroke is of ~10–20% of all strokes[1] and also the third most common cause of stroke, following cerebral embolism and thrombotic disease[2]. Unlike Ischemic stroke the overall incidence of ICH has not declined globally in any age groups during

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the past 3 decades[1] and the incidence of ICH in Asian individuals is roughly doubled than that in either black or white people[3]. ICH is the deadliest subtype among all types of strokes with an overall 1 month-mortality of 40% and 1-year mortality 54% with only 12% to 39% of patients achieving long-term functional independence[4]. As ICH does not have any definite treatment in contrast to other types of strokes, making understanding risks factors and causes of ICH is very important for suitable risk stratification, management and favorable outcome. The incidence of ICH is more in the older age group[5]. But in this century, Krishnamurthi et al.,[5] observed that there is a tendency towards increasing burden in young (45–59 years old). Studies reported proportions of ICH ranging from 10.0% to 38.5% in patients with stroke aged <45 years [6]. A young adult patient with ICH is usually described as aged between 18 years and 50 years, although the precise age range varies between studies and experts[7]. Regarding the upper age cut-off, older studies used 40 to 45 but the latest studies have used 50 or even 65 as the upper limit – a fact likely due to increased longevity in both developed and developing countries. ICH in the young contrasts from that in the elderly in several essential aspects: their risk factors and etiological spectrum are more distinct. Essentially, many more quality-weighted life years are lost in case severe ICH affects a young individual. An early diagnosis with stratification of the risk factor and evaluation of cause is pivotal for early treatment, optimization of health care resource allocation and improve outcome. Such a study was not performed in our population. So, this study will be performed to evaluate the risk factors, etiologic distribution, clinical features and hematoma characteristics of ICH in young patients.

Materials and Methods:

After ethical clearance from institutional review board, this study was conducted as a cross sectional study with 100 CT or MRI proven ICH of age 18-49 years in Stroke and Interventional Neurology Clinic, Indoor and Outdoor of Department of Neurology, BSMMU, Dhaka and Stroke unit in National Institute of Neurosciences & Hospital (NINS), Dhaka, Bangladesh from January 2020 to February 2022 after fulfilling the inclusion and exclusion criteria & giving consent to enrol in the study. Patients admitted after 72 hours of onset,ICH due to head injury and

tumor and hemorrhagic transformation of arterial ischemic stroke were excluded. The demographic details of the patients were noted. Their stroke risk factors such as hypertension, diabetes, smoking, family history, past history, pregnancy and puerperium history of drug abuse, anticoagulant, statin and antiplatelet therapy were also noted. The patient was considered hypertensive ifDeep hemorrhage (putamen, thalamus, pons, cerebellum) with prior hypertension(mention of elevated blood pressure by the patient, relative, or medical records or any use of blood pressure medication or ECG findings of left ventricular hypertrophy). New diagnosis of HTN will be done if arterial hypertension is demonstrated beyond 3 days after ICH (with at least two measurements above 140/90 mmHg in a patient not receiving blood pressure-lowering drugs or if the patient needs antihypertensive treatment to maintain blood pressure under 140/90 mmHg. Compliance to antihypertensive drugs was recorded. The patients were considered diabetic ifHbA1Ce™6.5% or FPG e™ 126mg/dl (7.0 mmol/l) or 2 Hours PG e™ 200mg/dl (11.1 mmol/l) or RPGe™ 200mg/dl (11.1 mmol/l) with classic symptoms of hyperglycemia or hyperglycemic crisis or patient is in use or any oral hypoglycemic agent or insulin. Hypocholesterolemia was deûned if cholesterol level was below 160 mg/dl and hypercholesterolemia if >200 mg/dl. The patient was considered smoker if e™ 10 cigarettes/day were consumed during the previous 6 months.Family history of stroke in the ûrst degree relatives was also noted. The severity was assessed by Glasgow Coma Scale (GCS) and NIHSS (National institute of health stroke scale) and modified rankin scale (mRS). CT scan or MRI ûndings were noted including location, size of hematoma and intraventricular extension. The volume of hematoma was calculated by the formula "a x b x c/2" [20]. Magnetic resonance angiography, CT angiography or digital subtraction angiography (DSA) ûndingswere noted. The location of hematoma was categorized into deep, lobar, brainstem and cerebellar. The etiology of hematoma was categorized according to SMASH-U classification system which includes includes six categories: structural causes, medication, amyloid angiopathy, systemic disease, hypertension and undetermined etiology. Continuous data were summarized in terms

of the mean with standard deviation (age and hematoma volume)and median with interquartile range (GCS, NIHSS). Categorical variables were presented by frequency with percentage (sex, presentations, time from onset to admission, risk factors, GCS, NIHSS, mRS, ICH score, hematoma location, IVH, Midline shift, Hydrocephalus, etiology, angiographic findings, acute complications, comorbidities).Statistical analysis was done using SPSS (Statistical package for social sciences) windows version 25 software program.

Result:

Total 116 patients with ICH between 18 and 50 years were included. Sixteen patients were excluded because of exclusion criteria, the study is based on 100 patients. Their mean age was 39.54 years with 63% in 40-49 years group and 46 (46%) were female. Altered level of consciousness (61%)was the most frequent clinical presentation. Other frequent presentations were hemiparesis (59%), vomiting (54%), headache (31%), Seizure (17%) and fall (18%,Table 1).37% young patients admitted within the 24 hours of onset of symptom. Among them only 8% patient in younger age group presented within 4 hours of onset. Hypertension was the most common risk factor (64%). Other risk factors were Hypotriglyceridemia (37.7%), smoking

(28%), previous vascular event (26%), presence of family history. (25%), Hypocholesterolemia (18.2%), irregular intake of antihypertensive (24%), use of antiplatelet (11%) and use of statin (7%), use of sympathomimetic agent (5%) and Peripartum period (1%). Regarding severity in admission, 24% patient had severe NIHSS (>20) with median NIHSS 15. Most of the patients belonged to 5-12 score (59%) and median GCS was 10. Rendering ICH score 18 %, 36%, 30%, 14%, 2% patients had score 0, 1, 2, 3, 4 respectively (figure 1). Thalamus and Basal Ganglia region (Deep) was the most common location of hematoma (69%). 25% had lobar hemorrhage whereas only 2% and 4% patients had cerebellar and brainstem hemorrhage. 45% patients had intraventricular hemorrhage and 24% and 29% had Midline shifting and hydrocephalus respectively. Mean hematoma volume was 17.11 ml with 17% had volume more than 30 ml (Table III). The etiological distribution according to SMASH-U classification showed most of the patients had hypertensive etiology (53%). Structural etiology accounts for 28% of the patients. 12% patient was of undetermined etiology. Among the structural causes 13% patients had aneurysm, 10% patients had AVM, 3% had Moyamoya disease, 1% had AVF and 1% had cavernoma.

Table-I

Presentation of ICH according to age (n=100)

Presentations^	Frequency (%)	Risk factors^	Frequency (%)
Hemiparesis	59 (59)	Hypertension	64 (64)
Headache	31 (31)	Irregular antihypertensive	24 (24)
Vomiting	54 (54)	Smoking	28 (28)
Dysphasia	6(6)	Previous vascular event	26 (26)25 (25)
Dysarthria	9 (9)	Family history	
Altered level	61 (61)	Hypotriglyceridemia (n= 163)	29 (37.7)
Of consciousness	17 (17)	Hypertriglyceridemia (n= 163)	20 (26)
Seizure	4 (4)	Hypercholesterolemia (n=163)	35 (45.5)
Vertigo	18 (18)	Hypocholesterolemia (n=163)	14 (18.2)
Fall		Antiplatelet therapy	11 (11)
		Statin therapy	7 (7)
		Use of sympathomimetic	5 (5)
		Pregnancy/Peripartum	1 (1)

^Multiple response considered
*P value measured by chi-square test
# Pvalue measured by Fisher Exact test
S= Statistically significant

Table-II

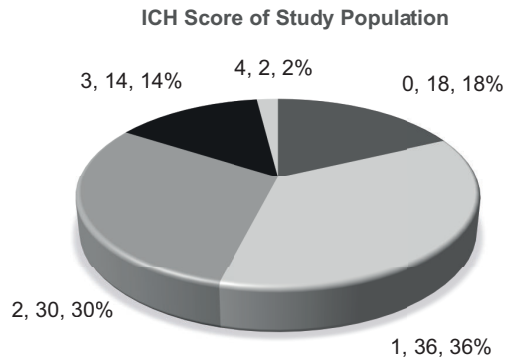*Severity of ICH in study population according to age (n=100)*

Severity Score	Frequency (%)	Severity Score	Frequency (%)
GCS		NIHSS	
3-4	9	Mild (0-4)	11 (11)
5-12	59	Moderate (0-15)	45 (45)
13-15	32	Moderate to severe (16-20)	20 (20)
Median (IQ)	10 (7)	Severe (21-42)	24 (24)
		Median (IQ)	15 (12.00)

GCS: Glasgow Coma Score, NIHSS: National Institutes of Health Stroke Scale,
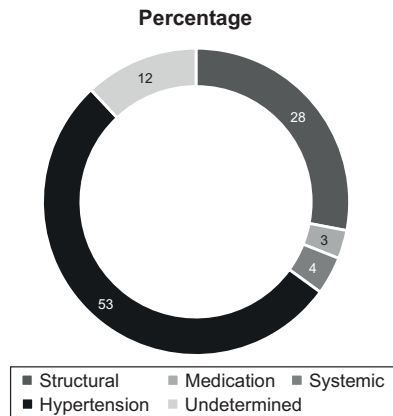IQ-Interquartile Range
*P value measured by chi-square test
# P value measured independent sample nonparametric test
S= Statistically significant

Fig.-1: *The ICH score of study population (n=100).*

Fig.-2: *Etiology of ICH in study population according to SMASH -U classification. (n=100).*

Table-III

Hematoma characteristics in study population (n=100)

Hematoma Characteristics	Frequency (%)	Angiogram findings	Frequency (%)
Location		Aneurysm	13 (13)
Deep	69 (69)	Arteriovenous Malformation	10
Lobar	25 (25)	Arteriovenous fistula	1
Brainstem	4 (4)	Cavernoma	1
cerebellum	2 (2)	Cerebral venous sinus thrombosis	4
Intraventricular	45 (45)	Moyamoya	3
hemorrhage	17 (17)	Normal	5
Volume	17.11 (±13.80)		
≥30 ml	24 (24)		
Mean (±SD)	29 (29)		
Midline Shift			
Hydrocephalus			

SD=Standard Deviation
*P value measured by chi-square test
# P value measured by Mann-Whitney U test
S= Statistically significant

Discussion:

Analysis of the data revealed that a majority of (63.0%) the patients were 40-49 years of age. The mean(±SD) age was 39.54(±7.17) years. The mean age of younger patient was 30.9(±10.5) years with a range from 16 to 45 years in one study in Bangladesh. They also found the maximum number of patients in the younger group were in the age group 16-25 years[8].In this study male predominance was apparent. About 54% of participants were male. In one study in South India, Hegde et al. found 70.5% of patients were males[9]. Hussain et al. also found male predominance which were 68.6%[8]. The INTERACT2 study found 63.7% were male in the young patients[10]. Altered level of consciousness (61%)was the most frequent clinical presentation. Other frequent presentations were hemiparesis (59%), vomiting (54%), headache (31%), Seizure (17%) and fall (18%,Table 2). Rutten et al found quite a similar result in young patients, they found presenting symptoms included severe headache (71.4 %), nausea (32.7 %), impaired consciousness (65.3 %), seizures (13.3 %) and focal neurological deficits (78.4 %) in young patients[11]. Koivunen et al.[12]found that presenting symptoms were motor hemiparesis (57.1%), headache (48.8%), nausea (35.7%), sensory hemiparesis (27.7%), vomiting (26.8%), dysphasia/ aphasia (31.3%), dysarthria (24.4%), seizure (11.6%), disorientation (11.3%), vertigo (9.2%) in young.Hypertension was the most common risk factor (64%). Our findings regarding the prevalence of hypertension are consistent with previous studies of ICH [12]where the frequency was quite high (65%). In the INTERACT2 study, 69.8 % of the young patient were hypertensive[10]. The increased frequencies of drug abuse were found among young patients with ICH in other studies[13]. Other risk factors in our study were smoking (28%), hypocholesterolemia (18.2%) and family history (25%). The result is consistent with the findings of a study conducted in India in which they found that 18.1% of patients had a history of smoking, 33.7% had hypocholesterolemia and 9.4% had family history of stroke as risk factors[14]. Regarding severity in admission, 24% patient had severe NIHSS (>20) with median NIHSS 15. Most of the patients belonged to 5-12 score (60%) and median GCS was 10. Rendering ICH score 18 %, 36%, 30%, 14%, 2% patients had score 0, 1, 2, 3, 4 respectively. Koivunen et al., 2015 found the NIHSS scores at admission among the young was 8[12]. The INTERACT2 trial found that 28.2 % of young patients had NIHSS >14 but the overall severe patient is less because they exclude the patient with GCS 3-4[10].Thalamus and Basal Ganglia region (Deep) were the most common locations of hematoma for both groups (69%) whereas only 2% and 4% younger patients had cerebellar and brainstem hemorrhage.. Radholm et al., (10) also found deep hematoma was 86.6%, brainstem hematoma 4.8% and cerebellum hematoma was 1.2%. In this study,mean (±SD) hematoma volume was 16.89 (±13.88) ml. Radholm et al. found the median volume was 12.4 (7.7–20.3) in patients of <52 years[10]. But Koivunen et al., (2015) found the mean hematoma volumes was 11 ml [3-36] in young patients[12]. Regarding Etiology of ICH, hypertension was the commonest etiology in both groups. 53% of young patients and 68% of older ones had hypertensive etiology. The structural lesion was 28% . 13% of patients had aneurysms, 10% of patients had AVM. Our findings are consistent with other studies in Asia and frequency of structural cause is quite similar (25.0%) in young[7]. Studies in Asian countries revealed hypertension is the most common cause of ICH compared to countries in western regions, where the vascular malformation is the most common cause . In one study in Bangladesh[8] the most common cause of ICH in young was the rupture of an AVM (45.7%). But their definition of young patient (<45 years) was different from ours and sample size was very small. In our study the etiology of 12% of young patients remains unknown. Hussain et al., (2010) found that the cause was undetermined in 28% of the patients respectively[8]. The decreasing trend of undetermined causes may be attributable to the more availability of investigations in recent days and more enthusiasm in findings the causes of ICH.

Conclusion:

ICH at young age is less frequent, but catastrophic incident and the spectrum of causes differs to that

of the elderly. Structural causes and hypertension cause approximately two third of the ICH among young. After careful work-up, an assumed cause could be identified in most young ICH patients.

Limitation: The study was done in a short period, also affected by COVID-19 pandemic situation.Method of sampling was not random rather purposive.Exclusion of those patients who undergo surgical hematoma evacuation.

Recommendation: Further large-scale study with long term follow up should be carried out with increased sample size. Method of sampling should be random. Consideration should be paid to detect and treat causes of ICH in young adults which will decrease treatment related cost.

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