

Original Article

Risk factors of Hemorrhagic Stroke- a Case-Control Study in Bangladesh.

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Abstract:

Background: Spontaneous intracerebral hemorrhage is one of the leading causes of mortality and morbidity. Genetic factors play an important role in this disease. Among the non-genetic causes Hypertension (HTN), IDDM (insulin dependent diabetes mellitus), NIDDM (non-insulin dependent diabetes mellitus), family history of hemorrhagic stroke, smoking, previous history of ischemic stroke, alcohol intake and education level are important.

Methods: The aim of the study was to evaluate the association between ICH and non-genetic risk factors. This was a case-control study with 120 participants. The place of the study was in the Neurosurgery department of Sylhet Women's Medical College Hospital (SWMCH) and the study period was 2 years.

Result: Alcohol consumption (RR=3, Odd=3.11) showed highest risk for ICH. Other risk factors of ICH were smoking (RR=2, Odd=2.36), family history (F/H) of ICH (RR=1.3, Odd=1.38), Hypertension (RR=1.1, Odd=1.39) and below 12 class education status (RR=1.08, Odd=1.63). The relative risk of IDDM, NIDDM, previous history (P/H) of ischemic stroke were less than 1.

Conclusion: There are few controllable risk factors of hemorrhagic stroke apart from genetic risk factors.

Keywords: Hemorrhagic stroke, risk factor, non-genetic risk factor

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Introduction:

Stroke is the second highest cause of mortality and morbidity in the developed countries.¹ Ischemic stroke (80%) is the commonest stroke.² Hemorrhagic strokes are two types: hemorrhagic stroke and subarachnoid hemorrhage. In the western countries hemorrhagic stroke (HS) is 15% of all strokes and this percentage is 22-35% in the Asian countries.

Hemorrhagic stroke is one of the serious medical conditions and the mortality of hemorrhagic stroke is reported between 40% and 50% within the first month of the stroke. HS is a multifactorial and heterogenic disease caused by both genetic and non-genetic factor. Approximately two-third ICH patients usually have known risk factors like hypertension, diabetes mellitus, smoking and obesity.³

The genes encoding proteins related to lipid metabolism and atherosclerosis are considered as risk factors of stroke. Apolipoprotein E (APOE) gene has a strong association with ICH.⁴ Among the non-genetic risk factors hypertension (RR=31.8) and education less than 12th grade (RR=28.4) had higher attributable risk. Previous history of ischemic stroke, use of warfarin and affecting first degree relatives with HS had shown significant risk. Daily alcohol intake more than 2 drinks and smoking did not show any significant relationship with HS. However, blood level with high cholesterol and consumption of less than 2 drinks per day reported as a protective effect of HS. Nearly one-fifth of the middle-age women showed at a lifetime risk of HS and this risk was one in six person in the case of a middle-age men.

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There is no particular evidence-based management is available for HS and the disability and mortality of HS is nearly 50%.⁶ It is reported that the lipid metabolism irregularities can play an important role in the pathophysiology of HS. According to the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) treating stroke patients with lipid lowering medication reduces attribute risk of ischemic stroke but raises the risk of hemorrhagic stroke (HS).⁷ According to the Genetic and Environmental Risk Factors for Hemorrhagic Stroke (GERFHS) hypercholesterolemia decreases the risk of HS by nearly 33%.⁸

This was a case-control study conducted at Sylhet Women's Medical College Hospital, Sylhet. The aim of the study was to find out the risk factors of hemorrhagic stroke (HS).

Selection criterion:

Inclusion criteria:

1. Participants diagnosed as spontaneous hemorrhagic stroke (HS) with normal coagulation profile were enrolled in the case group.
2. Participants with no history of hemorrhagic stroke (HS) and not consuming any lipid lowering drug were enrolled in the control group.

Exclusion criteria:

1. Subarachnoid hemorrhage (SAH), traumatic intracerebral hemorrhage and hemorrhage due to tumor / vascular malformation were not enrolled in the case group.

Methodology:

Ethical clearance certificate was received from the Intuitional Review Board (IRB) of Sylhet Women's Medical College (SWMC). The study place was the Neurosurgery department of (SWMC and the study period was 2 years (January 2020 to December 2021). After matching with the selection criterion the case and control group participants were enrolled. Informed consent was achieved from all the participants. Risk factors hypertension (HTN), insulin dependent diabetes mellitus (IDDM), non-insulin dependent diabetes mellitus (NIDDM), family history of hemorrhagic stroke,

smoking, previous history of ischemic stroke, alcohol consumption and educational status were documented. For the educational status 12 class was considered as the cutoff point. After collecting all the data they were transferred in the Microsoft Excel datasheet to make the master sheet. Simple descriptive calculation was done to detect percentage, mean and standard deviation. Categorical data were analyzed by chi-square test and numerical data were analyzed by independent t-test.

Results:

Total 120 participants were enrolled in this study. They were equally distributed into case and control group.

Table 1: According to gender and age groups

	Case (n=60)	Control (n=60)	p-value
Male	28	19	.0923
Female	32	41	.0923
Mean age	57.08	54.06	.124 [#]
30y and below	3	1	0.618 [*]
31 – 40 year	6	10	.282
41 – 50 year	13	16	.522
51 – 60 year	17	18	.840
61 – 70 year	13	9	.345
More than 70 year	8	6	.834

Chi-square, t-test (#) and Fisher Exact test (*) were performed.

Table-1 shows the distribution of participants according to gender and age groups. Female were higher in both the case and control groups. Mean age of cases was 57.08 years and it was 54.06 for controls. Highest frequency was in 51 to 60 year age group for both the groups. For both the groups 41-50 year age group was second in number. Lowest number of participants were from 30 year and below age group for both the groups.

Table 2: According to location of ICH and initial GCS.

	Number (n=60)	Percentage
Deep	40	67.0 %
Lobar	3	5.0 %
IVH	17	28.3 %
GCS 13-15	21	35%
GCS 9-12	33	55%
GCS 3-8	6	10%

Table-2 demonstrates the distribution of cases (n=60) according to location of ICH and initial GCS. More than two-third (67%) cases had deep ICH followed by IVH (28.3%) and lobar (5%). Initial GCS was in the 9-12 subgroup in more than half of the cases (55%). Nearly one-third had initial GCS of 13-15, whereas rest cases had initial GCS of 3-8.

Table-3: Distribution of different risk factors and their relative risk (RR) and odd ratio (OR)

	Case (n=60)	Control (n=60)	p-value	RR	Odd
HTN	45	41	.4177	1.1	1.39
IDDM	7	18	.0134	0.39	0.31
NIDDM	13	18	.2970	0.72	0.65
F/H of ICH	13	10	.4865	1.3	1.38
Smoking	16	8	.0678	2	2.36
P/H ischemic stroke	7	11	.3064	0.64	0.59
Alcohol	03	01	.6110*	3	3.11
Education < 12 class	52	48	.3271	1.08	1.63

Chi-square test done (* - with Yates correction)

Table-3 demonstrates that the number of IDDM participants were significantly lower ($p=0.0134$) in the case group. Alcohol consumption ($RR=3$, $Odd=3.11$) showed highest risk for ICH. Other risk factors of ICH were smoking ($RR=2$, $Odd=2.36$), family history (F/H) of ICH ($RR=1.3$, $Odd=1.38$), Hypertension ($RR=1.1$, $Odd=1.39$) and below 12 class education status ($RR=1.08$, $Odd=1.63$). The relative risk of IDDM, NIDDM, previous history (P/H) of ischemic stroke were less than 1.

Discussion:

The results of this study was compared with those of the national and international studies to find out the similarity and contrast.

Riaz BK published their case-control study on 171 participants of Bangladesh.⁹ It was a triple arm with one control group and the case groups were hemorrhagic stroke (HS) and ischemic stroke (IS). Hypertension ($OR\ 21$ for HS and 1.8 for IS), diabetes mellitus ($OR\ 1.3$ for HS and 0.8 for IS) frequent fatty diet ($OR\ 2.2$ for HS and 1.5 for IS), low fruit consumption ($OR\ 4.7$ for HS and 3.5 for IS), betel nut chewing ($OR\ 2.5$ for HS and 1.9 for IS) and aspirin intake ($OR\ 4.7$ for HS and 2.3 for IS) showed more risk for HS in comparison to IS. On the other hand low physical activity, raised waist-to-hip ratio, salt consumption, abnormal ECG and dyslipidemia were proven less risky for HS in comparison to IS. Smoking had equal risk ($OR\ 1.9$) for both the groups. In this study hypertension had a greater odd ratio in case of HS. There was no ischemic stroke group in this study.

Boehme et al divided the risk factors of stroke into non-modifiable and modifiable.¹⁰ Among the non-modifiable causes age, sex and race are significant. At the young age women are more vulnerable for stroke on the other hand male are accepted to develop stroke at higher age.¹¹ Pregnancy, hormonal imbalance and contraceptive pills considered as major aggravating factors for young women. African Americans have two fold more risk for stroke. Few cohorts of Latin Americans / Hispanic people have higher risk for stroke as well. Hypertension, diabetes, atrial fibrillation, cardiopathy, dyslipidemia, lifestyle, obesity, metabolic syndrome, alcohol consumption, abuse substances, smoking, inflammation and infections are known modifiable causes of stroke. In this study both modifiable and non-modifiable risk factors were evaluated. Alcohol consumption, smoking and lower education level were the modifiable risk factors.

Melmed et al published their study on ICH related to COVID-19.¹² Among the 416 enrolled participants mean age was 69.3 years. Nearly one-third (35.8%) were female and nearly one-third (34.9%) had history of therapeutic anticoagulation therapy. Mechanical ventilation, non-Caucasian race, older age and anticoagulation therapy were significantly ($p<0.01$) associated with ICH in COVID-19

diagnosed patients. In this study the mean age of the HS participants was 57.08 year. Female had a mild predominance.

According to Reymer M about 10-15% of all strokes were ICH.¹³ The mortality and morbidity of hemorrhagic stroke have not been changed in last 30 years. The mortality could reach up to 51-65% depending on the location of the ICH. Nearly half of the patients die within first two days. Nearly one-fifth of the patients become independent within 6 months of hemorrhagic stroke. The incidence of ICH increased with the age and male were more likely to be affected. Volume of the ICH blood and the GCS were considered to be the powerful predictors of mortality in the ICH.¹⁴ Intraparenchymal blood more than 30 ml had high mortality and patients with blood more than 60 ml had mortality more than 90%. Patients with intraventricular blood and brainstem hematoma showed higher mortality. Patients of age more than 80 years also reported as high death rate.¹⁵ In this study outcome of the HS was not measured. More than half (55%) HS cases had GCS between 9 and 12 when they were admitted.

After comparing with the national and international studies a fair similarity was found.

Conclusion: The site of the hemorrhagic stroke was in deep (basal ganglia and thalamus) in two-third of the cases. Alcohol consumption, smoking, family history of HS, Hypertension and below 12 class education status had higher risk for hemorrhagic stroke.

Conflict of interest: It was a self-funded study. None of the co-authors declared any conflict of interest.

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