

# Risk Factors for Acute Ischaemic Stroke in Young Adults in Armed Forces Medical Institute of Dhaka

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## ABSTRACT

**Background:** Stroke is a leading cause of death and disability in developing countries, afflicting individuals at a young age. The affection of economically productive group adds further to the overall disease burden. The contribution of established vascular risk factors to ischaemic stroke in young adults has not been evaluated systematically in CMH, Dhaka Cantonment. The purpose of the study is to detect the risk factors for acute Ischaemic stroke in adults.

**Materials and methods:** The case-control study was carried out in the department of Neurology and Medicine, CMH Dhaka during October 2019 to August 2020. Consecutive ischemic stroke patients who met the inclusion criteria and were hospitalized in the Department of Neurology and Medicine at CMH Dhaka were included in the study.

**Results:** The mean age of young patients with ischaemic stroke was 40.1 (SD± 6.6) years (Range 17-45 years). There were 40 (59.7%) male and 27 (40.3%) female with ratio of male to female was 1.5:1. Risk of acute ischaemic stroke was 2.7 times higher in smoker [36 (53.7%) vs 20 (29.9%) OR=2.7, 95% of OI=1.34-5.55, p<0.01] 2.4 times higher in diabetic [23 (34.3%) vs 12 (17.9%), OR=2.4, 95% of OI=1.07-5.35, p<0.05], 2.6 times higher in hypertensive patients [27 (40.3%) vs 14 (20.9%), OR=2.6, 95% of OI=1.19-5.49; p<0.05], 4.2 times higher in patients with atrial fibrillation [11 (16.4%) vs 3 (4.5%)]. The mean BMI of the respondents was 21.8 (SD± 3.3) Kg/M<sup>2</sup> in stroke patients of young and was 22.3 (SD 2.9) Kg/M<sup>2</sup> in control group (p>0.05).

**Conclusion:** Ischemic stroke in young patients has wider risk factors. Hypertension, diabetes mellitus, smoking and atrial fibrillation are the most common risk factors of acute ischemic stroke in young adults. Early identification of risk factors and proper prevention, treatment and life style modification may reduce the morbidity and mortality in young stroke patients.

## Key words

Acute ischaemic stroke; Atrial fibrillation; Risk factors; Young age.

## Introduction

Cerebrovascular insult or stroke is a crisis in cerebrovascular circulation and central nervous system function with focal neurologic dysfunction.<sup>1</sup> Stroke is defined as a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.<sup>2</sup> Stroke is the second leading cause of death worldwide and the vast majority of these stroke-related deaths occur in low and middle-

income countries.<sup>3,4</sup> Worldwide, about 15 million people have a stroke every year, of whom 5 million die and 5 million have a permanent deficit and roughly 20% of these deaths occurred in South Asia.<sup>5,6</sup> It is estimated that the number of deaths from stroke will increase to 6.3 million in 2015 and 7.8 million by 2030 with the bulk occurring in the poor countries of the world.<sup>7</sup> Stroke rates in middle-aged people are five to ten times higher in Pakistan, India, Russia, China, and Brazil, compared with the United Kingdom or the United States.<sup>3,4</sup> According to the World Health Organization (WHO) estimates, death from stroke in developing (Low-and middle-income) countries in 2001 accounted for 85.5% of stroke deaths worldwide, and the number of stroke-related disability-adjusted life years, which is comprised of years of life lost and years lived with disability, in these countries was almost seven times than in developed (High-income) countries.<sup>6</sup> South Asia is home to 20% of the world's population and has one of the highest burdens of cardiovascular disease in the world.<sup>8</sup> With an ageing population, there is an expected increase in the number of stroke cases and a corresponding increase in the burden of stroke in developing countries including South Asia.<sup>9,10</sup>

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Although stroke is considered to be a disease of the older population, it is not infrequent among adolescents and young adults and affects 5%-15% of patients under 50, with ischaemic stroke being predominant in this age group.<sup>11,12,2,13,14</sup> The magnitude of this increased susceptibility is higher for young Indian adults than older adults. Young stroke patients constitute 15-30% of all stroke patients in India, as opposed to 3.0-8.5% of all stroke patients in the West. However, it should be borne in mind that India is demographically younger than the more developed countries of the West.<sup>14,15,16,17</sup> According to Kittner et al the incidence of stroke is approximately 6/100,000 in Caucasians aged 15-39 years and approximately 2.5 times higher in persons of African descent. Stroke is also an important cause of mortality and morbidity in Bangladesh also.<sup>18,19</sup>

Stroke in the young is particularly tragic because of the potential to create a long-term burden for the victims, their families, and the community. However, effective stroke prevention in the young cannot be attempted until the risk factors are clearly documented.<sup>20</sup> The causes of ischaemic stroke in young adults are many and diverse. Such patients usually require more extensive investigations in order to find an underlying cause than more elderly patients. It is important that a comprehensive search is made since many of the underlying disorders are treatable. Principal causes are extracranial arterial dissection, cardioembolism, premature atherosclerosis, haematologic and immunological disorders and migraine. Drug abuse is becoming increasingly important but the risk of stroke in pregnancy remains unclear. Isolated angiitis of the central nervous system, heritable disorders of connective tissue and other genetically determined disorders account for a small proportion of ischaemic strokes in the young.<sup>21</sup>

To evaluate and quantitate risk factors for cerebral infarction in young adults, this study was performed, a case-control study of risk factors for cerebral infarction in people aged 45 years or younger.

### Materials and methods

This study was a case-control study carried out in the department of Neurology and Medicine, Combined Military Hospital, Dhaka Cantonment. The study period was October 2019 to August 2020. Consecutive ischaemic stroke patient admitted in the Department of Neurology and Medicine, Combined Military Hospital, Dhaka Cantonment, fulfilling the inclusion criteria were enrolled as study population, in this study. Inclusion Criteria are all diagnosed ischaemic stroke patients of

first-ever, Age between 18 to 45 years, regardless of gender, Control group was age and sex matched subjects and accompany person of the patient without history of any kind of stroke. Exclusion criteria were patients with haemorrhagic stroke, history of previous stroke, age above 45 years, head injury, those who refused to enroll in this study.

Data were processed and analyzed with the help of SPSS (Statistical Package for Social Sciences) version 16.0. Quantitative data were expressed in mean and standard deviation; and comparison was done between the groups by "Z" test. Qualitative data were expressed in frequency and percentage and comparison was done between groups by Chi-square ( $\chi^2$ ) and Fisher's Exact Test where applicable. Odds ratio was calculated between the groups to determine the risk factors. A probability value of  $<0.05$  ( $p < 0.05$ ) was considered statistically significant.

### Results

The age of the respondents ranged from 17 to 45 years with the mean age of 40.1 (SD $\pm$  6.6) years in group-A; whereas the age of the respondents of group-B ranged from 18 to 65 years with the mean age of 39.2 (SD $\pm$  7.8) years. There was no statistically significant difference of mean age of the respondents between the groups ( $Z=0.680$ ,  $p > 0.05$ ). Age distribution of the respondents was shown in Table I.

Table I showed the distribution of respondents by age. In group-A, 39 (58.2%) respondents were aged between 41 to 45 years, 13 (19.4%) were aged between 36 to 40 years, 7 (10.4%) were aged between 31 to 35 years, 4 (6.5%) were aged between 21 to 25 years, 3 (4.5%) were aged between 26 to 30 years and 1 (1.5%) respondents were aged between 16 to 20 years, it was 41 (61.2%), 8 (11.9%), 5 (7.5%), 6 (9.0%) and 2 (3.0%) respectively in group-B. There was no statistically significant difference of age of the respondents between the groups ( $\chi^2=2.807$ ,  $p > 0.05$ ). There were 40 (59.7%) male and 27 (40.3%) female in group-A, whereas 33 (49.3%) male and 34 (50.7%) female in group-B. The sex of the respondents of group-A and group-B did not show any statistically significant difference ( $\chi^2=1.475$ ,  $p > 0.05$ ).

\*Chi-square ( $\chi^2$ ) test was applied to test the level of significance. The mean BMI of the respondents was 21.8 (SD 3.3) Kg/M<sup>2</sup> in group-A and was 22.3 (SD 2.9) Kg/M<sup>2</sup> in group-B. The mean BMI of the respondents in both groups was almost identical ( $Z=0.831$ ,  $p > 0.05$ ). In group-A, 12 (17.9%) respondents had BMI  $>25$  Kg/M<sup>2</sup>, while in group-B 8 (11.9%) had BMI  $>25$  Kg/M<sup>2</sup>. The BMI of both groups was almost similar (OR=1.6 (95% of CI=0.61-4.23),  $\chi^2=0.940$ ,  $p > 0.05$ ).\* Z test and Chi-square ( $\chi^2$ ) test were applied to test the level of significance.

**Table I** Distribution of respondents by age, sex and BMI

Age Group (Years)	Study Group		p value
	Group-A (n=67)	Group-B(n=67)	
17-20	1(1.5)	2(3.0)	
21-25	4(6.0)	6(9.0)	
26-30	3(4.5)	5(7.5)	*p>0.05
31-35	7(10.4)	5(7.5)	
36-40	13(19.4)	8(11.9)	
Sex	Study Group		p value
	Group-A (n=67)	Group-B(n=67)	
Male	40 (59.7)	33 (49.3)	*p>0.05
Female	27 (40.3)	34 (50.7)	
Total	67 (100.0)	67 (100.0)	
BMI	Study group		Odds Ratio
	Group A (n=67)	Group B (n=67)	p Value
>25 Kg/M <sup>2</sup>	12(17.9)	8(11.9)	1.6 (0.61-4.23) †p>0.05
<24.9 Kg/M <sup>2</sup>	55(25.4)	59(88.1)	
Mean (±SD)	21.8(SD3.3)	22.3(SD2.9)	*p>0.05

Table II showed the respondents according to smoking status. Thirty six (53.7%) patients with acute ischaemic stroke were smoker and 20 (29.9%) control subjects were smoker. Risk of acute ischemic stroke was 2.7 times higher in smoker than non-smoker (OR=2.7, 95% of CI=1.34-5.55,  $\chi^2=7.853$ ,  $p<0.01$ ).

**Table II** Smoking status of respondents

Smoking status	Study group		Odds Ratio	p value
	Group-A (N=67)	Group-B (n=67)		
Smoker	36(53.7)	20 (29.9)	2.7	
Non-Smoker	31 (46.3)	47(70.1)	(1.34-5.55)	
Total	67(100.0)	67(100.0)		

\* Chi-square ( $\chi^2$ ) test was applied to test the level of significance. Figure in the parenthesis indicates corresponding percentage. OR: Odd Ratio, CI: Confident Interval.

Table III showed the respondents according to diabetes mellitus. Twenty three (34.3%) patients with acute ischemic stroke were diabetic and 12 (17.9%) control subjects were diabetic. Risk of acute ischemic stroke was 2.4 times higher in diabetic than non-diabetic (OR=2.4, 95% of CI=1.07-5.35,  $\chi^2=4.679$ ,  $p<0.05$ ).

**Table III** Distribution of the respondents according to diabetes mellitus

Diabetes mellitus	Study Group		Odds	p-Value
	Group-A (n=67)	Group-B (n=67)		
Diabetic	23 (34.3)	12 (17.9)	2.4	p<0.05
Non-diabetic	44 (65.7)	55 (82.1)	(1.07-5.35)*	
Total	67 (100.0)	67 (100.0)		

\* Chi-square ( $\chi^2$ ) test was applied to test the level of significance. Figure in the parenthesis indicates corresponding percentage.

Table IV showed the respondents according to hypertension. Twenty seven (40.3%) patients with acute ischaemic stroke were hypertensive and 14 (20.9%) control subjects were hypertensive. Risk of acute ischaemic stroke was 2.6 times significantly higher in hypertensive than normotensive (OR=2.6, 95% of CI=1.19-5.49,  $\chi^2=5.939$ ,  $p<0.05$ ).

**Table IV** Hypertension status of the respondents

Hypertension	Study Group		Odds	p-Value
	Group-A (n=67)	Group-B (n=67)		
Hypertensive	27 (40.3)	14 (20.9)	2.6	p<0.05
Normotensive	40 (59.7)	53 (79.1)	(1.19-5.49)*	
Total	67 (100.0)	67 (100.0)		

\*Chi-square ( $\chi^2$ ) test was applied to test the level of significance. Figure in the parenthesis indicates corresponding percentage.

Table V shows the respondents according to vulvular heart disease. In group-A, 3 (4.5%) respondents had vulvular heart disease, while in group-B 2 (3.0%) had vulvular heart disease. The vulvular heart disease of both groups was almost similar (OR=1.5, 95% of CI=0.25-9.42,  $\chi^2=0.208$ ,  $p>0.05$ ). \* Chi-square ( $\chi^2$ ) test was applied to test the level of significance. In group-A, 15 (22.4%) respondents had ischaemic heart disease, while in group-B 12 (17.9%) had ischaemic heart disease. The frequency of ischaemic heart disease was more frequent in ischaemic stroke group but did not reach the level of significance (OR=1.5, 95% of CI=0.57-3.09,  $\chi^2=0.417$ ,  $p>0.05$ ).

**Table V** Vulvular heart disease and Ischaemic heart disease status of the respondents

Vulvular Heart disease	Study Group		Odds	p-Value
	Group-A (n=67)	Group-B (n=67)		
Yes	3 (4.5)	2 (3.0)	1.5	p>0.05
No	64 (95.5)	65 (97.0)	(0.25-9.42)	
Total	67 (100.0)	67 (100.0)		
Ischaemic heart disease	Study Group		Odds	p-Value
	Group-A (n=67)	Group-B (n=67)		
Yes	15 (22.4)	12 (17.9)	1.3 (0.57-3.09)	p>0.05
No	52 (59.7)	55 (82.1)	(0.57-3.09)	
Total	67 (100.0)	67 (100.0)		

\* Chi-square ( $\chi^2$ ) test was applied to test the level of significance. Figure in the parenthesis indicates corresponding percentage.

Table VI showed that 11 (16.4%) respondents of acute ischaemic stroke had atrial fibrillation, while 3 (4.5%) respondents of control group had atrial fibrillation. Risk of acute ischaemic stroke was 4.2 times significantly higher in patients with atrial fibrillation than control (OR=4.2, 95% of 01=1.113-15.781,  $\chi^2=5.105$ ,  $p<0.05$ ).

**Table VI** Atrial fibrillation status of the respondents

Atrial fibrillation	Study Group		Odds (95% of CI)	p-Value
	Group-A (n=67)	Group-B (n=67)		
Yes	11 (16.4)	3 (4.5)	3.3 (1.197-5.4)	$p>0.05$
No	56 (83.6)	64 (95.5)		
Total	67 (100.0)	67 (100.0)		

Chi-square ( $\chi^2$ ) test was applied to test the level of significance. Figure in the parenthesis indicates corresponding percentage.

### Discussion

In this study the age of the young patients with ischaemic stroke ranged from 17 to 45 years with the mean age of 40.1 (SD± 6.6) years. This result was supported by Putaala et al. and Janssen et al. that mean age of their young patients with ischemic stroke was 41.3 (7.6) and 41.3 (SD±7.7) years respectively, while Nayak, reported the mean age of 34.7 (SD± 8) years and in another study Spengos and Vemmos reported the mean age of 35.3 ± 6.7 years among their young patients with ischaemic stroke.<sup>22-25</sup> This study also showed that 39 (58.2%) patients with ischemic stroke were aged between 41 to 45 years, 13 (19.4%) were aged between 36 to 40 years, 7 (10.4%) were aged between 31 to 35 years, 4 (6.5%) were aged between 21 to 25 years, 3 (4.5%) were aged between 26 to 30 years and 1 (1.5%) respondents was aged between 16 to 20 years. Similar results were observed by Nayak.<sup>24</sup>

This study showed that there were 40 (59.7%) male and 27 (40.3%) female with ratio of male to female 1.5:1. This result was supported by Janssen et al. where they found female preponderance of young ischemic stroke patients. But male preponderance was reported in other studies.<sup>20-25</sup>

In the present study 36 (53.7%) patients with acute ischaemic stroke were smoker and 20 (29.9%) control subjects were smoker. Risk of acute ischaemic stroke was 2.7 times higher in smoker than non-smoker (OR=2.7, 95% of 01=1.34-5.55,  $p<0.01$ ). This result was similar to the study of Lipska et al. that the risk of acute ischaemic stroke was 3.95 times higher in smoker than non-smoker (OR=3.95, 95% of 01=1.61-9.71,  $p=0.003$ ).<sup>26</sup> Similar result was also reported by Whisnant et al. (OR=1.4, 95% of 01=1.15-1.78,  $p=0.0015$ ).<sup>28</sup>

In the current study 23 (34.3%) patients with acute ischaemic stroke were diabetic and 12 (17.9%) control subjects were diabetic. Risk of acute ischaemic stroke was 2.4 times higher in diabetic than non- diabetic (OR=2.4, 95% of 01=1.07-5.35,  $p<0.05$ ). This result was in accordance with the study of Whisnant et al that the risk of acute ischaemic stroke was 2 times higher in diabetic than non- diabetic (OR=2.0, 95% of 01=1.46-2.83,  $p=0.0001$ ).<sup>28</sup> In this regard Das et al. found significant association of acute ischaemic stroke in young with blood sugar level when categorized as 120 mg/dl or above and <120 mg/dl ( $p< 0.05$ ).<sup>10</sup> But Lipska et al. did not find significant association of acute ischaemic stroke in- young with diabetes mellitus.<sup>26</sup>

In this study 27 (40.3%) patients with acute ischaemic stroke were hypertensive and 14 (20.9%) control subjects were hypertensive. Risk of acute ischaemic stroke was 2.6 times significantly higher in hypertensive than normotensive (OR=2.6, 95% of 01=1.19-5.49,  $p<0.05$ ). This result was in accordance with the study of You et al. that the risk of acute ischaemic stroke was higher in patients with hypertension than without hypertension (OR=4.9, 95% of 01=3.3-13.9,  $p<0.001$ ).<sup>27</sup> Whisnant et al. also supported the result (OR=2.0, 95% of 01=1.61-2.52,  $p<0.0001$ ).<sup>28</sup>

In the present study 3 (4.5%) respondents of acute ischaemic stroke had vulvular heart disease, while 2 (3.0%) respondents of the control group had vulvular heart disease. The vulvular heart disease of both groups was almost similar (OR=1.5, 95% of 01=0.25-9.42,  $p>0.05$ ). This result was different from the study of Whisnant et al that mitral valve disease was significantly more frequent in acute ischaemic stroke patients than control (OR=2.4, 95% of 01=1.45-4.12,  $p=0.0008$ ) but mitral valve prolapse and aortic valve disease did not show statistically significant difference (OR=0.8, 95% of 01=0.37-1.67,  $p=0.5328$ ) and (OR=1.8, 95% of 01=0.94-3.46,  $p=0.0751$ ) respectively.<sup>28</sup>

In the current study 15 (22.4%) respondents of acute ischaemic stroke had ischaemic heart disease, while 12 (17.9%) respondents of control group had ischaemic heart disease. The frequency of ischaemic heart disease was more frequent in ischaemic stroke group but did not reach the level of significance (OR=1.5, 95% of 01=0.57-3.09,  $p>0.05$ ). This result was different from the study of Whisnant et al. that ischaemic heart disease was significantly more frequent in acute ischaemic stroke patients than control (OR=2.1, 95% of 01=1.64-2.78,  $p=0.0001$ ).<sup>28</sup>

This study showed that 11 (16.4%) respondents of acute ischaemic stroke had atrial fibrillation, while 3 (4.5%) respondents of control group had atrial fibrillation. Risk of acute ischaemic stroke was 4.2 times significantly higher in patients with atrial fibrillation than control (OR=4.2, 95% of CI=1.113-15.781,  $p<0.05$ ). This result was in agreement with the study of Whisnant et al that atrial fibrillation was significantly more frequent in acute ischaemic stroke patients than control (OR=2.0, 95% of CI=1.49-2.75,  $p=0.0001$ ).<sup>27</sup>

In the present study, 3 (4.5%) respondents of acute ischaemic stroke had migraine; while 1 (1.5%) respondents of control group had migraine. The frequency of migraine was more frequent in ischaemic stroke group but did not reach the level of significance (OR=3.1; 95% of CI=0.31-30.52;  $p>0.05$ ). This result was supported by Naess et al. (OR=1.7, 95% of CI=0.9-3.2,  $p>0.05$ ).<sup>11</sup>

### Conclusion

In conclusion, ischemic stroke in young patients has wider risk factors. Key components like hypertension, diabetes mellitus, smoking and atrial fibrillation associated with stroke as the most common risk factors of acute ischemic stroke in young adult patients. Early identification of risk factors and proper prevention, treatment and life style modification may reduce the morbidity and mortality in young stroke patients. Our findings highlight the value of focusing screening and prevention efforts on young adults to lower the incidence of ischemic stroke in this age group.

### Disclosure

All the authors declared no competing interest.

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