

# Association of Hypertriglycerideamia with Ischaemic Stroke

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## Abstract:

*Stroke is one of the foremost causes of morbidity, mortality and is a socioeconomic challenge. This is particularly true for developing countries like Bangladesh, where health support system including the rehabilitation system is not within the reach of common people. Hypertriglyceridemia has an effective influence in the pathogenesis of Ischaemic Stroke (IS). So, the focus of this study was to evaluate and assess the association of serum triglyceride level in patients of IS.*

*This case control study was carried out in the Department of Neurology in collaboration with Department of Biochemistry, BSMMU, Dhaka from July 2011 to June 2013. In this study, 60 diagnosed cases of ischaemic stroke patients and 60 age and sex matched healthy controls were enrolled. Risk factors of Ischemic Stroke (IS) patients were assessed (adjusted Odds Ratio) in comparison with healthy adults. In this study, being married [OR. 1.95, 95% CI (0.40-9.42), p=0.409], smoker [OR. 1.65, 95% CI (0.57 - 4.82), p= 0.357], DM [OR. 1.48, 95% CI (0.36-6.06), p=0.582], IHD [OR. 1.51, 95% CI (0.29 - 7.89), p=0.624], HTN [OR. 3.66, 95% CI (1.11-12.12), p=0.033], overweight [OR. 2.31, 95% CI (0.77 - 6.91), 0.135] and obesity [OR. 16.19, 95% CI (1.31-200.6), p=0.030], increased level of serum TC [OR. 8.24, 95% CI (2.07 - 32.83), p=0.003], TG [OR. 9.40, 95% CI (1.17 - 75.86), p=0.035], LDL [OR. 0.45, 95% CI (0.10-2.05), p=0.308], and decreased level of HDL [OR. 3.37, 95% CI (1.03 - 12.25), p=0.045] were found as risk factors in developing IS. Independent t-test was done to find out the statistically significant differences of continuous variables like serum lipid profile between case and control group. The mean (SD) value of TG which is focus of this study, was found 237.67 (61.74) in case group, and 169.97 (26.95) in control group which was highly statistically significant (p < 0.0001).*

*All of the significant variables were entered into stepwise logistic regression analysis model. From the logistic regression model, it can be finally concluded that hypertension, obesity, increased level of TC, increased level of TG and decreased level of HDL were statistically significant risk factors for development of IS.*

**Abbreviation:** IS (ischemic stroke), TC (total cholesterol), TG (triglyceride), HDL (high density lipoprotein), LDL (low density lipoprotein).

## Introduction:

Stroke is one of the leading causes of death in the world<sup>1</sup> and low and middle income countries have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide<sup>2</sup>. Each year, about 4.4 million people die of stroke globally, of whom almost three millions are from developing countries<sup>3</sup>. According to WHO, stroke will remain second leading cause of death both in developed and developing countries in 2020<sup>4</sup>. A survey carried out by the Indian Council of Medical Research in Kolkata, showed the average annual incidence of stroke as 145 per 100,000 persons per year<sup>5</sup>. Estimated annual incidence in Pakistan is 250/

100,000 translating to 350,000 new cases every year<sup>6</sup>. Incidence of stroke in Bangladesh is 2.55 per 1000 population per year in both sexes<sup>7</sup>. Another study showed prevalence of stroke is 46.2% in rural area, 27.4% in semi urban area and 26.4% in urban population<sup>8</sup>.

Multiple risk factors are associated with Stroke. The Non-modifiable risk factors are age, sex, family history, race and ethnicity and the modifiable risk factors include hypertension, cardiac disease, diabetes mellitus, dyslipidaemia, cigarette smoking, alcohol abuse, physical inactivity, carotid stenosis, and transient ischaemic attack<sup>9</sup>. Hyper-

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cholesterolaemia, high LDL and low HDL are established risk factor for ischaemic stroke<sup>10,11</sup> but some studies<sup>12-15</sup> showed significant correlation between hypertriglyceridemia and others<sup>16-18</sup> failed to prove this. Hypertriglyceridemia may lead to IS as Triglyceride-rich lipoproteins, including very-low-density lipoprotein and intermediate-density lipoprotein, in addition to LDL-C particles, become trapped in blood vessel walls and have been demonstrated in human atherosclerotic plaques. Hypertriglyceridemia may also endothelial dysfunction, oxidative stress due to lipid-derived free radicals, and impairment of endothelium-dependent vasodilatation<sup>19</sup>. In addition to a direct atherogenic effect of triglyceride rich lipoproteins, elevated triglycerides have been associated with several abnormalities of the clotting-fibrinolytic systems<sup>20</sup>.

In Bangladesh, food grain, particularly rice plays a key role in the consumption of food as well as for supplying calories and nutrients for the people of Bangladesh<sup>21</sup>. As the content of dietary carbohydrate is elevated (>55% of energy) and fat in the diet is reduced, triglycerides in the blood rises. This paradoxical phenomenon is known as carbohydrate-induced hypertriglyceridemia<sup>22</sup>. As a result, Bangladeshi people may have high triglyceride level and this study is carried out to see the association between ischaemic stroke and serum triglyceride level.

#### **Methodology:**

This case control study was carried out on 60 ischaemic stroke patients admitted in the Neurology Department, BSMMU and 60 age and sex matched controls from July 2011 to June 2013. All participants were above 18 years of age and ischaemia was confirmed by either CT scan or MRI of brain. Patients having venous thrombosis, cardioembolic events – AF, MI (within 6 weeks), prosthetic heart valve, endocarditis or taking anti lipid drugs are excluded from the study. After overnight fasting, serum lipid profile was done by automated analyzer in Biochemistry Department within 72 hours of

stroke onset. Diabetes Mellitus was defined as per ADA diagnostic criteria. Hypertensive were those people having blood pressure more than 140/90 mmHg. Hypercholesterolaemia, having TC more than 200 mg/dl; hypertriglyceridemia, having TG more than 150mg/dl; high LDL having LDL more than 130mg/dl and low HDL, having HDL less than 40mg/dl was set to define abnormal lipid profile. Smoker were those people who had a smoking history for a certain period of time (≥ 1 years) either regularly or irregularly. Overweight was defined as having BMI more than 25 but less than 30 and obese were those people having BMI 30 or more. SPSS 21.0 was used for analysis of the data. The Chi-square test was used to compare proportions and Student t test to compare continuous variables between groups. Logistic regression analysis was used to assess the independent contribution of risk factors to stroke. For all statistical tests, we considered p value <0.05 as statistically significant.

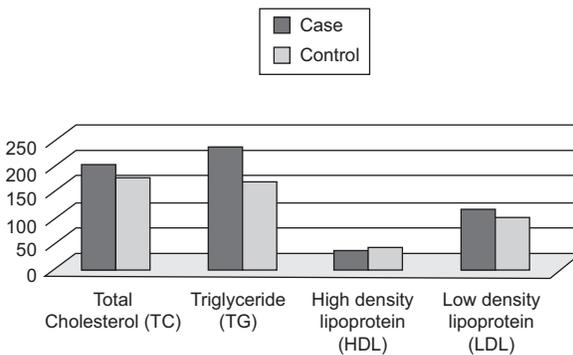
#### **Results:**

The mean age (SD) in the study was found 58.95 (12.23) years in case group and 52.90 (13.78) years that of control group (p=0.94). Most of the correspondents were belong to 60-69 years age group. Among the study sample, 56 were married in case group and 48 in control group. Statistically significant (p=0.018) difference was noted regarding the smoking status of case and control (36 Vs 22). 65% of the case and 68.3% of the control lived in urban area. (Table I) Around 51.67% of cases presented with hemiparesis, 20% monoparesis, 16.67% aphasia, 5% visual disturbance and 6.67% had cranial nerve involvement. The mean value of TG was found 237.67 (61.74) in case group, and 169.97 (26.95) in control group which was highly statistically significant (p < 0.0001). There was also statistically significant difference (p < 0.05 in other parameters in case and control groups [TC: 204.36 (39.57) vs. 179.83 (22.08) mg/dl; HDL: 39.75 (6.51) vs. 43.54 (5.04) mg/dl and LDL: 117.07 (42.44) vs 102.30 (22.59) mg/dl]. (Figure 1)

**Table-I**  
*Characteristics of case and control group*

	Case(n=60)	Control(n=60)	p value
1. Age (SD) years	58.95 (12.23)	52.90 (13.78)	0.94
2. Married (%)	56 (93.3%)	48 (80.0%)	0.60
3. Urban dweller	39 (65.0%)	41 (68.3%)	0.846
4. Smoker	36 (60.0%)	22 (36.7%)	0.018 <sup>#</sup>
5. Overweight	53.33%	36.67%	0.025 <sup>#</sup>
6. Obesity	10.0%	3.33%	0.025 <sup>#</sup>
7. Hypercholesterolaemia	51.7%	20.0%	0.001 <sup>#</sup>
8. Hypertriglyceridaemia	96.7%	75.0%	0.034 <sup>#</sup>

Comparison of lipid profile of case and control



**Fig.-1:** Bar diagram showing mean value of lipid profile in case group and control group.

The following variables were entered into logistic regression model to find out adjusted OR for ischemic stroke: Marital status, smoking, urban living, Diabetes Mellitus, IHD, hypertension, overweight, obesity, hypercholesterolemia, Hypertriglyceridemia, high LDL and low HDL. This model revealed having hypertension [adjusted or(95% CI), 3.66 (1.11 - 12.12); p =0.033], obesity [adjusted or(95% CI), 16.19 (1.31 - 200.69); p=0.03], increased level TC [adjusted or(95% CI), 8.24 (2.07 - 32.83); p=0.003], increased level TG [adjusted or(95% CI), 9.40 (1.17 - 75.86); p= 0.035] and decreased level of HDL [adjusted or(95% CI), 3.37 (0.93 - 12.25); p = 0.05] as statistically significant risk for ischemic stroke. Other risk factors did not attain statistically significant value. (Table II)

**Table-II**  
*Risk factors for ischemic stroke*

	Adjusted OR (95% CI)	p value
1. Married	1.95 (0.40-9.42)	0.409
2. Smoking	1.65 (0.57 - 4.82)	0.357
3. Urban living	0.86(.40 - 1.84)	0.699
4. Diabetes Mellitus	1.48 (0.36 -6.06)	0.582
5. IHD	1.51 (0.29 - 7.89)	0.624
6. Hypertension	3.66(1.11-12.12)	0.033 <sup>#</sup>
7. Overweight	2.31(0.77-6.91)	0.135
8. Obesity	16.91(1.31-200.6)	0.030 <sup>#</sup>
9. Hypercholesterolemia	8.24(2.07-32.83)	0.003 <sup>#</sup>
10. Hypertriglyceridemia	9.40(1.17-75.86)	0.035 <sup>#</sup>
11. High LDL	0.45(0.10-2.05)	0.308
12. Low HDL	3.37(0.93-12.25)	0.045 <sup>#</sup>

<sup>#</sup> Statistically significant

Logistic Regression Analysis was done to find correlation

### Discussion:

The main findings in this study were high triglycerides which constitutes an independent risk factor for ischemic stroke along with high cholesterol, low HDL, hypertension and obesity. Multiple studies along with a meta-analysis showed association of TG with ischemic events. Triglycerides are present in all plasma lipoproteins and make triglyceride-rich lipoproteins highly heterogeneous. This heterogeneity leads to complex relationship between triglycerides and cardiovascular disease. Although concurrent hypertriglyceridemia, hypertension, diabetes mellitus, obesity, and other dyslipidemias are well known as “metabolic syndrome”, Hypertriglyceridemia can cause stroke independently.

The metabolic pathways of triglycerides and HDL-C are related, and an increase in one will usually be accompanied by a decrease in the other<sup>23</sup>. Predicting ischemic risk in light of low HDL may most likely underestimate the role of triglyceride. The meta-analysis of prospective studies by the Asia-Pacific Cohort Studies Collaboration (APCSC) showed significant correlation between triglyceride and ischemic stroke<sup>13</sup>. In the Copenhagen City Heart Study, Lindstrom et al found a strong linear association between nonfasting triglyceride levels and cerebral ischemic events<sup>15</sup>. For every 1 mmol/l increment in non-fasting triglycerides, the RR increment for ischemic events was 1.12 (95% CI 1.07–1.16). In the Blood Lipids and First-Ever Ischemic Stroke/Transient Ischemic Attack in the Bezafibrate Infarction Prevention (BIP) registry the odds ratio for IS of triglyceride levels >200 mg/dl was 1.47 (95% CI 1.19–1.8)<sup>12</sup>. Wiely et al in their prospective study showed completely opposite result, where stroke was not associated with total cholesterol, triglyceride or HDL but increased risk of ischemic stroke of those having LDL>130 mg/dl (adjusted HR, 3.81; 95% CI, 1.53–9.51)<sup>24</sup>. In Finnmark study, a significant association between nonfasting triglyceride levels and stroke was found for women only [RR 1.29 (95% CI 1.05–1.57)]<sup>14</sup>. In Bangladesh Uddin et al, although found significant correlation between all components of lipid profile but not for TG<sup>10</sup>. Again, Bowman et al and Sridharan found no association of triglyceride level and ischemic stroke<sup>11, 18</sup>. To our best knowledge, this is the first study in Bangladesh to show correlation between TG and ischemic stroke. In the present analysis, we demonstrate the additive risk conferred by cholesterol fractions and high triglycerides.

#### Limitations:

Recall bias, inherent to all case-control study, and we are not different. This study is conducted in a single center involving small number of sample, which might not represent the actual condition of whole Bangladeshi people. In logistic regression model, we found wide confidence interval, which may be occurred due to small sample size.

#### Conclusion:

Blood lipids improve the prediction of ischemic stroke beyond traditional risk factors. Specifically, this study shows for the first time that high triglycerides is associated with increased risk of ischemic stroke. The renewed interest in the role of lipids for stroke, further research should focus on blood lipids, including serum triglycerides, as part of the global risk assessment and potentially modifiable risk factors for ischemic stroke.

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