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Association of Hypertriglyceridemia with Ischemic Stroke, Study in a Tertiary Care Hospital in Bangladesh

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Abstract

Background: *Hypertriglyceridemia fosters the development of atherosclerosis via several mechanisms and lead to ischemic stroke (IS) through its contribution to thrombogenicity. The association of hypertriglyceridemia with ischemic stroke was evaluated in this study.*

Methods: *This was a case control study conducted in the Department of Medicine, Dhaka Medical College Hospital and data was collected in a questionnaire from January to June'2013. Patients presented with ischemic stroke, confirmed by CT scan of Head/ MRI of brain from 1 day to 6 months and other than ischemic stroke patients were considered as case and control respectively.*

Results: *The mean age was found 61.0±8.3 years in case group and 60.5±8.1 years in control group. Male were predominant in both groups which was 80 (80.0%) in case group and 84 (84.0%) in control group. More than two third (68.0%) in cases and one fourth (25.0%) in controls patients had hypertension. 12 (12.0%) in cases and 2 (2.0%) in controls patients had heart disease. Normal triglycerides was found 52 (52.0%) in cases and 72 (72.0%) in control. The mean TG was found 179.9±62.8 mg/dl in cases and 148.0±51.9 mg/dl in controls. Desirable cholesterol was found 16 (16.0%) in cases and 25 (25.0%) in controls. The mean cholesterol was found 238.0±4.0 mg/dl in cases and 213.0±42.0 in controls. Optimal LDL was found 12 (12.0%) and 18 (18.0%) in case and control group respectively. Mean LDL was found 167.0±35.2 mg/dl in cases and 141.0±36.1 mg/dl in controls. Low HDL was found 64 (64.0%) in cases and 26 (26.0%) in controls. Mean HDL was found 41.2±10.6 mg/dl in case group and 49.0±8.6 mg/dl in control group.*

Conclusion: *Ischemic stroke is significantly associated with a higher level of TC, TG, LDL and HDL (inversely). Therefore, Hypercholesterolemia and Hypertriglyceridemia may be a risk factor for ischemic stroke.*

Keywords: *Ischemic stroke, Triglyceride (TG), Low density lipoprotein (LDL), High density lipoprotein (HDL).*

Introduction:

Stroke is one of the leading causes of death in the world, and the leading cause of acquired disability in adults in most regions.[1-2] Countries of low and middle income have the largest burden of stroke, accounting for more than 85% of stroke mortality worldwide, but few reliable data are available to identify risk factors for stroke in most of these regions, and particularly for hemorrhagic stroke.[1-5]

In Asia, the problem of stroke has a particularly strong impact, not only because more than half of the world's population lives in Asia, but stroke is the predominant vascular disease in many parts of Asia.[1] In1990 alone, World Health Organization estimated that there were over 2.1 million people who died of stroke In Asia.[2] The burden of stroke is likely to increase substantially in the near future because of the aging population. Stroke is the second leading cause of death worldwide, and the leading cause of acquired disability in adults in most regions. Apart from implementing effective stroke prevention programs, identification of factors associated with more severe stroke may help to ease the burden of this coming epidemic.[3-5]

Due to the tremendous burden that stroke places on our society, there have been major efforts to identify modifiable risk factors that could reduce the incidence of ischemic stroke (IS). Multiple independent risk factors for IS have been identified. The most prevalent of these include hypertension, diabetes mellitus, smoking, atrial fibrillation, coronary artery disease, congestive heart failure and disorders of lipid metabolism. Epidemiologic studies suggest that elevated total cholesterol and low-density lipoprotein cholesterol (LDL-

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C), as well as low levels of high-density lipoprotein cholesterol (HDL-C) are possible risk factors for IS.[6-7] Cholesterol and triglycerides are the 2 main lipids found in the body. Triglycerides (triacylglycerols) are the main storage form of fatty acids. They are esters of fatty acids and trihydric-alcohol-glycerol.

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 (a rise in the HDL-C level will be accompanied by a drop in the triglyceride level, and vice versa).[8-9]

Hypertriglyceridemia may lead to IS through its contribution to atherosclerosis and/or thrombogenicity. Studies suggest that hypertriglyceridemia fosters the development of atherosclerosis via several mechanisms. Postprandial hypertriglyceridemia in diabetic patients was found to produce endothelial dysfunction, oxidative stress due to lipid-derived free radicals, and impairment of endothelium-dependent vasodilatation.[10] 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.[11] Transient hypertriglyceridemia, induced by intravenous infusion of a triglyceride emulsion, was associated with decreased vascular reactivity in young healthy men who had no risk factors for coronary heart disease (CHD).[12] Chronic hypertriglyceridemia was independently associated with endothelial dysfunction in an observational study of patients with normal LDL-C.[13] Increased expression of adhesion cell molecules is considered to be a marker of endothelial cell dysfunction.[14] An increase in cell adhesion molecules has been noted in patients with hypertriglyceridemia.[14-15] Many prospective epidemiological studies have reported a positive relationship between serum triglyceride levels and incidence of CHD.[16-18]

Materials and Methods

This case control study was carried out in Department of Medicine, Dhaka Medical College Hospital from January 2013 to June 2013. A total of 100 Ischemic stroke patients who met the inclusion criteria were recruited as cases from the admitted patient of Medicine Department, DMCH. Age and sex matched apparently healthy persons were recruited as controls. Those who give informed written consent were finally enrolled in this study. All patients presenting with ischemic stroke, confirmed by CT scan of head/MRI of brain from 01 day to 6 months were included as cases. Patients of venous thrombosis, severely ill patients, those who were taking anti lipid drugs, history of Cardioembolic events – AF, MI (within 6 weeks of acute stroke), prosthetic heart valve, endocarditis were excluded from this study.

Stroke was defined as a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and at times global loss of brain function, with symptoms lasting >24 hours or leading to earliar death, and with no apparent cause other than that of vascular origin. *Hypertriglyceridemia* is *defined* as plasma levels of TG ≥200 mg/dL[12]. (it corresponds to a high *hypertriglyceridemia according* to the *ATP III*).Serum total cholesterol, HDL cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides were measured by standard enzymatic procedures.

After collection of information, these data were checked, verified for consistency and edited for result. After editing and coding, the coded data were entered directly into the computer by using software. Data cleaning validation and analysis were performed using the SPSS\PC software and graph and chart by MS Excel. The result was presented in tables in mean, standard deviation (SD) and percentage. A "p" value <0.5 were considered as significant.

Results:

100 patients with ischemic stroke and 100 control subjects were included in the study. It was observed that male were predominant in both groups which was 80 (80.0%) in case group and 84 (84.0%) in control group. The difference was not statistically significant (p>0.05) between two groups.

Among the study patients according to past medical history (n=200) it was observed that more than two third (68.0%) in cases and one fourth (25.0%) in controls patients had hypertension. Ten (10.0%) patients had diabetes in cases and 4 (4.0%) in controls. Twelve (12.0%) in cases and 2 (2.0%) in controls patients had heart disease. Hypertension and heart disease difference was statistically significant (p<0.05) between two groups. In this Normal triglycerides were found in 52 (52.0%) cases and in 72 (72.0%) of control. The mean TG was found to be 179.9±62.8 mg/dl in cases and 148.0±51.9 mg/dl in controls. Desirable cholesterol was found 16 (16.0%) in cases and 25 (25.0%) in controls. The mean cholesterol found was 238.0±4.0 mg/dl in cases and 213.0±42.0 in controls. Optimal LDL was found 12 (12.0%) and 18 (18.0%) in case and control group respectively. Mean LDL was found to be 167.0±35.2 mg/dl in cases and 141.0±36.1 mg/dl in controls. Low HDL was found in 64 (64.0%) cases and 26 (26.0%) in controls. Mean HDL was found to be 41.2±10.6 mg/dl in case group and 49.0±8.6 mg/dl in control group. The difference was statistically significant (p<0.05) between two groups.

Table-I

Distribution of the study patients according to age (n=200)

Age (years)	Case (n=100)		Control (n=100)		P value
	n	%	n	%	
26 - 35	4	4.0	3	3.0	
36 - 45	8	8.0	6	6.0	
46 - 55	24	24.0	25	25.0	
56 - 65	20	20.0	19	19.0	
66 - 75	28	28.0	33	33.0	
>75	16	16.0	14	14.0	
Mean±SD	61.0±8.3		60.5±8.1		0.667^{ns}
Range (min,max)	(26 -77)		(27-79)		

Table-II

Distribution of the study patients according to occupational status (n=200)

Occupational status	Case (n=100)		Control (n=100)	
	n	%	n	%
House-wife	20	20.0	19	19.0
Day labour	28	28.0	30	30.0
Non govt. service	16	16.0	15	15.0
Govt. service	8	8.0	7	7.0
Business	20	20.0	22	22.0
Others-Farmer	8	8.0	7	7.0

Table-III

Distribution of the study patients according to complications (n=200)

Complications	Case (n=100)		Control (n=100)		P value
	n	%	n	%	
Weakness of the body (Rt)	64	64.0	0	0.0	0.001^{s}
Weakness of the body (Lt)	36	36.0	0	0.0	0.001^{s}
Aphasia	40	40.0	0	0.0	0.001^{s}
Unconsciousness	25	25.0	0	0.0	0.001^{s}
Headache	11	11.0	8	8.0	0.469^{ns}
Vomiting	16	16.0	4	4.0	0.004^{s}
Others	8	8.0	88	88.0	0.001^{s}

Table-IV

Distribution of the study patients according to past medical history (n=200)

Past medical history	Case (n=100)		Control (n=100)		P value
	n	%	n	%	
Hypertension					
Yes	68	68.0	25	25.0	0.001^{s}
No	32	32.0	75	75.0	
Diabetes					
Yes	10	10.0	4	4.0	0.096^{ns}
No	90	90.0	96	96.0	
Heart Disease					
Yes	12	12.0	2	2.0	0.005^{s}
No	88	88.0	98	98.0	

Table-V

Distribution of the study patients according to fasting lipid profile (n=200)

Fasting lipid profile		Case (n=100)		Control (n=100)		P value
		n	%	n	%	
Triglycerides (TG)	Normal (< 150 mg/dl)	52	52.0	72	72.0	
	Borderline high (150-199 mg/dl)	32	32.0	22	22.0	
	High (200-499 mg/dl)	14	14.0	6	6.0	
	Very high (>500 mg/dl)	2	2.0	0	0.0	
	Mean±SD	179.9 ±62.8		148.0 ±51.9		0.001^{s}
	Range (min,max)	(110 ,520)		(100,290)		
Total cholesterol	Desirable (< 200 mg/dl)	16	16.0	25	25.0	
	Increased (> 200 mg/dl)	84	84.0	75	75.0	
	Mean±SD	238.0 ±43.0		213.0 ±42.0		0.001^{s}
	Range (min,max)	(150 ,280)		(150 ,250)		
Low-density lipoprotein (LDL)	Optimal (< 130 mg/dl)	12	12.0	18	18.0	
	Increased (> 130 mg/dl)	88	88.0	82	82.0	
	Mean±SD	167.0±35.2		141.0±36.1		0.001^{s}
	Range (min,max)	(120,189)		(100,159)		
High-density lipoprotein (HDL)	Low (< 40 mg/dl)	64	64.0	26	26.0	
	Increased (> 40 mg/dl)	36	36.0	74	74.0	
	Mean±SD	41.2±10.6		49.0 ±8.6		0.001^{s}
	Range (min,max)	(38,60)		(39 ,66)		

Discussion:

This case control study was carried out with an aim to determine the level of triglyceride among ischemic stroke patients and to measure and compare the serum triglyceride level including comparing partial demographic variation between cases and controls.

In this present study it was observed that the age of 28.0% patients in case group and 33.0% in control group was within 66-75 years and the mean age was 61.0±8.3 years varied from 26 – 77 years in case group and 60.5±8.1 years varied from 27 – 79 years in control group, which was almost alike between two groups, no difference was found. Similarly, Tanne et al.[11] showed the mean age was 61.8±6.5 years Ischemic Stroke/TIA and 59.6±7.1 years in no CVD patients. Similarly, Bowman et al.[18] showed the mean age was 61.5±7.2 years and 59.9±8.7 years in case and control respectively. On the other hand, Hsieh et al.[19] has observed higher mean age in Ischemic Stroke Group and control group, which were 69±11 years and 63±23 years respectively. They have stated that the higher age range maybe due to increased life expectancy, geographical and racial influences may have significant impacts on Ischemic Stroke.

In this current study it was observed that male were predominant in both groups which was 80.0% in case group and 84.0% in control group and male to female ratio was almost 4:1 in both groups. The difference was not statistically significant ($p>0.05$) between two groups. Similar observations regarding the sex incidence were also made by Tanne et al.[11], Hsieh et al.[19]

Regarding the complications it was observed in this present study that weakness of the body (Rt) (64.0%), weakness of the body (Lt) (36.0%), aphasia (40.0%) and unconsciousness (25.0%) were more common in the case group whereas headache was present in 11.0% and vomiting 16.0% in this group. Islam[20] showed that 50.0% of the Ischemic patients presented with left sided abnormality, 40.0% had right sided, 10.0% had both sided abnormality and 24.0% had vomiting. Report from Akbar and Mushtaq[21] showed that the bilateral stroke was 15.5% in the 103 study patients.

Regarding the past medical history it was observed in this current study that more than two third of patients (68.0%) in cases and one fourth (25.0%) in controls had hypertension. Ten percent patients had diabetes in cases and 4.0% in controls. Twelve percent patients in cases and 2.0% in controls had heart disease. Hypertension and heart disease were significantly ($p<0.05$) higher in case groups. Tanne et al.[11] showed hypertension, in 43.0% Ischemic Stroke/TIA group and 32.0% in NO CVD group. Diabetes mellitus found 34.0% and 20.0% in Ischemic Stroke/TIA and No CVD respectively.

Hypertension is the most important modifiable risk factor for both ischemic stroke and ICH. However, hypertension appears to be a stronger risk factor for ICH than for ischemic stroke reported by Qureshi et al.[23], Lewington et al.[24] The risk of stroke increases exponentially with increasing diastolic blood pressure (DBP) mentioned by MacMahon et al.[25] However, hypertension is a highly preventable risk factor; a systematic review of 17 randomized clinical trials showed that lowering DBP by 5– 6 mmHg and systolic blood pressure (SBP) by 10–12 mmHg resulted in a 38% reduction in strokes.[23-25] Hypertension alone may also increase the risk of rupture related to degenerative changes of small arterioles documented by Qureshi et al.[23] In this present study it was observed that 28.0% patients had diabetes mellitus in case group and 7.0% in control groups. Al most one third (32.0%) patients had hypertension in case group and 19.0% in control group. Alost one fourth (24.0%) patients had stroke in case group and 9.0% in control group. Only 4.0% and 19.0% had obesity in cases and controls respectively. Eight (8.0%) patients had dyslipidemia in cases and 18.0% in controls. diabetes mellitus, hypertension and stroke were significantly ($p<0.05$) higher in case group, however obesity and dyslipidemia were significantly ($p<0.05$) higher in control group. Bowman et al.[18] found diabetes 12.8% and 3.4% in case and control respectively.

In only some a severe hypercholesterolemia (total-C levels > 8 mmol/L) was associated with ischemic stroke obtained by Lindenstrom et al.[26] or non fatal stroke in men reported by Wannamethee et al.[27]. It was observed in this current study that normal triglyceride was found 52.0% in cases and 72.0% in control. The mean TG was found 179.9±62.8 mg/dl in cases and 148.0±51.9 mg/dl in controls, which was significantly ($p<0.05$) higher in case group. Austin MA et al.[13] found that the mean average of TG was 169.71 mg/dl in patients and 148.68 mg/dl in controls. Tanne et al.[11] showed the mean TG 178±108 mg/dL in Ischemic Stroke/TIA and 164±102 mg/dL in No CVD. Bowman et al.[18] (2003) obtained that the mean average of TG was 192.3±155.9 mg/dl in patients and 157.0±93.0 mg/dl in controls.

In this series it was observed that desirable cholesterol was found 16.0% and 25.0% in case and controls respectively. The mean cholesterol was found 238.0±4.0 mg/dl in cases and 213.0±42.0 in controls. That was significantly ($p<0.05$) higher in case group. Tanne et al.[15] found the mean total cholesterol 228±43 mg/dL and 225±43 mg/dL in Ischemic Stroke/TIA and No CVD respectively. Similarly, Bowman et al.[18] obtained that the mean TC level was 231.7±51.1 mg/dL in case group and 228.6±46.5 mg/dL in control group. Similar identical findings also found by Hsieh et al.[19].

In this study it was observed that optimal LDL was found 12.0% in case and 18.0% in control group. Mean LDL was found 167.0±35.2 mg/dl in cases and 141.0±36.1 mg/dl in controls, which was significantly ($p<0.05$) higher in case group. Tanne et al.[11] found the mean LDL-C level was 157±38 mg/dL in Ischemic Stroke/TIA and 54±37 mg/dL in No CVD. Similar findings also obtained by Hsieh et al.[19]. The above findings are consistent with the current study.

A low HDL-C level has been reported by Bowman et al.[18] to be associated with ischemic stroke in many studies. In another, hypertriglyceridemia was weakly associated with ischemic stroke in women but not in men obtained by Abbott RD et al.[22]. In this present series it was observed that low HDL was found 64.0% and 26.0% in case and controls groups respectively. Mean HDL was found 41.2±10.6 mg/dl in case group and 49.0±8.6 mg/dl in control group, which was significantly ($p<0.05$) lower in case group. Bowman et al.[18] showed the mean HDL-C to be 49.0±15.9 mg/dL and 52.4±16.0 in cases and control respectively. Similarly, Tanne et al.[11] and Hsieh et al.[19] had observed identical HDL level of the patients and thus, support the present study.

Laloux et al.[17] showed in controlled study that ischemic stroke/TIA is associated significantly with a higher level of total-C, LDL-C, HDL-C (inversely) and TG. Therefore, their results confirm that hypercholesterolemia and hypertriglyceridemia may be a risk factor for ischemic cerebrovascular disease. However, the issue of whether hyperlipidemia is related more to any particular stroke subtype remains unsettled. Although two studies have shown that a high level of total-C and TG was significantly associated with atherothrombotic stroke as compared to control. The above findings closely resemble the findings of the current study.

Conclusion

This study was undertaken to evaluate the association of hyper-triglyceridemia with ischemic stroke. Ischemic Stroke was more common in 6^{th} and 7^{th} decade and male predominant. Weakness of the body (Rt), weakness of the body (Lt), aphasia and unconsciousness were the more common complications of ischemic stroke patients. Hypertension, heart disease, smoking**,** diabetes mellitus were significantly ($p<0.05$) associated with ischemic stroke. On the other hand ischemic stroke is associated significantly with a higher level of total-C, LDL-C, HDL-C (inversely), and TG. Therefore, this current study result confirms that hypercholesterolemia and hypertriglyceridemia may be a risk factor for ischemic stroke.

Limitations of the study

1. The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not be reflect the exact picture of the country.
2. The present study was conducted within a very short period of time.
3. Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size.

Conflict of Interest : None

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