

ORIGINAL ARTICLES

Association of Dyslipidaemia in Young Patients with Recent Ischaemic Stroke

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Abstract:

Background: The relation between serum lipids and ischemic stroke remains controversial in young patients. The aim was to determine the serum lipid profile and the vascular risk factors for ischaemic stroke in a series of patients under 45 with an ischemic stroke and to compare them with a series of controls of the same age.

Material and method: This case-control study was conducted in the Department of Neurology and Department of Biochemistry of BSMMU, Dhaka, between the period of July 2007 and June 2009 for duration of two years. A total number of 50 patients presented with recent ischemic stroke and 50 control person were enrolled in this study. All patients of both sexes, aged between 15 to 45 years presented with ischemic stroke, from 0 day to 1 month that was confirmed by CT scan of head/MRI of brain. Vascular risk factors were recorded and blood sample was collected from the cases and the controls and analyzed at the Dept. of Biochemistry, BSMMU for estimation of serum fasting lipid profile. **Result:** Multivariate analyses showed that other than serum lipids- family history of dyslipidaemia, family history of stroke or TIA, history of HTN and smoking habit are found significant risks for stroke in young adult. **Conclusion:** The present study does not confirm the role of serum lipids as risk factors for ischemic stroke in young adult. Other than serum lipids- family history of dyslipidaemia, family history of stroke or TIA, history of HTN and smoking habit are found significant risks for stroke in young adult.

Keywords: Ischemic stroke; young people; lipoproteins.

Introduction:

Stroke is a major global health problem. It is a major cause of mortality, morbidity and disability in developed and increasingly in less developed countries. Ischemic stroke in young adults has been considered a relatively rare event, with fewer than 5% of all cerebral infarctions occurring below the age of 45 years, (Nedeltchev et al. 2005)¹. Studies of lipid related risk factors in cerebrovascular disease have varied greatly in their findings and also in their definition of the cerebrovascular end points²⁻³. Several clinical trials showed an association between high concentrations of serum cholesterol and ischemic stroke⁴⁻⁶. On the other hand, case-control studies of stroke which examined cholesterol as a risk factor have generally produced negative findings⁷⁻⁸ and

prospective studies have generally failed to show a direct and strong association⁹. Present study is designed to evaluate the serum lipid profile as a risk factor for young ischemic stroke patients less than 45 years in Bangladesh.

Materials and Methods:

This case control study was conducted in the Department of Neurology, BSMMU, Dhaka from July 2007 to June 2009 for duration of two years. Total 100 subjects were included in this study and of them 50 were young ischemic stroke patients, who were enrolled as cases and 50 were clinically healthy individual, enrolled as controls.

Subjects were selected following the inclusion and exclusion criteria-

1. Assistant professor. Department of Neurology. Sylhet M A G Osmani Medical College.

2. Professor. Department of Neurology. Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

Inclusion criteria for cases:

1. Patients with clinical features of ischemic stroke proved by computed tomography scan and/MRI of head within 4 weeks of attack.
2. Young patients in between the age of 16 to 45 years.
3. Patients, who gave consent and complied with the study procedure, were included.

Exclusion criteria for cases:

1. Patients who refused to be included in the study
2. Patient with intracranial space occupying lesion (ICSOL) presenting with stroke like features.
3. Systemic disease like vasculitis, e.g. systemic lupus erythematosus (SLE), polyarteritis nodosa (PAN).
4. Head injury
5. Infective disease of brain and meninges
6. Abnormal cardiac condition giving rise to stroke e.g. valvular heart disease, atrial fibrillation.
7. Those patients who were on lipid lowering drugs.

Inclusion criteria for control:

1. Age group and sex matched with the cases
2. Clinically healthy individual voluntarily agreed to undergo the study protocol.
3. Agreed to collection of blood sample for biochemical test

Exclusion criteria for control:

Those who did not voluntarily agree to the study protocol after full explanation.

Data were collected in a structured questionnaire at stroke clinic and neurology ward in BSMMU. Collection of blood sample & estimation of serum lipid profile from the cases and the controls were done at the department of Biochemistry, BSMMU.

Statistical analysis:

The relationships between different variables of both case and control group was analyzed with the Chi-squared test; Student's t test where applicable. Risk factor was analyzed by multiple logistic regression model. The findings of the study are presented here.

Results:

Table 1, showed the distribution of the respondents by age. Mean \pm SD of age of the cases was 39.88 \pm 7.26 years. Among the cases most common age group was 36-45 years (82.0%) followed by 26-35 and 16-25. Mean \pm SD of age of the control was 39.68 \pm 5.90 years. There is statistically no significant difference in age between the case and control ($p > 0.05$).

Table II showed the sex distribution of the respondents of both case and control group. Male and female ratio was approximately 2:1 in each group. There is statistically no significant difference in sex between the case and control ($p > 0.05$).

Table III revealed that out of all respondent of case and control group 40.0% and 10.0% had family history of diabetes mellitus, 34.0% and 16.0% had hypertension, 12% and 8.0% had familial history of

Table-I
Distribution of the respondents by age (n=100)

Age (in year)	Group		Total
	Case (n=50)	Control (n=50)	
16-25	3 (6.0) [#]	3 (6.0)	6 (6.0)
26-35	6 (12.0)	6 (12.0)	12 (12.0)
36-45	41 (82.0)	41 (82.0)	82 (82.0)
Total	50 (100.0)	50 (100.0)	100 (100.0)
Mean \pm SD	39.88 \pm 7.26	39.68 \pm 5.90	

[#]Figure within parenthesis indicates in column percentage.

Table-II
Distribution of the respondents by sex (n=100)

Sex	Group		Total
	Case (n=50)	Control (n=50)	
Male	32 (64.0)#	32 (64.0)	64 (64.0)
Female	18 (36.0)	18 (36.0)	36 (36.0)
Total	50 (100.0)	50 (100.0)	100 (100.0)

#Figure within parenthesis indicates in column percentage.

Table-III
Distribution of the respondents by family history of different diseases by group (n=100)

Family history	Group		p value*	Odd ratio
	Case	Control		
Diabetes	20 (40.0)#	5 (10.0%)	0.001	6.00 (2.03-17.73)
HTN	17 (34.0%)	8 (16.0%)	0.038	2.71 (1.04-7.04)
IHD	6 (12.0%)	4 (8.0%)	0.505	1.568 (0.41-5.93)
Dyslipidaemia	18 (36.0%)	3 (6.0%)	0.001	8.81 (2.39-32.41)
Stroke/TIA	24 (48.0%)	9 (18.0%)	0.001	4.205 (1.69-10.45)

*Chi-square test was done to measure the level of significance.

#Figure within parenthesis indicates in column percentage. Multiple responses

IHD, 36.0% and 6.0% had dyslipidaemia and 48.0% and 18.0% had family history of stroke/TIA respectively. There is statistically significant difference in family history of diabetes, hypertension, IHD, dyslipidaemia and stroke/TIA between the case and control ($p < 0.05$).

From Table IV, in case group 34.0% and in control group 10.0% had diabetes and patients with diabetes mellitus showed a risk of having stroke 4.64 times more than that of non diabetics. Out of all patients of case group 62.0% and in control group 10.0% had hypertension. Respondents having hypertension are 14.48 times more prone to develop stroke. There is statistically significant difference in respondents history of diabetes, hypertension in the case and control ($p < 0.05$).

In table V, 24.0% of the case group and 13.0% in control group had smoking habit, in case group 14.0% and in control group 03.0% had history of alcohol intake, in case group 25.0% and in control group 09.0% were tobacco chewer .

Table VI showed mean (\pm SD) total serum cholesterol, triglyceride, HDL and LDL level for case

group were 201.32 (\pm 43.47), 145.48(\pm 40.11), 34.26(\pm 8.59), 137.96(\pm 41.38) mg/dl respectively and in control group were 178.18(\pm 38.62), 136.38(\pm 57.11), 40.16(\pm 8.05), and 110.74(\pm 35.03) mg/dl respectively.

The table VII showed that in case group 54.0% had normal and 46.0% had abnormal level of total cholesterol. In control group 80.0% had normal and 20.0% had abnormal level of cholesterol. Statistically significant difference was observed between groups in term of total serum cholesterol level ($p < 0.05$).

Table VIII showed In case group 60.0% had normal and 40.0% had abnormal level of triglyceride. In control group 68.0% had normal and 32.0% had abnormal level of triglyceride. No statistically significant difference was observed between groups in term of triglyceride level ($p > 0.05$).

Table IX showed In case group 24.0% had normal and 76.0% had abnormal level of HDL cholesterol. In control group 44.0% had normal and 56.0% had abnormal level of HDL cholesterol. Statistically significant difference was observed between groups in term of HDL cholesterol level ($p < 0.05$).

Table-IV
Distribution of the respondents history of diseases by group (n=100)

Diseases	Group		p value	Odds ratio (CI)
	Case (n=50)	Control (n=50)		
Diabetes	17 (34.0)#	5 (10.0)	0.004*	4.64(1.55-13.84)
HTN	31 (62.0)	5 (10.0)	0.001*	14.48(4.96-43.51)
IHD	5 (10.0)	0 (.0)	0.056**	
Dyslipidaemia	4 (8.0)	1(2.0)	0.360**	
Stroke	2 (4.0)	0 (.0)	0.153**	

*Chi-square test was done to measure the level of significance.

**Fisher's exact test was done to measure the level of significance.

#Figure within parenthesis indicates in column percentage. Multiple responses

Table-V
Distribution of the respondents by personal habit by group (n=100)

Personal habit	Group		p value*	Odds ratio (CI)
	Case	Control		
Smoking habit	24 (48.0)	13 (26.0)	0.023	2.63(1.13-6.09)
Alcohol intake	7 (14.0)	3 (6.0)	0.182	2.55(0.62-10.49)
Tobacco leaf chewer	25 (50.0)	9 (18.0)	0.001	4.56(1.83-11.32)

*Chi-square test was done to measure the level of significance.

#Figure within parenthesis indicates in column percentage .Multiple responses

Table-VI
Distribution of the respondents fasting lipid profile level by group

Fasting lipid profile	Normal value	Mean \pm SD	
		Case	Control
Total serum cholesterol	<200mg/dl	201.32 \pm 43.47	178.18 \pm 38.62
Triglyceride	<150mg/dl	145.48 \pm 40.11	136.38 \pm 57.11
HDL cholesterol	>40mg/dl	34.26 \pm 8.59	40.16 \pm 8.05
LDL cholesterol	<130mg/dl	137.96 \pm 41.38	110.74 \pm 35.03

Table-VII
Distribution of the respondents by total serum cholesterol by group (n=100)

Total serum cholesterol	Group		p value*	Odd ratio
	Case(n=50)	Control (n=50)		
Normal	27 (54.0)	40 (80.0)	0.006	3.41 (1.40-8.28)
Abnormal	23 (46.0)	10 (20.0)		
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-VIII
Distribution of the respondents by triglyceride level by group

Triglyceride	Group		p value*	Odd ratio
	Case (n=50)	Control (n=50)		
Normal	30 (60.0)	34 (68.0)	0.405	1.42 (0.62-3.22)
Abnormal	20 (40.0)	16 (32.0)		
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-IX
Distribution of the respondents by HDL cholesterol by group

HDL cholesterol	Group		p value*	Odd ratio
	Case	Control		
Normal	12 (24.0)	22 (44.0)	0.035	2.49 (1.06-5.86)
Abnormal	38 (76.0)	28 (56.0)		
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table X showed In case group 44.0% had normal and 56.0% had abnormal level of LDL cholesterol. In control group 76.0% had normal and 24.0% had abnormal level of LDL cholesterol. Statistically significant difference was observed between groups in term of LDL cholesterol level ($p < 0.05$).

Table XI showed, logistic regression analysis of Odds ratios for characteristics of the patients likely to develop stroke. The variables revealed to be significantly associated with stroke by bivariate analyses were all entered into the model directly.

Variables entered into the model were family history of DM, HTN, dyslipidaemia, stroke/TIA, personal history of DM, HTN, smoking habit, tobacco leaf chewer, total serum cholesterol, HDL cholesterol LDL cholesterol were found to be the independent predictors of stroke with Odd ratios being 4.60, 1.66, 21.27, 4.48, 1.23, 11.70, 4.71, 2.44, 3.72, 3.25 and 2.52 respectively. Of them family history of dyslipidaemia, family history of stroke/TIA, personal history of HTN and smoking habit were found significant predictors.

Table-X
Distribution of the respondents by LDL cholesterol level by group

LDL cholesterol	Group		p value*	Odd ratio
	Case (n=50)	Control (n=50)		
Normal	22 (44.0)	38 (76.0)	0.001	4.03 (1.71-9.49)
Abnormal	28 (56.0)	12 (24.0)		
Total	50 (100.0)	50 (100.0)		

*Chi square test was done to measure the level of significance.

Table-XI
Logistic regression analysis for predictors of stroke in young

	B	S.E.	Wald	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
						Lower	Upper
Family H/O DM	1.527	0.952	2.571	0.109	4.604	0.712	29.768
Family H/O HTN	0.504	0.743	0.461	0.497	1.656	0.386	7.103
Family H/O dyslipidaemia	3.057	1.180	6.717	0.010*	21.267	2.107	214.663
Family H/O stroke/TIA	1.500	0.726	4.272	0.039*	4.481	1.081	18.584
H/O DM	0.204	0.866	0.055	0.814	1.226	0.225	6.697
H/O HTN	2.460	0.764	10.379	0.001*	11.702	2.620	52.262
Smoking habit	1.550	0.769	4.061	0.044*	4.711	1.043	21.268
Tobacco leaf chewer	0.890	0.696	1.638	0.201	2.436	0.623	9.525
Total serum cholesterol	1.314	1.093	1.444	0.229	3.720	0.437	31.703
HDL cholesterol	1.180	0.762	2.394	0.122	3.253	0.730	14.495
LDL cholesterol	0.926	0.907	1.041	0.307	2.524	0.426	14.936
Constant	-4.455	1.018	19.165	0.001	.012		

* Significant predictor

Discussion::

All respondents were enrolled in this study from the age group of 16 to 45 years with a male and female ratio of 2:1. Majority of the cases presented at 36 to 45 years of life [Mean (± SD) age of case group was 39.88 (± 7.26) and control group was 39.68 (± 5.90)] with male and female ratio of 2:1. There is no statistically significant difference in sex between the case and control (p>0.05) (Table 2).

In present study out of all respondent of case and control group 40.0% and 10.0% had family history of diabetes mellitus, 34.0% and 16.0% had hypertension, 12% and 8.0% had family history of IHD, 36.0% and 6.0% had dyslipidaemia and 48.0% and 18.0% had family history of stroke/TIA respectively.

Respondents having family history of diabetes, hypertension, IHD, dyslipidaemia and stroke/TIA are 6.0, 2.71, 1.57, 8.81 and 4.20 times more chance to develop stroke than respondents not having this type of family history respectively. These risk factors were measured by bivariate analysis.

Respondents having family history of stroke/TIA had 4.20 times more chance to develop stroke (p<0.05)

than respondents not having this type of family history. Few studies have examined FHS as a risk factor for specific stroke types or in early-onset stroke cases. A matched case-control study conducted in India showed a significant 2.5-fold increased risk of stroke associated with FHS after adjusting for stroke risk factors (Zodpey et al. 2000)¹⁰. In a population-based case-control study of Japanese men and women aged 20 to 70 years, the risk of ischemic stroke was significantly increased in those with a FHS in any first- or second-degree relative (Kubota 1997)¹¹. In a large prospective study conducted in Finland, an adjusted RR of 1.8 (p =0.03) for ischemic stroke and 2.8 (p =0.11) for SAH was found in those with an early parental history of stroke compared to those with no parental history in women aged 25 to 64 years (Jousilahti et al. 1997)¹². These risk estimates were very similar in magnitude to those found in the current study of young patients aged 35 to 45 years (unadjusted OR [95% CI] =4.205 [.69-10.45]) and adjusted OR [95% CI] = 4.48 [1.08-18.58] for ischemic strokes.

In a study conducted by Jalal Uddin (2006), 20% of the patients with ischemic stroke had family history

of stroke while in control only 2% had positive family history¹³. All these findings are consistent with the findings of present study.

In case group of present series 34.0% and in control group 10.0% had history of diabetes and participants with positive personal history of diabetes mellitus showed a risk of having stroke 4.64 times that of negative personal history of diabetes mellitus. In Jalal Uddin (2006)¹³ series diabetic persons had 3.917 times higher risk of ischemic stroke than non diabetic persons which is consistent with our findings. In Albucher et al (2000)¹⁴ series Odds ratio for development of stroke in diabetes mellitus patients was 1.058.

Hypertension was one of the most important risk factor of cerebral infarction in this study, found in 62% of patient. This figure is almost similar to that reported by Safeer et al (2008)¹⁵, Ali-L et al (1997)¹⁶ and Al-Rajeh et al (1993)¹⁷ and lower than reported by Burgin et al (65%)¹⁸ and Feigin et al (85%)¹⁹.

In the present study respondents not having hypertension were 14.48 times more prone to develop stroke than respondents not having hypertension. In multivariate analysis this risk reached 11.70 times. In Albucher et al (2000)¹⁴ series Odds ratio for development of stroke for hypertensive patients were 18.67. About 60% patients of stroke group and 20% respondents of control group were hypertensive in Jalal Uddin series (2006) ($P < 0.05$). Hypertensive persons showed a risk of having ischemic stroke 6 times higher than those of non-hypertensive persons in their series. Similar observation was also made in the present series.

In the present series among all respondents of case and control group 48.0% and 26.0% were smoker respectively. Smoker had 2.63 in bivariate analysis and 4.71 in multivariate analysis, times more chance to develop stroke than non smoker.

In Jalal Uddin series, 54% of case and 52% of the control group were smokers ($p > 0.05$). Smokers showed a risk of having ischemic stroke 1.084 times higher than those of non-smokers in his series¹³. Similar result was found by Khan (2000)²⁰. In his

series 55% of ischemic stroke patients were smoker but in control group, only 33% were smoker.

Smoking is associated with increased risk of cerebral infarction (Pancioli 1998)²¹. In Safeer et al (2008)¹⁵ study smoking was found in 31% of patients. The figure is slightly higher than other reported studies in Pakistan (Javed 1998)²² and much lower than studies reported in Greenland (81%) (Kjaergaard and Gelvan 2004)²³.

The serum cholesterol–stroke association remains an enigma. If low serum cholesterol concentration is associated with an increased risk of hemorrhagic stroke (Iso et al., 1989; Yano et al., 1989)^{24,25}, increased cholesterol is associated with an increased risk of ischemic stroke (Iso et al., 1989; Knuiman and Vu, 1996)^{24,26}. Studies in men subsequently showed increases in ischemic stroke rates at higher levels of total cholesterol, particularly for levels above 240 to 270 mg/dl (Iso et al., 1989;). The Asia Pacific Cohort Studies Collaboration found a 25% increase in ischemic stroke rates for every 1 mmol/L increase in total cholesterol (Zhang et al; 2003)²⁷. Dyslipidaemia was present in 32% of Khan et al (2009) series which is higher than 11-23% reported in other studies (Ali et al., 1997;)¹⁶.

In Jalal uddin (2006) series the total cholesterol level was 210 ± 7.89 (mean \pm SE) mg/dl and 187 ± 4.53 (mean \pm SE) mg/dl in case and control groups respectively ($p < 0.05$). Previous case-control study conducted by Khan (2000) found the value of serum total cholesterol 201 ± 5.52 (mean \pm SE) mg/dl in ischaemic stroke patients and 169.13 ± 3.49 (mean \pm SE) mg/dl in corresponding control ($p < 0.05$). Thus the result of the present study is consistent with the previous studies mentioned above although the age strictly was not matched.

LDL cholesterol level of patients with ischemic stroke in Jalal Uddin (2006) study was 156.99 ± 7.53 (mean \pm SE) mg/dl in stroke group and was 126.44 ± 4.47 mg/dl in control group ($p < 0.01$). The values of HDL-c in case and control groups of the Jalal Uddin series were 30.34 ± 0.91 vs. 41.04 ± 0.87 (mean \pm SE) mg/dl ($p < 0.01$). Low level of serum HDL-c was significantly associated with ischemic stroke in a previous case-control study conducted by Khan (2000)²⁰.

In this study high level of total serum cholesterol and LDL-c level and low level of HDL-c have odds of 3.41, 2.49 and 4.03 to develop stroke than that of normal level of these lipid profiles.

After adjustment with other predictors increased level of total serum cholesterol, lower level of HDL and higher value of LDL cholesterol had ODDs ratio (95% CI) of 3.72 (0.44-31.70), 3.25 (0.73-14.50) and 2.52 (0.43-14.94) respectively to develop stroke in young people.

In the present study after doing multiple logistic regression model- family history of DM, HTN, dyslipidaemia, stroke/TIA ; personal history of DM, HTN, smoking habit, tobacco leaf chewer ; total serum cholesterol, HDL cholesterol LDL cholesterol were found to be the independent predictors of stroke with Odd ratios being 4.60, 1.66, 21.27, 4.48, 1.23, 11.70, 4.71, 2.44, 3.72, 3.25 and 2.52 respectively. Of them family history of dyslipidaemia, family history of stroke/TIA, personal history of HTN and smoking habit were found significant predictors ($p < 0.05$).

In this study bivariate analysis showed lower level of HDL- cholesterol and higher value of total cholesterol and LDL-c as risk factors for stroke but after adjusted these variables by other known risk factors no significant result has come out. So, this study does not conclude having any relation between ischemic stroke in young patients and serum lipid profile.

Conclusion :

The present study does not confirm the role for lipids as risk factors for ischemic stroke in young adult. Rather than lipids, family history of dyslipidaemia, family history of stroke or TIA, personal history of HTN and smoking habit were found significant risks for stroke. As the present study conducted in a single center in Dhaka city with small sample size, to find out such potential risk factors, more study is needed to see association of serum lipids as a risk factor for young ischemic stroke in our ethnic population.

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