Article

Association of Apo B, Apo A_1 and lipid Profile with Early Onset Stroke

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Abstract

Background: Early onset of stroke is a devastating illness and dyslipidaemia are widely accepted risk factors for coronary heart disease (CHD). High Apolipoprotein B (Apo B), low Apolipoprotein A_1 (Apo A_1) and the Apo B/Apo A_1 ratio are used as the predictors of stroke for CHD. **Objective:** To evaluate the association of Apo B, Apo A_1 and lipid profile with early onset stroke. **Methods:** This case-control study was conducted in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University, Dhaka from Jan'2008 to Dec'2008. Total 100 stroke patients of both sexes were included, diagnosed by CT scan and MRI. Fifty stroke patients of early onset (EOS-P; age d"45 yrs) were included as case and 50 stroke patients of late onset (LOS-P; age >50 yrs) were taken as control. Serum lipid profile (TAG, TC, LDL-C & HDL-C), lipid ratios (TC/HDL-C, LDL-C/HDL-C & TAG/TC), Apo B, Apo A_1, and Apo B/Apo A_1 ratio were measured in all patients. Mann Whitney U test, Odds Ratio, unpaired t-test were used for statistical analysis. **Results:** In this study, serum Apo A_1, and TAG were significantly higher in EOS-P than those of LOS-P. Again, with respect of cut off value, odds ratio of 2.29 indicates that high serum Apo B concentration is associated whereas odds ratio of 0.38 indicates that low serum Apo A_1 concentration is not associated with EOS **Conclusion:** From this study it can be concluded that, higher level of TAG is a risk factors for early onset stroke and high Apo B is associated with early onset stroke.

Key-words: Early onset stroke, lipid profile, lipid ratios, Apolipoprotein.

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Introduction

Stroke is a major public health problem. According to World Health Organization (WHO), stroke has caused about 5.54 million deaths worldwide in 1999 with two-thirds of these deaths occurring in less developed countries[1]. Indian studies have shown that about 10% to 15% of strokes occur in people below the age of 40 years[2]. Whereas, 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 descents[3]. Although stroke is considered to be a disease of the older population, it is not infrequent among adolescent and young adult. Young onset of stroke is a devastating illness and it brings misery and disability in the golden years of life. It carries significant morbidity, psychological effect and financial constrain for the person as well as for family [4] .

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The available data indicate that stroke occurring in young people is more often atherothrombotic in origin in developing countries[5-6]. Abnormal lipid parameters including increased level of triglycerides (TAG), total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) along with decreased level of high density lipoprotein cholesterol (HDL-C) are the probable risk factors for ischemic stroke, largely due to their link to atherosclerosis[7]. Apo B is present in VLDL, IDL, large buoyant LDL & small dense LDL (sd-LDL) which are the atherogenic particles. Among them sd-LDL particles are the most atherogenic, as they are easily oxidized & promote an inflammatory response & growth of plaques[8-10]. Larger Apo B containing particles, such as VLDL & IDL, can also enhance the risk of atherothrombosis by inhibiting the fibrinolytic system & by stimulatory cytokine production[11]. Apo A_1 is the inherent apolipoprotein of HDL & has anti-atherogenic properties. This apoprotein promotes fat efflux, including cholesterol from tissues to the liver for excretion. It is a cofactor for lecithin HYPERLINK "https://en.wikipedia.org/wiki/Lecithin%E2%80%94cholesterol_acyltransferase" cholesterolacyl transferase (LCAT) which is responsible for the formation of most plasma cholesteryl HYPERLINK "https://en.wikipedia.org/wiki/Cholesteryl_ esters" esters[12]. Apo A_1 was also isolated as a prostacyclin (PGI_2) stabilizing factor and thus may have an anticlotting effect[13].

HDL cholesterol sometimes gives misleading results, since the cholesterol composition of HDL can vary in response to various physiological and pathological conditions. Hence, the measurement of Apo A_1, the protein part of HDL is a better predictor of stroke. Again, the small dense particles of LDL are associated with risk of atherosclerosis. They contain less cholesterol and hence, the measurement of LDL cholesterol does not accurately reflect their plasma concentrations. Apo B (the protein part of LDL) predicts the development of stroke better than LDL cholesterol. This is because each of the atherogenic particles (VLDL, IDL and LDL) contains one molecule of Apo B and therefore, plasma Apo B measures the total number of atherogenic particles. So Apo B, Apo A_1, and the Apo B/Apo A_1 ratio can be used as the predictors of stroke along with the traditional lipid profile measurements [14]. Dyslipidaemia, low Apo A_1 and high Apo B are widely accepted as the risk factors for coronary artery disease. In contrast, the correlation has not been well established for stroke. So, the present study was undertaken to evaluate the association of Apo B, Apo A_1 and lipid profile with early onset stroke.

Methods

This case-control study was carried out in the Department of Biochemistry, BSMMU, Dhaka from January to December 2008. A total number of 100 stroke patients of both sexes were included in this study and they were diagnosed by CT scan and MRI. Among them, 50 stroke patients of early onset (EOS-P; age d"45 yrs) were included and 50 stroke patients of late onset (LOS-P; age >50 yrs) were taken as control for comparison. All of the subjects were selected from Department of Neurology of DMCH & BSMMU by simple random sampling. This protocol was approved by Institutional review board of BSMMU. After selection of the subjects, the nature, purpose, benefit and risks of the study were explained in details. They were encouraged for voluntary participation. Informed written consent was taken from the participants. Before taking blood, detailed family and medical history were taken and recorded in a prefixed data schedule. Serum Apo B, Apo A_1, Apo B/Apo A_1 ratio and lipid profile (TAG, TC, LDL-C & HDL-C), lipid ratios (TC/HDL-C, LDL-C/HDL-C & TAG/TC), of all the subjects were measured. However, Apo B, Apo A_1 were measured by Immuno nephelometric method[15,16], TC by

CHOD-PAP method[17], TG by GPO-PAP method[18], HDL-C by enzymatic colometric phosphotunstate-magnesium method[19], LDL-C by Fried-Wald formula[20]. Statistical analysis was performed by unpaired t-test, Mann Whitney 'U' test & Odds Ratio. 95% confidence limit ($p<0.05$) was taken as level of significance.

Results

The mean age and sex distribution of early onset and late onset stroke (EOS) are shown in Table I.

In this study Apo A_1 found significantly ($p<0.05$) higher in EOS compared to that of LOS. On the other hand, Apo B & Apo B / Apo A_1 ratio were found almost similar and the difference was not statistically significant between EOS and LOS (Table II).

Again, with respect to cut off concentration of Apo B (>1 g/l), 38 patients in EOS and 29 patients in LOS found to have high Apo B concentration. Calculated odds ratio of 2.29 indicates that high serum Apo B concentration is associated with EOS .With respect to the cut off value of 1gm/l; low concentration of Apo A_1 was found in 07 patients and in 15 patients among the EOS and LOS respectively. Calculated odds ratio of 0.38 indicates that low serum Apo A_1 concentration is not associated with EOS (Table III).

Moreover, with respect to the cut off ratio of 0.9, 23 patients in EOS and 28 patients in LOS found to show high Apo B/Apo A_1 ratio. Odds ratio of 0.67 advocates the high Apo B/Apo A_1 ratio is not a risk factor of EOS (Table III)..

The lipid profile status and lipid ratios in EOS and LOS are shown in Table IV. TAG in EOS was found significantly ($p<0.05$) higher compared to that of LOS; but with respect to TC, LDL-C HDL-C, TC/HDL-C ratio, LDL-C/ HDLC ratio and TAG/TC ratio, EOS and LOS did not differ significantly ($p<0.05$)

Table I: Grouping of the study subjects with age & sex distribution (n= 100)

Group	Male (n=57)	Female (n=43)	Age (years)
Case (no.)	27	23	38.22±7.70
(Early onset stroke) Age < 45 yrs			(18-45)
Control(no.)	30	20	65.80±8.66
(Late onset stroke) Age >50 Yrs			(52-85)

Data for age expressed as mean± SD ;Parenthesis indicates range.

Table II: Serum Apo B, Apo A-I & Apo B/Apo A-I ratio in two groups (n= 100)

Parameters	Case(n = 50)	Control(n = 50)
Apo B (g/L)	1.18	1.05
Apo A-I (g/L)	1.33	1.19*
Apo B /Apo A-I ratio	0.87	0.90

Data are expressed as median. For statistical analysis Mann Whitney U test was done. *p <0.05.

Table III: Association of Apo B , Apo $A_{1\ and}$ Apo B/Apo AI ratio with Early onset Stroke (n= 100)

Group	Apo B		Apo A_1		Apob/Apo A-I	
	> 1g/L	< 1 g/L	< 1 g/L	> 1g/L	> 0.9	<0.9
Early onset stroke (n = 50)	38	12	07	43	23	27
Late onset stroke (n = 50)	29	21	15	35	28	22
Total	67	33	22	78	51	49
Odds Ratio (C I)	2.29(0.97-5.41)		0.38(0.14-1.0 4)		0.67(0.30-1.97)	

Table IV: Comparison of lipid profile and lipid ratios in two groups (n= 100)

Parameters	Case(n = 50)	Control(n = 50)
TC (mg%)	161.28±54.72	158.34±73.99
TAG (mg%)	156.50±77.76*	126.14±57.05
LDL-C (mg%)	96.64±45.59	01.82±62.07
HDL-C (mg%	5.00±1.41	5.34±1.76
TC/HDL-C ratio	5.00±1.41	5.34±1.76
LDL-C/HDL-C ratio	2.95±1.20	3.37±1.32
TAG/TC	1.04±0.55	0.87±0.34

Data are expressed as Mean±SD. Statiscal analysis was done by Unpaired 't'test. TC= total cholesterol, TAG= triacylglycerol, LDL-C= low density lipoprotein cholesterol, HDL= high density lipoprotein cholesterol, *p<0.05.

Discussion

Present study showed that serum TC, LDL-C & HDL-C didn't differ significantly but serum TAG was significantly higher in early onset stroke group. A study also found significant association of plasma TAG with stroke that was concordant with our findings [21]. Many studies also show TAG as a risk factor for atherosclerosis[22-23]. Though, controversies exist about the association between TAG concentration & risk of stroke[24], TC/HDL-C, LDL-C/HDL-C & TAG/TC ratios did not also differ significantly in this study. Conflicting results exist in the literatures about the correlation between total plasma cholesterol of the patient & the risk of stroke. Dyslipidemia in stroke in young patients was not found to be associated in some studies[25,26] but some other studies[27-28] found association against community based control.

Apo B is present in VLDL, IDL, large buoyant LDL & small dense LDL (sd-LDL), with one molecule of Apo B in each of these atherogenic particles. Thus total Apo B reflects the total number of atherogenic particles. Usually >90% of all Apo B in blood is found in LDL. In case where LDL-C is in the normal/low range, high apo B level may indicate an increased number of sd-LDL particles which are the most atherogenic particles because they are easily oxidized & promote an inflammatory response & growth of plaques [8-10]. Larger Apo B containing particles, such as VLDL & IDL can also enhance the risk of atherothrombosis by inhibiting the fibrinolytic system & by stimulatory cytokine production[11]. In our study calculated risk ratio revealed high Apo B is associated with early onset stroke, but with comparative analysis LDL-C & Apo B concentration found no significant difference between early & late onset stroke patients. Probably it may be due to increased number of sd-LDL particles.

Apo A_1 has anti-atherogenic properties & higher value of Apo B/Apo A_1 ratio indicates more cholesterol is likely to be deposited in the arterial wall, thereby provoking atherogenesis [12]. Present study revealed significantly higher Apo A_1 in early onset stroke patients rather than late onset, which indicated protective role of this protein against early onset stroke, but Apo B/Apo A_1 ratio

didn't differ significantly. Some studies are not concordant with our study[29], where cases are compared with healthy control. Again, in this study calculated risk ratio revealed high Apo B is associated with early onset stroke, but with comparative analysis LDL-C & Apo B concentration found no significant difference between early & late onset stroke patients may be due to increased number of sd-LDL particles. Yet it needs to be rigorously searched through study with large sample size.

Conclusion

From this study it can be concluded that, higher level of TAG is a risk factors for early onset stroke. Again, high Apo B is strongly associated with early onset stroke.

Conflict of interest : None

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References

1. Prasad K, Singhal KK. Stroke in young, An Indian perspective. Neurol India. 2010;58(3):343-350
2. Kaul S. Stroke in young. Neurol India. 2007; 7(5): 23-24.
3. Kettner SJ, Stern BJ, Wozniak M, Buchholz DW, Earley CJ, Feese BR, Johnson CT, Macko RF, McCarter RJ, Price TR, Sherwin R, Chi B, Sloan MA, Wityk RJ. Cerebral infarction in young adult. Neurol. 1998; 50: 890-4.
4. Tripathi M, Vibha D. Stroke in young in India. Stroke Res Treat Online [Internet]. 2010 Dec 16 [cited 2011]: [6p]. Available from http://dx.doi.org/10.4061/2011/368629
5. Hankey GJ. Potential new risk factors for ishemic stroke. Stroke. 2006; 37: 2181-8.
6. Hayee MA, Haque A, Ullah AKMA, Hoque A and Akter N. Analysis of risk factor of stroke in 427 cases. Bangladesh J Neurosci. 1998; 14(2): 41-5.
7. Bihari VM, Szekely J, Grube E. Plasma high density lipoproteins in coronary, cerebral and peripheral vascular disease. The influence of various risk factors. Atheroscler. 1981; 40(3-4): 337-45.
8. Chein KL, Sung FC, Hsu H, Su T, Lin RS, Lee Y. Apolipoprotein A_1 and B and stroke events in a community-based cohort in Taiwan. Stroke. 2002; 33: 39-44.
9. Christophe R, Kailasanatha KM, Nagaraja D, Tripathi M. Case-control study of serum lipoprotein (a) and apolipoproteins A_1 and B in stroke in the young. Acta Neurologica Scandinavica. 1996; 94(2): 127-30.
10. Dixon JL, Biddle J, Lo C, Stoops JD, Li H, Sakata N, Phillips TE. Apolipoprotein B is synthesized in selected human non-hepatic cell lines but not processed into mature lipoprotein. J Histochem Cytochem. 2002; (50): 629-39.
11. Walldius G and Jugner I. Rationale for using apolipoprotein A_1 as indicators of cardiac risk and target for lipid-lowering therapy. Eur Heart J. 2005; 26(3): 210-12.