Research Article

Study of Lipid Profile in Non Diabetic Stroke in Young

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Abstract: Stroke is an abrupt onset of a neurological deficit that is attributable to a focal vascular cause. It is encountered quite frequently in clinical practice. The role of circulating lipids and lipoproteins in the pathogenesis of young stroke remains uncertain even after decades of research. Diabetes is an important cause for dyslipidaemia. In this present study an attempt is made to evaluate the association between serum lipids and young non diabetic stroke patients. This study was conducted on 30 patients of young nondiabetic stroke patients. Our study included 25 patients of Ischemic stroke, 5 patients of Hemorrhagic stroke and 30 age and sex matched healthy controls. Duration of study was from September 2010 to October 2013. Patients with cerebrovascular diseases associated with diabetes, head injury, pregnancy, puerperium, infections, hepatic encephalopathy, uraemic encephalopathy, nephrotic syndrome and patients on lipid lowering drugs were excluded. Venous blood was collected for the estimation of serum total cholesterol, triglycerides, LDL-C, HDL-C, VLDL-C by standard methods. Most common age group in our study was 37-45 years comprising 53.33% of cases. Males (76.7%) were more than females (23.3%) 63.41% of patients had elevated total cholesterol (mean 210.33 ± 71.61). 70% had elevated triglycerides (mean 184.93 ± 74.49), High LDL-C value (mean 131.78 ± 61.49) was seen in 46.7% of cases. The HDL-C levels (mean 44.71 ± 17.43) was seen in 43.3% of cases, High VLDL-C value (mean 33.94 ± 15.18) was seen in 56.7% of cases. The levels of total cholesterol, Triglycerides, LDL-C, TC/HDL-C, LDL-C/ HDL-C in cases were significantly raised when compared to control group ($p<0.001$). The levels of VLDL-C was significantly raised when compared to controls ($p<0.004$). The levels of HDL-C was not significantly decreased in cases when compared to control group ($p<0.853$). Dyslipidaemia was seen in 70% of cases. Dyslipidaemia was the first major risk factor followed by smoking (26.7%) and hypertension (23.3%). Among stroke patients smokers had significantly lower HDL-C (mean 41.23 ± 15.27) and higher TC/HDL-C (mean 6.05 ± 4.34) levels when compared to non smokers. Alcoholics had significantly higher HDL-C (mean 46.87 ± 0.19) & lower TC/HDL-C (mean 5.01 ± 3.87) levels than non alcoholics ($P<0.01$).Total cholesterol, Triglycerides, LDL-C, VLDL-C, TC/HDL-C, LDL-C/HDL-C were significantly raised in young stroke patients when compared to controls and had a positive correlation with the risk of stroke. Dyslipidaemia is one of the major risk factor in young non diabetic stroke patients. Thus early identification of dyslipidaemia and treatment can reduce the risk of stroke in young adults.

Keywords: Non Diabetic Stroke, Lipid Profile, Young adults.

INTRODUCTION

Stroke is the most common cause of death in the developed world after cancer and ischemic heart disease. It has been reported to be the most common cause of physical disability. Stroke is a common medical emergency. The incidence is raising steeply in many developing countries due to the adoption of less healthy life styles [1]. The treatment is difficult to treat and is still not effective. Prevention is the best option but ability to forecast the stroke is challenging. Detailed study of risk factors is essential [2].

The risk factors include diabetes, hypertension, dyslipidaemia, atherosclerosis, age, smoking and other rare causes. There is good evidence that modification of modifiable risk factor will reduce the risk of the stroke [3, 4]. Studies have shown that elevated levels of serum lipids are important risk factors for the development of atherosclerosis which is the precursor of stroke [5]. So, aggressive treatment of dyslipidaemia will decrease the risk of stroke [3].

The amount of evidence relating to relation between serum lipids, lipoproteins and cerebrovascular accidents is not adequate. The meager reports are

available in Indian patients who have different social, living and dietary habits compared to the western population [6].

Hence the study has been taken up to study lipid abnormalities in non diabetic young stroke patients in our setup

Aims and Objectives

To study serum lipid profile in patients with cerebrovascular disease and to determine the significant correlation between them.

MATERIALS AND METHODS

A total of 30 non-diabetic young patients aged more than 18 years & less than 45yrs both male and females diagnosed to have cerebrovascular disease have been the subjects of the study. Age and sex matched 30 healthy persons were taken as controls.

Criteria for selection

- Abrupt or relatively rapid onset of focal neurological disturbance which persisted for more than 24 hours.
- Gradual onset with smooth or stuttering progression over few hours. CT scan brain or MRI brain evidence of infarction or hemorrhage.

Cerebrovascular accidents associated with head injury, pregnancy, puerperium, dehydration, infections, hematological disturbances, uraemic and hepatic encephalopathy, Nephrotic syndrome, CVT, with previous neurological deficits and TIAs. CT/MRI scan

evidence of old infarcts, patients who were on lipid lowering drugs, and who came after the first week of onset of stroke were not included in the study. The purpose of elimination was to obtain a pure picture of the relationship between cerebrovascular disease and serum lipids.

Samples for analysis were taken in the first week of post cerebral infarction period. Each patient was subjected to thorough clinical examination. CT/MRI scan brain, CBC, fasting and post prandial blood sugars, blood urea, Sr. creatinine, fasting lipid profile, CXR, ECG, 2D Echo, Abdominal U/S, were done in all cases.

Blood sampling and preparation of serum

The serum samples were analyzed the same day or within 48 hours. The lipid and lipoprotein assay was done using the Dr. Lange LP 700 equipment. Estimation of Serum Total Cholesterol was by Carr and Drekter Method:

The serum total cholesterol concentration was calculated as follows:

$$\text{Total Cholestrol} = \frac{\text{OD of the test}}{\text{OD of the Standard}} \times 200 \text{mg/dl}$$

(OD- optical density)

RESULTS

A Comparative two group clinical study with 30 Cases and age and sex matched 30 controls is undertaken to study the levels of serum lipid profile in young non diabetic stroke patients.

Table 1: Age distribution of patients studied:

Age in years	Cases		Controls	
	No.	%	No.	%
18-27	5	16.67	5	16.67
28-37	9	30	9	30
>37	16	53.33	16	53.33
Total	30	100.0	30	100.0
Mean $\pm$ SD	35.23$\pm$7.37		35.27$\pm$7.39	

Samples are age matched with p=0.986

The youngest patient in the study was 18 years and the eldest was 44 yrs old. Maximum number of patients 53.33% was more than 37 years age and less than 45 yrs group. Mean age with standard deviation was 35.23 $\pm$ 7.37. Samples are age matched with P = 0.986.

Gender distribution was equal among both the groups with 23 males (76.7%) and 7 females (23.3%)

Equal number of males and females were selected in both the groups to eliminate the confounding effect of sex on lipid levels. In our study, male: female ratio is 3.2:1.

Most common presenting complaint was aphasia in 76.7% of the patients followed by altered sensorium 53.3%, right hemiplegia 40%, left hemiplegia in 36.7%,

Table 2: Incidence of risk factors in the cases

Risk factors	Number of patients (n=30)	%
Dyslipidaemia	21	70
Smoking	8	26.7
Hypertension	7	23.3
Alcohol	7	23.3
Serum Homocysteine	6	20
Obesity	5	16.7
Family H/o CVA	5	16.7
APLA	2	6.7
ANA	2	6.7
Protein C & S	1	3.3
TIA	1	3.3

Dyslipidaemia (70%) was the first major risk factor for stroke followed by smoking (26.7%), hypertension (23.3%) and alcohol (23.3%). Least was found to be TIA (3.3%).Among the 30 stroke patients studied 25 patients (83.3%) had Ischemic Stroke & 5 patients (16.7%) had Hemorrhagic stroke.

Ischemic stroke was seen in 83.3% of the stroke & hemorrhagic stroke was seen in 16.7%. Among the ischemic stroke Middle Cerebral Artery was involved in 56.7% of the cases. Among the hemorrhagic stroke it is only the MCA territory which was involved.

Table 4: Distribution of lipid profile in cases and control groups

Lipid parameters	Cases (n=30)		Controls (n=30)		p-value
	No.	%	No.	%	
Total cholesterol mg/dl					
<200	11	36.7	30	100	
200-239	11	36.7	0	0.0	<0.001
≥ 240	8	26.7	0	0.0	
Triglycerides mg/dl					
<150	9	30.0	30	100	
150-200	9	30.0	0	0.0	
200-499	12	40.0	0	0.0	<0.001
≥ 500	0	0	0	0.0	
HDL mg/dl					
<40	13	43.3	0	0.0	
40-60	13	43.4	30	100	<0.008
>60	4	13.3	0	0	
LDL mg/dl					
<100	5	16.6	20	66.7	
100-129	11	36.7	10	33.3	
130-159	11	36.7	0	0.0	<0.001
160-189	0	0.0	0	0.0	
≥190	3	10.0	0	0.0	
VLDL mg/dl					
<30	13	43.3	25	83.3	
≥30	17	56.7	5	16.67	<0.004

The mean levels of triglycerides (184.1 ±74.49) in cases was significantly raised when compared to control group (113.35 ± 24.91). This increase in Triglyceride levels inyoung stroke patients was statistically highly significant (p<0.001).

The mean values of VLDL-C among cases (33.94 ± 15.18) was raised when compared to the control group (25.30 ± 16.38). This increase in VLDL-C levels in stroke patients was statistically highly significant (p<0.004).

The mean values of LDL-C among cases (131.78 ± 61.49) was also significantly raised when compared to the control group (89.29 ± 26.20). This increase in LDL-C levels in stroke patients was statistically highly significant (p<0.001).

The mean levels of HDL-C among cases (44.71 ± 17.43) was not significantly decreased when compared to the control group (45.32 ± 9.20). This

decrease in mean HDL-C levels in cases was statistically not significant (p=0.853).

The mean ratio of TC/HDL-C (5.09+3.73) and LDL-C/ HDL-C (3.17 +2.07) among cases were also increased when compared to the control group TC/HDL-C (3.26 + 0.60) and LDL-C/HDL-C (1.92 + 0.53). This increase in cases was also statistically highly significant (p<0.001).

The total cholesterol is <200mg/dl in 40% of ischemic cases but it is 20% in hemorrhagic. It is in the range of border line high 200-239mg/dl is seen in 32% of ischemic cases & 60% in hemorrhagic. ≥ 240mg/dl that is high as per ATP3 guide lines seen in 28% of ischemic cases and 20% in hemorrhagic with p<0.001 and is statistically highly significant.

Normal levels of Triglycerides (<150mg/dl) levels were seen in 24% of the ischemic cases & 40% in the hemorrhagic. Border line high (150-199mg/dl) is seen in 32% in ischemic cases and 40% in hemorrhagic cases. High (200-499mg/dl) levels are seen in 44% in ischemic cases 20% in hemorrhagic. Very high (≥ 500mg/dl) levels are not seen in either hemorrhagic or ischemic cases with P<0.001 and is statistically highly significant.

The HDL cholesterol was found low (<40mg/dl) in 52% of the ischemic cases & none in hemorrhagic. Normal values (>40mg/dl) were seen in 48% of the ischemic cases & 100% in hemorrhagic. High values (>60mg/dl) were seen in 4% in the ischemic & 60% in hemorrhagic cases with P<0.005 and is statistically highly significant.
LDL cholesterol optimal (<100mg/dl) levels were seen in 20% of the ischemic cases & none in hemorrhagic strokes, near optimal (100-129mg/dl) levels are seen in 36% of the ischemic cases & 40% in hemorrhagic. Border line high (130-159mg/dl) values were found in 36% the ischemic cases & none in hemorrhagic. High (160-189mg/dl) are not seen either in hemorrhagic or the ischemic cases. Very high values (≥ 190 mg/dl) were seen in 8% of the ischemic cases & 10% of hemorrhagic cases with P<0.001 and is statistically highly significant

Normal levels of VLDL-C (<30mg/dl) levels were seen in 40% of the ischemic cases & 60% of hemorrhagic cases. High (≥ 30mg/dl) values are seen in 60% of the ischemic cases & 40% of hemorrhagic cases with P<0.598 and is statistically not significant.

Table 6: Comparison of mean values of lipid profile in ischemic & hemorrhagic cases:

Lipid profile	Ischemic (n=25)	Hemorrhagic (n=5)	p-value
Total cholesterol (mg/d1)	209.12+ 76.21	216.4+ 47.72	0.840
Triglycerides (mg/d1)	193.48+ 75.87	142. 2+ 54.32	0.164
HDL-C (mg/d1)	39.97+ 10.66	68.4+ 26.06	<0.001**
LDL-C (mg/d1)	127.9+ 63.1	151.18+ 54.45	0.449
VLDL-C (mg/d1)	35.59+ 15.8	25.7+ 8.44	0.188

Incidence of dyslipidaemia is not statistically similar in male and female cases with p=0.977. 21(70.0%) patients had dyslipidaemia. Females (85.71%) had higher incidence than males (65.21%).

Incidence of dyslipidaemia in ischemic strokes is 64% but 100% in hemorrhagic strokes.

Smokers had significantly lower HDL-C (41.23 + 15.27) and the ratio of TC/HDL-C (6.05 + 4.34) was increased when compared to non smokers HDL-C (47.24 + 16.01) and TC/HDL-C (5.11 + 3.29). This decrease in HDL-C and increase in the ratio of TC/HDL-C was statistically highly significant p<0.01.

Alcoholics had significantly higher HDL-C (46.87 + 0.19) and the ratio of TC/HDL-C (5.01 + 3.87) was decreased when compared to non alcoholics HDL-C (40.07 + 0.51) and TC/HDL-C (5.97 + 3.28). This increaseof HDL-C and decrease in the ratio of TC/HDL-C was statistically highly significant p<0.01.

DISCUSSION
Stroke is the third leading cause of death after heart diseases and cancer in the developed countries with an average incidence of approximately 1 in 1000 population. It is the leading cause of morbidity and mortality worldwide. Identification of potential cerebrovascular disease victims for preventive medical and surgical management would seem essential if the impact of this common and devastating illness is to be substantially reduced.

An epidemiological study conducted by the Indian council of medical research in 1986 revealed that the main risk factors are hypertension, tobacco smoking. The combination of hypertension and tobacco smoking increased the risk of stroke 20 times.

Carotid and vertebral artery atherosclerosis is associated with hypercholesterolemia patients with elevated lipid levels are at higher risk of atherothrombotic brain infarction than those with normal values and this applies mainly to premature ischemic Cerebrovascular diseases. So dyslipidaemia has emerged clearly as a major risk factor associated

with increased risk of atherosclerosis either alone or in combination with other risk factors in young stroke patients.

Farid *et al.* [7] in their study observed high frequency of abnormalities involving increases in pre beta lipoprotein fraction in patients with ischemic stroke patients.

Genetic influence also plays an important role in the development of stroke. De Graba T.J. *et al.* [8] in 1995 in their study they showed that many 49 risk factors for stroke are under genetic influence. Epidemiologic studies show that parental and sibling histories of cerebral ischemic events are associated with an increased risk of stroke. In the present study family history of stroke was observed in 16.7% of cerebrovascular disease patients.

In the present study age group range was from 18-44 years. The peak incidence of stroke was between 37-44 years contributing 53.33%. In 2009 Jukka Putaala *et al.* [9] in their study of ischemic cerebrovascular disease in young adults aged 15 to 49 years found with the maximum number of cases were around 44 years. In 2000, JF Albucher *et al.* [10] in their study of ischemic stroke in young adults aged between 15 to 45 years found that mean age group was 35.8 ±8.2.

In 1997 S. Dinesh Nayak *et al.* [11] in their study of ischemic stroke of young adults reported that mean age was 34.7 ± 8.0 years. In the present study male: female ratio was 3.2:1.0 This was comparable with the study conducted by Jukka Putaala *et al.* [9] in 2009 in which M:F ratio was found to be 1.7:1.0.

Most common presenting complaint was Aphasia in 76.7% of the patients followed by altered sensorium 53.3%, right hemiplegia 40%, left hemiplegia in 36.7% seizures seen in 20%, cerebellar & sensory deficit in 20%. patients presented with giddiness in another 20%.

This is comparable with the study done by S. Dinesh Nayak *et al.* [11] who reported that in 177 patients they studied speech was affected in 54%, right hemiplegia 49%, left hemiparesis in 35% loss of consciousness in 19% headache (31%), vomiting (17%), seizures in 7%.

The incidence of dyslipidaemia was 70% which was the commonest risk factor followed by smoking (26.7%), hypertension (23.3%) followed by alcohol (23.3%).

In 1997 S. Dinesh Nayak *et al.* [11] in their study of ischemic stroke of young adults found that dyslipidaemia was 42%, hypertension was 18.0%, smoking 47% and family history in 6% of the patients.

Most common radiologic finding was parieto-temporal infarct (43.3%) followed by putamen bleed 10% and basal ganglia bleed 6.7% it was comparable with the study done by K. Sreedhar *et al.* [4] in 2010.

In the present study among the 30 patients ischemic stroke was seen in 25 cases that were 83.3% of the total & hemorrhagic stroke was seen in 5 cases that were 16.7% of the total. Among the arterial distribution it is the MCA territory involved in 56.75 of the Ischemic stroke and in hemorrhagic stroke it is only the MCA territory which is involved about 16.7% Among the ICH it is putamen hemorrhage found to be more common about 10%. It was comparable with study done by K Sreedhar *et al.* [4] in 2010 in which it was reported that among the nondiabetic stroke patients 62.5% are Ischemic & 37.5% are hemorrhagic stroke.

Comparison of HDL-C levels in relation to smoking & alcohol

It is known that smoking adversely affects HDL-C. In the present study the incidence of smoking was 26.7% and HDL-C(41.23 ± 15.27) levels are significantly low in smokers compared to non smokers (47.24± 16.01) with the (p<0.01). TC/HDL-C levels (6.05±4.34) which was increased compared with non smokers (5.11 ±3.29) with p value<0.01.

This is comparable with the study done on 849 medical students in 2003 by Ioannis N Mammas *et al.* [12] smoking was related to higher triglyceride (p=0.032), and lower HDL cholesterol (p=0.037) serum levels. Total cholesterol, LDL-cholesterol, and the TC/HDL cholesterol ratio were strongly related with the level of smoking.

In relation to alcohol in the present study the incidence of alcohol consumption was found to be 23.3% & HDL-C levels (46.87 ±0.19) are higher compared to nonalcoholics (40.07 ± 0.51) & TC/HDL-C levels (5.01 ±3.87) which was decreased compared with non alcoholics (5.97± 3.28) with statistically highly significant p value<0.01. It is comparable with the study done by S.R. Choudhary *et al.* [13] where they reported that alcohol drinkers had higher HDL-C levels & lower LDL-C levels than nonalcoholics. There is an anti atherogenic effect of alcohol on the Lipid profile in alcoholics. In the study done by Hyejin Park *et al.* [14] on lipid profile in Alcoholic Hypertensive men it was found that alcohol consumption was negatively associated with risk of low HDL-C; whereas risk of high triglycerides increased with increasing alcohol consumption.

Incidence of dyslipidaemia

Out of 30 patients studied 21 had Dyslipidaemia (70%). Among these 21, 19 cases (63.4%) had high Total cholesterol levels. All 21 cases (70%) had high Triglyceride levels, the HDL-C levels was found to be low in 13 cases (43.3% LDL-C was

high in 13 cases (43.3%) and VLDL-C was found to be high 17 cases (56.7%).This is compatible with the study conducted by Jukka Putaala *et al*. [9] in 2009 in young patients aged 15-49 reported that dyslipidaemia was found to be 60%.

Total cholesterol

The value of total cholesterol was significantly elevated in patients with CVA when compared to controls in our study (p<0.001). This observation supports the earlier reports. In a study by Jukka Putaala *et al*. [9] showed that the most frequent risk factor for stroke was dyslipidaemia 60%& TC was found to be the risk factor for large vessel atherosclerosis.

However in contrary, the studies done by Lipska *et al*. [15] reported that mean cholesterol in cases did not differ from the controls.

Triglycerides

The serum triglyceride levels were significantly higher in cases of stroke patients than in controls. This observation is in full agreement with the studies conducted by Lipska *et al*. [15] in 2006 and S. Dinesh Nayak *et al*. [11] in 1995.

HDL-C

In the present study levels of serum HDL-C, which was significantly decreased in cases of stroke patients when compared to controls but the p value (P=0.853) is not found to be statistically significant. In a study by Lipska *et al*. [15] in 2007 on 216 young ischemic stroke patients in south India showed that lower HDL-C associated with risk of stroke in young south Indian adults.

In a study by Kameshwar Prasad *et al*. [16] concluded that along with smoking, HTN Fasting lipid profile in young stroke patients shows low HDL-C levels & TC/HDL-C the ratio was high in both cases & controls. A unit increase in the ratio of TC/HDL-C doubles the risk of stroke. But a large volume of publications on this subject are consistent with low HDL-C association with the risk of stroke but in the present study low HDL-C was not statistically found to be significant.

LDL-C

LDL-C is believed to be the most atherogenic lipoprotein. Majority of cholesterol in plasma is found in LDL-C. The present study revealed significant increase in levels of serum LDL-C in stroke patients, when compared to controls (p<0.001). This is in accordance with previous study by Sreedhar K *et al*. [4] which showed a positive correlation between the elevated serum LDL-C, serum Triglyceride, total cholesterol in Non diabetic stroke. Anseil B.J. *et al*. [17] in 2000 concluded that patients with established atherosclerosis should be treated with a statin to achieve

LDL-C levels less than 100mg/d1 for the reduction of stroke incidence.

VLDL-C

VLDL-C levels were significantly elevated in stroke patients when compared to controls in our study (p<0.001). S. Das *et al*. [18] in 1984 noticed there was no differentiation in mean values of lipid fractions between controls and patients of CVA with regard to any parameters (TC, TG, HDL-C, LDL-C). The only common lipid abnormality in their study was raised VLDL-C and VLDL-C/TC. A similarly raised VLDL-C and VLDL-C/TC was one of the notable features in the present study in addition to significantly elevated TC, TG, LDL-C & Low HDL-C.

The mean ratios of TC/HDL-C(5.09 $\pm$ 3.73) and LDL-C/ HDL-C (3.17 $\pm$ 2.07) among cases were also increased when compared to the control group TC/HDL-C (3.26 $\pm$ 0.60) and LDL-C/HDL-C (1.92 $\pm$ 0.53). This increase was also statistically highly significant (p<0.001). This was comparable with the study done by Kameshwar Prasad *et al*. [16]

Comparison of lipid profile among ischemic & hemorrhagic patients

In the present study the lipid profile was compared between ischemic & hemorrhagic patients and found that it is only the mean HDL-C(39.97 $\pm$ 10.66) levels which was significantly decreased in Ischemic stroke patients when compared to hemorrhagic (68.4 $\pm$ 26.06) with p<0.001. There was no statistically significant difference between the TC, TG, LDL-C & VLDL-C lipid values in ischemic and hemorrhagic stroke patients.

This was comparable with the study done by J F Albucher *et al*. [10] where he found that low HDL-C is the only lipid index associated with the increased risk of stroke among ischemic stroke patients.

CONCLUSION

Total cholesterol, Triglycerides, LDL-C, VLDL-C, the ratio of TC/HDL-C, LDL-C/HDL-C were significantly raised in young stroke patients when compared to controls and had a positive correlation with the risk of stroke. Dyslipidaemia is one of the major risk factors in nondiabetic young stroke patients. Thus early detection of dyslipidaemia and treatment of the same can reduce the risk of stroke in young.

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