



CORRELATION OF COMMON LIPID PROFILE AND CAROTID ARTERY INTIMA MEDIA THICKNESS IN PATIENTS OF ISCHEMIC STROKE

Cardiology

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ABSTRACT

AIM: The present study was postulated to correlate common lipid profile and carotid artery intima media thickness (cIMT) in patients of ischemic stroke.

MATERIALS AND METHODS: This was a single-centred, case-control study which included a total of 100 patients, from which 50 patients were of ischemic stroke (cases) and 50 patients without ischemic stroke (controls). The cIMT of each subject was measured at 8 sites in the carotid artery both sides using Doppler carotid imaging and mean cIMT was measured. Total lipid profile, cardiovascular and common baseline investigation were performed for each patient.

RESULTS: Mean cIMT in subjects with stroke and in subjects without stroke was found to have statistically significant difference (0.913 ± 0.120 mm vs. 0.732 ± 0.119 mm, $p < 0.0001$, respectively). Total serum cholesterol, serum triglycerides and LDL level demonstrated positive correlation with the cIMT and HDL level was found to be negatively correlated with cIMT.

CONCLUSION: Deranged lipid profile was found to be associated with the increased cIMT and with occurrence of ischemic stroke. Hence, estimation of cIMT and blood lipid component can help in early manifestation of risk of stroke.

KEYWORDS

Carotid intima media thickness, high density lipoprotein, ischemic stroke, low density lipoprotein, total serum cholesterol

INTRODUCTION

Stroke is the devastating neurological disease, with the second leading cause of mortality worldwide [1]. More than two-third of the global burden of stroke is borne by developing countries, where the average age of patients with stroke is 15 years younger than that of developed countries [2, 3]. In developing country like India, stroke is one of the principal causes of death and disabilities [4]. The numbers obtained from past studies revealed that in India, the prevalence of ischemic stroke was higher (80-85%) than haemorrhagic stroke (15-20%) [2].

Ischemic stroke can be thrombotic or embolic. Brain ischemia originates as a result of an impediment to normal perfusion, caused by severe arterial stenosis or occlusion due to atherosclerosis and co-existing thrombosis. Among all the documented risk factors for atherosclerosis, abnormalities in plasma lipoproteins and derangement in lipid metabolism rank as the most firmly established and best understood one [3]. Atherosclerotic plaque may develop at any point along the carotid artery and the vertebrobasilar system, but the most common site includes bifurcation of common carotid artery into external and internal branch [5].

Nowadays, carotid artery intima media thickness (cIMT) is widely used as a non-invasive alternative marker of atherosclerosis and can help to predict future vascular events. Furthermore, there are studies which have shown correlation of various lipid components to the extent of cIMT [6-8]. The cIMT is also found to be associated with the higher prevalence of future development of stroke [2]. Hence, the present study was postulated to correlate common lipids (total serum cholesterol, serum triglyceride, HDL and LDL level) and cIMT in patients of ischemic stroke.

MATERIALS AND METHODS

This was a single-centred, case-control study conducted at the tertiary care centre in India. The present study included a total of 100 patients, from which 50 patients with ischemic stroke were considered as cases and 50 patients without ischemic stroke were considered as controls. The study was approved by the Institutional Ethics Committee of the hospital and informed consent was taken from all the patients before the start of the study.

Patients with ischemic stroke and who have given consent were included in the study. Patients of stroke having history of trauma, surgery, liver disease, renal failure, malignancy, cerebral haemorrhage, acute myocardial infarction, rheumatic heart disease (RHD) or other causes of cardiac embolism, deep vein thrombosis (DVT) or on anticoagulant treatment, chronic inflammatory diseases or acute infectious conditions, underwent invasive operations (e.g. angiography within last 6 weeks) were excluded from the study.

A detailed history of each patient was recorded and a thorough neurological examination was performed. Patients were designated as having ischemic stroke if CT scan recognized the presence of infarction in form of hypodensity or MRI showed infarction following indication by clinical examination.

The cIMT of each subject was measured at 8 sites in the carotid artery on both sides using Doppler carotid imaging and mean cIMT was measured. Lipid profile for each subject was investigated, including total serum cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides and very low density lipoprotein (VLDL).

The pulse rate, blood pressure, jugular venous pressure, palpitation, cardiac auscultation and cervical bruit from carotid bifurcation, vertebral artery origin and heart were examined for investigation of cardiovascular system. All the patients underwent baseline investigations which included full blood count, plasma glucose level, syphilis serology, urine analysis, ECG, chest X-ray, MRI and echocardiogram (if required).

Qualitative data were analysed using Chi-square test and quantitative data were analysed using independent t-test. All the data were analysed using SPSS version 15 (Chicago, IL, USA).

RESULTS

In the present study, total 100 patients were studied, out of which 50 patients having ischemic stroke were designated as cases and 50 patients without ischemic stroke were designated as controls.

The baseline characteristics of cases and controls are represented in **Table I**. Mean age of patients in cases was 60.26 ± 10.90 years and in controls was 55.06 ± 9.15 years. There were 35 (70%) and 30 (60%) males and 15 (30%) and 20 (40%) females in cases and controls, respectively. Among stroke patients 37 (74%) and among non-stroke patients 12 (24%) were hypertensive. Nineteen (38%) stroke patients and 6 (12%) non-stroke patients were diabetic. In cases, 5 (10%) patients were designated with transient ischemic attack (TIA). The cases contained 44% and controls contained 18% smokers. Eleven patients with stroke and 6 patients without stroke were alcoholic.

Total serum cholesterol was found to be 196.86 ± 53.54 mg/dl in cases and 152.92 ± 75.13 mg/dl in controls with p -value of <0.001 . The serum triglyceride level was found to be 180.44 ± 37.82 mg/dl and 133.63 ± 62.30 mg/dl in cases and controls with p -value of 0.1655. The HDL level, LDL level and VLDL level showed statistically significant difference between cases and controls ($p = 0.012$, $p = 0.0001$ and $p = 0.028$, respectively).

The cIMT of each patient was measured at 8 sites and the mean cIMT was correlated with different baseline parameters as depicted in **Table II**. Difference in mean cIMT in patients with stroke and in patients without stroke was found to be statistically significant (0.913 ± 0.120 mm vs. 0.732 ± 0.119 mm, $p < 0.0001$, respectively). The value of cIMT in patients with age of >60 years was found to be 0.866 ± 0.150 mm and in patients with age of <60 years was found to be 0.822 ± 0.148 mm but no statistically significant difference ($p = 0.174$) was observed. Male patients were found to have higher value of cIMT (0.865 ± 0.159 mm) as compared to female patients (0.785 ± 0.122 mm) with a p -value of <0.001 .

Hypertensive subjects had significantly higher cIMT as compared to non-hypertensive subjects (0.896 ± 0.131 mm vs. 0.749 ± 0.134 mm, $p < 0.0001$). Similarly, diabetes mellitus was also found to be positively associated with cIMT ($p = 0.04$).

Mean cIMT was also correlated with mean lipid profile of the study patients. Total serum cholesterol level >200 mg/dl showed significantly thicker cIMT compared to <200 mg/dl (0.913 ± 0.111 and 0.802 ± 0.159 , respectively) ($p = 0.017$). Similarly, LDL level >100 mg/dl and triglycerides level >160 mg/dl also showed thicker cIMT compared to <100 mg/dl LDL and <160 mg/dl triglycerides ($p = 0.1655$ and $p = 0.0001$, respectively). Mean cIMT for subjects with HDL level <40 mg/dl was found to be higher (0.874 ± 0.137 mm) compared to HDL >40 mg/dl (0.727 ± 0.113 mm) with $p = 0.0001$.

DISCUSSION

Stroke is the detrimental disease that affects 15 million patients worldwide and out of which the prevalence of ischemic stroke accounts for around 80% [9]. The underlying pathophysiology of most ischemic stroke is atherosclerosis and cIMT act as a surrogate marker of atherosclerosis [10, 11]. Deranged lipid metabolism is one of the important risk factor for development of carotid atherosclerosis. Hence, the present study was hypothesized to correlate serum lipid profile and cIMT in patient with ischemic stroke.

In this study, significant difference in age between cases and controls was observed but increased in age was not found to be associated with the cIMT. Rajeev H et al. [10] studied in different age groups from 41-70 years and stated that with increase in age, mean cIMT also increased drastically in stroke patients. O'Leary DH et al. [12] also established that cIMT has been dependent on age and it increases at a rate of 0.005 - 0.010 mm/year. The conflicting result was observed in our study compared to previous studies as the mean age was 60.26 ± 10.90 years in patients with stroke, hence to prove this it should be studied in more number of patients with varying age.

Hypertension (HTN) has been considered as one of the strongest and most prevalent risk factor for stroke [13]. In current study, mean IMT in hypertensive patients and non-hypertensive patients significantly varied with p -value of <0.0001 and this was supported by the results of Kota SK et al. [2]. Likewise, STANISLAS cohort study also stated that subjects with the history of HTN were more likely to have cIMT $>900 \mu\text{m}$ and had higher mean cIMT ($p < 0.001$) [14].

In the present study, the correlation of diabetes mellitus was also established with stroke and cIMT. The results manifested that diabetic patients were more prone for development of ischemic stroke compared to non-diabetic patients ($p = 0.003$). The value of mean cIMT was also significantly higher in diabetic patients with stroke compared to non-diabetic patients with stroke ($p = 0.04$).

It has been found that cIMT is the independent marker of atherosclerosis and cerebrovascular disease [2, 6, 10]. The current study showed significantly increased value of mean cIMT in patients with ischemic stroke as compared to patients without ischemic stroke ($p < 0.0001$). Similarly, Rotterdam study stated that increasing cIMT is the direct risk factor for stroke [15] and the study by Kota SK et al. [2] also concluded that an increase in cIMT more than 0.8 mm increases the risk of development of ischemic stroke. Furthermore, in the cross sectional study by Harris S. [16], 259 patients with the age group of 31-75 years were included and divided into the stroke group ($n=131$) and non-stroke group ($n=128$). He also concluded that increased cIMT has been correlated with the stroke which was in analogous with the present finding.

The mean cIMT was found to be significantly higher in patients with serum total cholesterol level >200 mg/dl as compared to <200 mg/dl with p -value of 0.017 . The total serum cholesterol level was also compared in patients with and without ischemic stroke and its level was found to be significantly higher in stroke patients ($p < 0.001$). The

results of study by Senagupta D. et al. [6] were equivalent with our study in which they enrolled 50 patients with stroke as cases and 50 without stroke as controls. The result of their study displayed significantly higher level of serum cholesterol in cases compared to control ($p < 0.001$). They also demonstrated a positive correlation of average cIMT with serum cholesterol level ($p < 0.001$). The study by Kota SK et al. [2] also established positive correlation of cIMT with total serum cholesterol ($p < 0.001$).

The LDL level was found to be positively associated with the prevalence of stroke when compared between cases and controls ($p = 0.001$). Furthermore, the LDL level >100 mg/dl demonstrated significantly higher mean cIMT as compared to <100 mg/dl ($p = 0.0001$). It was observed that patients with stroke having HDL level >40 mg/dl showed significantly lesser mean cIMT ($p=0.0001$). Plenty of studies demonstrated HDL as the independent negative predictor of atherosclerosis as it displayed pleiotropic effects. Recently, the research has been focused on the HDL based therapy in acute ischemic stroke as it may have leukocyte modulation and platelet activation property along with antioxidant, anti-inflammatory and anti-apoptotic properties [17]. In the study of Senagupta D. et al. [6], they correlate the LDL:HDL ratio between stroke and non-ischemic stroke patients. They also demonstrated significant difference in the LDL:HDL ratio in both case and control groups (2.79 ± 0.93 vs. 1.42 ± 0.28 ; $p < 0.001$) and also showed a positive correlation to average cIMT compared to other lipid parameters. Several previous studies also displayed alliance of LDL and HDL level with carotid atherosclerosis development and stroke [2, 18, 19].

On comparison of serum TG level in patient with and without stroke no significant difference was observed ($p = 0.1655$) which was antagonistic to the finding of Senagupta D. et al. [6] But, higher level of serum TG (>160 mg/dl) was found to be positively linked with mean cIMT which supported the findings of Kota SK et al. [2] and Senagupta D et al. [6].

Diabetes mellitus, HTN and altered lipid profile, all together contribute to the characteristic of atherogenic profile and may accelerate the atherosclerotic process which results in pathophysiological changes in cerebral vessels and increases risk of stroke [20].

STUDY OF LIMITATIONS

The limitations of the present study include small sample size such that individual risk factors were not properly assessed and it was a single centred study.

CONCLUSION

In conclusion, deranged lipid profile was found to be associated with the increased cIMT and with occurrence of ischemic stroke. This study also concluded that increased cIMT has a strong correlation with the event of ischemic stroke; hence its estimation can help in the early manifestation of stroke.

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CONFLICT OF INTEREST: None Declared

Table I: Baseline characteristics of cases and controls

Parameters	Case (n=50)	Control (n=50)	P-value
Age (mean \pm SD, years)	60.26 \pm 10.90	55.06 \pm 9.15	0.011
Male, n (%)	35 (70%)	30 (60%)	0.295
BMI, n (%)			
< 25 kg/m ²	36 (72%)	39 (78%)	0.488
≥ 25 kg/m ²	14 (28%)	11 (22%)	0.488
HTN, n (%)	37 (74%)	12 (24%)	<0.0001
DM, n (%)	19 (38%)	6 (12%)	0.003
Smokers, n (%)	22 (44%)	9 (18%)	0.005
Alcoholic, n (%)	11 (22%)	6 (12%)	0.183
Total serum cholesterol (mean \pm SD, mg/dl)	196.86 \pm 53.54	180.44 \pm 37.82	<0.0001
Triglycerides (mean \pm SD, mg/dl)	152.92 \pm 75.13	133.63 \pm 62.30	0.1655
HDL (mean \pm SD, mg/dl)	42.55 \pm 9.02	47.11 \pm 8.83	0.012
LDL (mean \pm SD, mg/dl)	124.66 \pm 47.20	106.48 \pm 34.00	0.0001
VLDL (mean \pm SD, mg/dl)	32.64 \pm 16.48	26.06 \pm 12.74	0.028
Mean cIMT (mm \pm SD)	0.913 \pm 0.120	0.732 \pm 0.119	<0.0001

SD: standard deviation, **BMI:** body mass index, **HTN:** hypertension, **DM:** diabetes mellitus, **HDL:** high density lipoprotein, **LDL:** low density lipoprotein, **VLDL:** very low density lipoprotein and **cIMT:** carotid intima media thickness

Table II: Correlation of cIMT with different parameters

Parameters	Mean cIMT (mm ± SD)	P-value
Stroke		
Subjects with CVA	0.913 ± 0.120	<0.0001
Subjects without CVA	0.732 ± 0.119	
Age		
>60 years	0.866 ± 0.150	0.174
<60 years	0.822 ± 0.148	
Gender		
Male	0.865 ± 0.159	0.0006
Female	0.785 ± 0.122	
BMI		
≥ 25 kg/m ²	0.880 ± 0.151	0.114
< 25 kg/m ²	0.835 ± 0.160	
Smoking		
Smoker	0.876 ± 0.164	0.809
Non-smoker	0.869 ± 0.127	
Alcohol		
Alcoholic	0.853 ± 0.152	0.126
Non-alcoholic	0.776 ± 0.142	
HTN		
Hypertensive	0.896 ± 0.131	<0.0001
Non-hypertensive	0.749 ± 0.134	
DM		
Diabetics	0.907 ± 0.125	0.04
Non-diabetic	0.835 ± 0.118	
Serum total cholesterol		
>200 mg/dl	0.913 ± 0.111	0.017
<200 mg/dl	0.802 ± 0.159	
Triglycerides		
>160 mg/dl	0.814 ± 0.177	0.003
<160 mg/dl	0.791 ± 0.117	
HDL		
<40 mg/dl	0.874 ± 0.137	0.0001
>40 mg/dl	0.727 ± 0.113	
LDL		
>100 mg/dl	0.888 ± 0.141	0.0001
<100 mg/dl	0.788 ± 0.136	

cIMT: carotid intima media thickness, **CVA:** cerebrovascular accident, **BMI:** body mass index, **HTN:** hypertension, **DM:** diabetes mellitus, **HDL:** high density lipoprotein and **LDL:** low density lipoprotein

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