

Original Research Article

Association between serum lipid and ischaemic stroke in a tertiary hospital in Northern Andhra Pradesh, India

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ABSTRACT

Background: The incidence of cerebrovascular disease increases with age and the number of strokes is projected to increase as the elderly population grows. A stroke occurs when blood vessels that carry blood to the brain suddenly blocked or burst, preventing blood flow to the brain. The most common cause of blood vessel blockages is thrombosis (a blood clot) or an embolism (floating clot). Blood clots may form in the arteries that are damaged by atherosclerosis. Atherosclerosis is an aging process but some factors (risk factor) precipitate it to occur earlier. To find out the risk factors properly are of tremendous importance as risk factor change could directly influence or indirectly affect case fatality by altering the natural history of the disease. Serum lipids are thought to interact with the pathogenesis of stroke through the atherosclerotic mechanism. Objective was to identify the high serum lipid as an independent risk factor of stroke.

Methods: This is a hospital-based case-control study. Seventy cases of stroke patients and age, sex-matched 70 healthy control subjects were enrolled by non-random sampling. 12 hours of fasting plasma lipids were estimated in both cases and control subjects. Then it was compared between cases and controls.

Results: Hypercholesterolemia was higher in the case group than control but not statistically significant. Mean LDL-cholesterol, and triglycerides were significantly higher in the case group than the control group. The mean value of serum HDL-cholesterol was not significantly lower in the case group than the control group.

Conclusions: Serum lipids are significantly higher in ischaemic stroke patients than the control group (LDL cholesterol and triglyceride). So, it may be an independent risk factor of ischemic stroke.

Keywords: Hypercholesterolaemia, Ischaemic stroke, Risk factors

INTRODUCTION

Stroke is a disease of neurologic mortality and disability. The incidence of cerebrovascular diseases increases with age and the number of strokes is projected to increase as the elderly population grows, with a doubling in stroke death in the United States by 2030.¹ Similarly, gradually the segment of the elderly population is increasing and so inviting many diseases, which are due to aging process.² Stroke can be divided into two major categories based on whether the disrupted blood supply to the brain is caused

by the blocked blood vessel (known as ischaemic stroke) or a burst blood vessel (known as hemorrhagic stroke).³ The most common causes of blood vessel blockages are thrombosis (a blood clot) or an embolism (floating clot). Blood clots may form in arteries that are damaged by atherosclerosis (also known as hardening of the arteries).²

Authors know that the incidence of stroke increases with age. Atherosclerosis is also an aging process but some factors precipitate it to occur earlier.⁴ These factors are known as risk factors. To know and find out the risk

factors properly are of tremendous importance as risk factor change could directly influence or indirectly affect case fatality by altering the natural history of the disease.²

Certain risk factors like age, sex, and genetic factors are the definite and non-modifiable factors, but blood pressure, smoking, diabetes mellitus, heart disease, stenosis of precerebral arteries and transient ischaemic attacks (TIA) and alcohol are the definite modifiable risk factors; and lipids, fibrinogen, and hematocrit, obesity, female sex hormones are the probable risk factors for stroke.⁵

The relation between serum lipids and ischemic stroke remains controversial. Studies of lipids related risk factors in cerebrovascular disease have varied greatly in their findings and also in their definition of cerebrovascular endpoints. Serum lipids are thought to interact with the pathogenesis of stroke through an atherosclerotic mechanisms.⁵ Besides these, there is mounting epidemiologic evidence to support the relationship of lipid as a risk factor for ischaemic stroke.⁶

In the process of atherosclerosis dyslipidemia (hypercholesterolemia and hypertriglyceridemia) plays a major role through the formation of fibrofatty intimal plaque on the arterial wall (deposition of cholesterol and cholesteryl ester from the plasma protein into the arterial wall). The risk is correlated with the level of serum low-density lipoprotein (LDL), formed from the catabolism of very-low-density lipoprotein (VLDL). LDL carries 70% of total serum cholesterol. Risk is inversely related to the HDL level, perhaps because HDL helps clear cholesterol from vessel wall lesion.⁷ Cholesterol is present in tissues and plasma as free cholesterol or as a storage form, combined with a long-chain fatty acid as cholesteryl esters. In plasma, both forms are transported in lipoproteins. A little more than half the cholesterol of the body arises by synthesis (almost 70%) and the remainder is provided by the average diet. Plasma LDL is the vehicle of uptake of cholesterol and cholesteryl esters into many tissues. Free cholesterol is removed from the body either unchanged or after conversion to bile acid in the process known as reverse cholesterol transport.⁸

Triglycerides (triacylglycerol) are found in fat. It is an important constituent of other blood lipids (triacylglycerol-16%, phospholipid-30%, cholesterol-14%, cholesteryl esters-36% and free fatty acid-4%). They are formed from the digestion of fats in food and the synthesis within the liver from acetyl-co A, derived mainly from carbohydrates and uptake of free fatty acid from the circulation (lipogenesis from carbohydrate).⁸

However, recent data also have affirmed the primary role of triglycerides in the genesis of atherosclerosis. This process involves the overabundance of triglyceride-rich lipoprotein particles, which paradoxically, can be enriched with cholesterol through the action of cholesterol ester transfer protein. These particles appear

to be especially atherogenic. Also, low-density lipoproteins become smaller and denser-small, dense phenotype or pattern B- in hypertriglyceridemia states.⁹ Several proposed connection appears to exist between hypertriglyceridemia and atherosclerosis including the inverse correlation between triglyceride and HDL. The presumed atherogenicity of triglyceride-rich lipoprotein remnant particles, the potential resultant increase in the serum concentration, and atherogenicity of low density of lipoprotein (LDL) and proposed interaction between serum triglyceride and fibrinolytic/coagulation systems.¹⁰

Authors know that triglycerides are the neutral fat synthesized from carbohydrate for storage in adipose tissue; i.e. excess carbohydrate, which is not utilized by the body, was stored in the adipose tissue as a depot fat.¹¹

METHODS

In this hospital-based case-control study 70 cases with ischemic stroke and 70 age and sex-matched controls without stroke were selected based on their clinical and CT scan of brain findings from Great Eastern Medical School Hospital through the convenient sampling from March 2018 to December 2018. Institutional Ethics Committee approved the study.

All the study subjects were free from heart disease (Myocardial infarctious, congenital heart disease, valvular heart disease with or without atrial fibrillations), diabetes mellitus, previous history of transient ischemic attack (TIA) or any case history of haemorrhagic stroke. Informed written consent was taken from all study subjects before their enrollment. For all study subjects performed questionnaires were used to collect data. Blood samples were collected aseptically from all study subjects after 12 hours fasting for the measurement of fasting lipid profile. Blood samples of the cases (stroke patients) were collected within 48 hours of the attack to avoid the effect of stroke and hospital diet on lipid profile.⁴

Data were analysed using SPSS. To find out the statistical significance p-value <0.05 was considered as statistically significant.

RESULTS

In this case-control study, 70 diagnosed ischaemic stroke cases (male-39 and female-31) with mean age 54.8 years (age range 40-65 years) and 70 healthy control subjects (male-40, female-30) with mean age 57.2 years (age range 40-65 years) were enrolled (Table 1). In the stroke patient's median plasma total cholesterol concentration was 196 mg/dl with a range of 152.3-318 mg/dl and in the control subject, it was found to be 183.4 mg/dl. With the range of 148-289.3 mg/dl. The paired T-test shows that the plasma concentration of total serum cholesterol was not significantly higher ($p > 0.05$) in the case group than control subjects. But mean LDL cholesterol and

triglyceride were significantly higher in the case group ($p < 0.05$) than the control group (120.4 and 94.5 mg/dl and 216.8 and 367.42 mg/dl respectively). But HDL

cholesterol level was 42.86 mg/dl in case group and 43.4 mg/dl in control group (Table 2) which was not statistically significant ($p > 0.05$).

Table 1: Age and sex distributions of the study subjects.

Subject	Total number	Mean age (yrs)	Age range (yrs)	Male	Female
Cases (Ischemic stroke patient)	70	54.8	40-65	39	31
Control (Without stroke)	70	57.2	40-65	40	30

Table 2: Comparison of serum lipids value between cases and control.

Serum lipids(mg/dl)	Subjects		Subjects	
	Cases	Control	Cases	Control
	Mean	Range	Mean	Range
Total Cholesterol	196	152.3-318	183.4	148-289.3
HDL Cholesterol	42.86	35.6-47.6	43.4	37.8-49.4
LDL Cholesterol	120.4	90.2-176.8	94.5	48.6-154.3
Triglycerides	216.8	136.5-367.42	164.3	129.8-346.5

DISCUSSION

This study was carried out to find the serum concentration of fasting lipid in stroke (ischaemic) patients and to compare it to age and sex-matched control subjects to establish the lipid as a risk factor of ischaemic stroke.

This study has revealed the median plasma total cholesterol in cases was 196 mg/dl and that in the control group was 183.4 mg/dl which was statistically insignificant. In our study, mild hypercholesterolemia was detected in the case group, but in the study of other people sometimes significant hypercholesterolemia is detected in ischemic stroke patients.

In a similar study by Quraishi and Latif et al showed the direct relationship of ischaemic stroke with hypercholesterolemia and thus listed relationship with blood lipid i.e hyperlipidemia as a risk factor for ischaemic stroke.¹²

Mayer JS, Rogers RL, Mortel KF, Judd BW showed in their study that cerebral blood flow level was reduced among a group of TIA patients with an elevated level of either cholesterol or triglyceride compared with the TIA patients with normal lipids levels.¹³ Cazzato g, Zorzoan M, and Monit F. showed in their study that the mean total cholesterol concentration was significantly higher in male patients affected by TIA and cerebral infarction.¹⁴ Armin JG et al also showed in their study that hypercholesterolemia was particularly common in both microangiopathic stroke (44%) and macroangiopathic stroke (41.4%) and least frequent cardioembolism combined other aetiologies (21.9%).¹⁵

In our study, the mean level of HDL-cholesterol is nearer to cases and control (42.86 mg/dl and 43.4 mg/dl respectively).

Due to et al showed in their study of eighty-eight age and sex-matched control with seventy-nine patients. Those patients had HDL-C and HDL-C/APO A1 ratio was significantly lower than control.¹⁶

Albuicer JF et al concluded in their study of serum lipids in young patients with ischaemic stroke a case-control study that low HDL-cholesterol was only serum lipid index to be associated to an increased risk of stroke in that population.⁶

Though our small scale study does not correlate with these studies in many other researcher’s studies showed that HDL- cholesterol is a risk factor of ischemic stroke. Regarding LDL-cholesterol in our study, cases have significantly higher ($p < 0.05$) LDL-cholesterol (120.4 mg/dl) than control (94.5 mg/dl).

Hachinski V et al, showed that LDL-cholesterol levels were significantly higher among the patients with atherothrombotic strokes and transient ischemic attacks than among the control subjects.¹⁷ In another study Lalaux P, Galanti L, and Janeant I. showed in their case-control study of lipids in ischaemic stroke subjects that a significant increase in the LDL-cholesterol level and a significant decrease in HDL-C were only observed in LVD (large vessel Disease).¹⁸

Triglyceride level was also significantly higher in the case group than the control group in our observations which has similarities with many other studies.

A study of cholesterol and the risk of ischaemic stroke by Bowman TS, et al showed that total cholesterol, HDL, and triglyceride were not significantly associated with ischaemic stroke risk.¹⁹ But in later time researches have shown that high triglycerides - a type of blood fat are a strong independent predictor of a person's risk for stroke.¹¹ It is also shown that low-density lipoprotein becomes smaller and denser small, dense phenotype or pattern β - is hypertriglyceridemia states.⁹ Besides this Morag NK, Eran C, Gold B. showed that about a quarter of the patient of stroke had a triglyceride level of 200 mg/dl and higher than control.¹¹ Tame D, Koren-Morag N, Graff E, Goldbilatom V. showed that patient experienced an ischaemic stroke/TIA had a higher mean level of triglycerides, lower levels of HDL cholesterol and lower percentages of cholesterol contained in HDL cholesterol moiety (%HDL, $p < 0.01$ for all).²⁰

Though it is well-established fact that higher serum lipids are directly related to coronary artery disease but it remains still controversial about the relations between serum lipids and ischaemic stroke.²¹ But more recent studies showed some direct and indirect relationships of serum lipids with stroke.¹⁹ Besides these South Asian populations in the U.K. have a high percentage of coronary heart disease, central obesity (high waist to hip ratios), insulin resistance, non-insulin dependent diabetes, hypertension, and high stroke mortality, but there is no good information on incidence. This seems to be due partly to genetic susceptibility (high serum lipoprotein levels) in these people potentiated by dietary and lifestyle-induced changes in lipid levels.²²

Our study populations have also reflected the above-mentioned idea about the ischaemic stroke and lipid level, ie. higher lipid levels (total cholesterol, LDL-cholesterol, and triglyceride) was found in ischaemic stroke patients than control people.

CONCLUSION

As stroke is more preventable than looking for a cure. So, at present in the country like ours, need more effort to control the risk factors like lowering of serum lipid level to reduce the incidence of stroke. For this, a simultaneous community screening program for dyslipidaemias with other controllable risk factors (smoking, hypertension, diabetes mellitus) on a large scale basis for middle-aged to elderly group people may be an effective measure to reduce the incidence of stroke.

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