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Original Research Article

A Hospital-Based Study to Assess the Lipid Profile and Oxidative Stress in Patients of Ischemic and Hemorrhagic Stroke: A Case-Control Study

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess lipid profile in patients of cerebrovascular stroke and controls.

Methods: The present study was carried out in the Department of Biochemistry. Informed consent was taken from patient / relative and control subjects. The study was conducted for the period of one year. Study Groups: 50 Patients (age 30-90 years) of cerebrovascular stroke referred by hospitals were selected.

Results: The mean age of cases and controls were 56.54 ± 12.48 and 48.32 ± 7.83 years respectively Maximum number of cases was in the age group of 51-60 years (34%). On comparing mean cholesterol, TG, HDL, LDL and VLDL between cases and controls, the p value was < 0.01 in all above test parameters which was found to be statistically significant. On comparing, levels of total cholesterol, HDL cholesterol and LDL cholesterol between ischemic and hemorrhagic stroke, p value was statistically significant while difference between triglyceride level and VLDL was not significant. On comparing, the difference between mean MDA values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). On comparison by student t test, the difference between mean SOD values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). Also on comparison between hemorrhagic stroke and control the difference in mean MDA and SOD values was found to be statistically significant ($p<0.01$).

Conclusion: The difference in lipid profile between ischemic and hemorrhagic stroke should be taken into consideration while starting statin therapy as primary preventive measure to reduce incidence of first stroke in high risk patients, as well as during secondary prevention in case of ischemic strokes.

Keywords: cerebrovascular stroke, lipid profile, oxidative stress, ischemic stroke, hemorrhagic

Introduction

Stroke is a clinical syndrome divided into two broad categories that define its pathophysiology: Ischemic strokes are caused by sudden occlusion of arteries supplying the brain, either due to a thrombus at the site of occlusion or formed in another part of the circulation accounting for 50%–85% of all strokes worldwide. Hemorrhagic strokes are caused by subarachnoid hemorrhage or intra-cerebral hemorrhage accounting for 1%-7% and 7%-27% respectively of all strokes worldwide. [1] Stroke is the second leading cause of death worldwide and one of the main causes of long term disability. [2] Improved stroke care, aging, and growth of the population combined with the increased prevalence of many modifiable stroke risk factors are likely to be the main drivers in the increased number of stroke survivors and people affected by stroke. [3] Many risk factors for stroke have been documented, including hypertension, current smoking, diabetes, abdominal obesity, poor diet, inactivity, excessive alcohol consumption, cardiac causes and stress/depression. [4] Dyslipidemia is a modifiable risk factor for stroke and is associated with a 1.8- to 2.6-times relative risk of stroke. [5]

In the central nervous system, lipids and lipid mediators are essential to sustain the normal structure and function of brain tissue. Pathways leading to post-stroke brain deterioration include the metabolism of polyunsaturated fatty acids (PUFAs). The lipids released are utilized in either enzymatic or non-enzymatic reactions, generating diverse classes of short-lived, lipid mediators, e.g.,

eicosanoids. These molecules have either neuroprotective or neurodegenerative effects on the post-stroke brain tissue; thus, they largely contribute to the outcome and recovery from stroke. Oxidative stress is defined as "an imbalance between oxidants and antioxidants, in favor of the oxidants, potentially leading to damage". is involved in the pathogenesis of acute stroke. [6]

The brain cellular membrane lipids are very rich in polyunsaturated fatty acid side chains, which are highly prone to free radical attack resulting in lipid peroxidation and biomarkers such as malondialdehyde (MDA) can be estimated to assess the amount of damage to brain tissue. [7] Endogenous antioxidants involve enzymatic and non-enzymatic antioxidants, all of which consists of the cellular protective antiradical mechanism. Superoxide dismutase (SOD) is the most studied antioxidant enzyme in stroke. [8] Considering the relation of lipid parameters and oxidative stress with cerebrovascular stroke, the present study was undertaken to get a better understanding of their association in stroke patients. [9]

The aim of the present study was to assess the serum levels of total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), very low-density lipoprotein (VLDL) and triglyceride (TG) in patients of cerebrovascular stroke and controls. [10,11]

Materials and Methods

The present study was carried out in the Department of Biochemistry, Jan Nayak Karpuri Thakur Medical College and Hospital, Madhepura, Bihar, India. Informed consent was taken from patient / relative and control subjects. The study was conducted for the period of one year. Study Groups: 50 Patients (age 30-90 years) of cerebrovascular stroke referred by hospitals to Jan Nayak Karpuri Thakur Medical College and Hospital, Madhepura, Bihar, India were selected as cases based on inclusion and exclusion criteria. 50 normal individuals (age and sex matched) belonging to same socioeconomic status participated as controls.

Inclusion criteria: Patients presenting with focal neurological deficit of acute onset in the form of hemiparesis, hemi anesthesia or aphasia, or having evidence of presence of ischemic or hemorrhagic stroke on CT/MRI scan of brain were included in study complying with the WHO definition of stroke.13Patients with new onset of stroke presenting within 72 hours of onset of stroke were included. Clinical examination including vitals and detailed neurological examination were carried by physicians and neurologist.

Exclusion criteria: Patients with history of recent myocardial infarction or acute coronary syndrome(within last three months) , neoplastic disease, hepatic failure, chronic alcoholics and smokers, with infectious diseases, on NSAIDs, statins, hormone replacement therapy, antioxidants , post partum stroke, TIA were excluded Collection of Blood Sample: About 3-5 ml of venous blood after overnight fasting was collected in vacutainer by means of sterile needle, from anterior anticubital vein. It was allowed to clot for few minutes and was subjected to centrifugation for 10 minutes at 3000 rpm to separate the serum and kept at -20o C until analysis was carried out. Concentration of serum lipids was measured By Dimension Rxl Fully automated analyzer using The kits supplied By Siemens . LDL and VLDL were estimated by Friedwalds formula14. Serum Malondialdehyde (MDA) was estimated using the thiobarbituric acid [TBA] method (cited by Nourooz ZadehJ, TajaddiniSarmati J ,Mccarthy)

.15Super oxide dismutase(SOD) levels in serum were estimated spectrophotometrically using the method by S Marklund and G Marklund .16The following parameters were estimated

1. Lipid profile (total cholesterol, HDL, TG, LDL ,VLDL).
2. Serum MDA (malondialdehyde)
3. Serum SOD (superoxide dismutase)

The chemicals and reagents used for the procedure were of analytical grade

Statistical analysis: Mean and standard deviation were worked out for estimating the levels of lipid profile, serum MDA and SOD in patients of ischemic and hemorrhagic stroke and age matched controls. Using the student's t-test values, the 'p' values (probability values) were obtained. 'p' value less than 0.01 was considered as statistically significant.

Results

Table 1: Age wise distribution of cases

Age in years	N%
31-40	6 (12)
41-50	6 (12)
51-60	17 (34)
61-70	9 (18)
71-80	9 (18)
81-90	3 (6)

The mean age of cases and controls were 56.54 ± 12.48 and 48.32 ± 7.83 years respectively Maximum number of cases was in the age group of 51-60 years (34%).

Table 2: Comparison of mean cholesterol, TG, HDL, LDL and VLDL between cases and control

Parameters	Cases	Controls
Total cholesterol(mg/dl)	214.96±36.76	192.88±14.764
TG(mg/dl)	177.43±21.89	125.95±20.32
HDL(mg/dl)	33.7±5.18	45.5±7.33
LDL(mg/dl)	147.23±42.48	98.42±16.44
VLDL(mg/dl)	36.94±4.16	24.36±4.24

On comparing mean cholesterol, TG, HDL, LDL and VLDL between cases and controls, the p value was < 0.01 in all above test parameters which was found to be statistically significant.

Table 3: Comparison of mean cholesterol, TG, HDL, LDL and VLDL between cases of ischemic stroke and cases of hemorrhagic stroke

Parameter	Ischemic stroke	Hemorrhagic stroke	P value
Total cholesterol(mg/dl)	244±24.76	180.22±21.79	0.0001
TG(mg/dl)	182.58±22.58	172.18±18.72	0.2220
HDL(mg/dl)	31.79±3.77	36.54±5.70	0.007
LDL(mg/dl)	176.54±26.44	111.89±26.34	0.001
VLDL(mg/dl)	35.70±4.34	35.85±3.87	0.2209

On comparing, levels of total cholesterol, HDL cholesterol and LDL cholesterol between ischemic and hemorrhagic stroke, p value was statistically significant while difference between triglyceride level and VLDL was not significant.

Table 4: Comparison of mean serum MDA and SOD between ischemic stroke, Hemorrhagic stroke and control group

Parameters	Cases		Controls
	Ischemic stroke Mean±SD	Hemorrhagic stroke Mean±SD	Mean±SD
MDA(nmol/ml)	3.04±0.47	2.86±0.72	1.58±0.32
SOD(U/ml)	2.64±0.22	2.84±0.16	3.14±0.16

On comparing, the difference between mean MDA values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). On comparison by student t test, the difference between mean SOD values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). Also on comparison between hemorrhagic stroke and control the difference in mean MDA and SOD values was found to be statistically significant ($p<0.01$).

Discussion

Two third of all strokes occur in people over the age of 65 years, with men more commonly affected as compared to women. [12] Developing countries like India are facing a double burden of communicable and non-communicable diseases. The estimated adjusted prevalence rate of stroke range is, 84-262/100,000 in rural and 334-424/ 100,000 in urban areas. The incidence rate is 119-145/100,000 based on the population based studies. [13] Stroke is a clinical syndrome divided into two broad categories that define its pathophysiology: Ischemic strokes are caused by sudden occlusion of arteries supplying the brain, either due to a thrombus at the site of occlusion or formed in another part of the circulation accounting for 50%–85% of all strokes worldwide. The potential risk factors which have gained importance in recent years are dyslipidemia and oxidative stress. Several clinical trials showed an association between high concentrations of serum cholesterol, TGs, LDL, VLDL and ischemic stroke. [14] On the other hand, case-control studies of stroke which examined cholesterol as a risk factor have generally produced negative findings and prospective studies have generally failed to show a direct and strong association. [15] Therefore, the association between cholesterol and stroke may not be as straight forward as for coronary heart disease. [16]

The mean age of cases and controls were 56.54 ± 12.48 and 48.32 ± 7.83 years respectively Maximum number of cases was in the age group of 51-60 years (34%). These findings matched with most of the previous studies. [14,16,17] Dyslipidemia is a known risk factor for stroke. Improved detection, modification or control of risk factors, life style modification, diet and physical activity could significantly reduce the incidence of ischemic stroke and reduce the impact of this disease. [17] Lipid peroxidation, with accumulation of thiobarbiturate reactive material, is consistently found in cerebral ischemia. Amount of oxidative stress and acute changes of antioxidant capacity

might influence the prognosis of cerebral ischemia. On comparing mean cholesterol, TG, HDL, LDL and VLDL between cases and controls, the p value was < 0.01 in all above test parameters which was found to be statistically significant. [18]

On comparing, levels of total cholesterol, HDL cholesterol and LDL cholesterol between ischemic and hemorrhagic stroke, p value was statistically significant while difference between triglyceride level and VLDL was not significant. Ahmed W et al [14] ,Sreedhar et al [19], Younis et al. [20] who showed in their study that, the difference in values of TC, HDL, LDL, TG in study group and controls was found to be highly significant ($p<0.001$). This reflects the anti-atherogenic role, of HDL cholesterol in facilitating reverse cholesterol transport. On comparing, the difference between mean MDA values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). On comparison by student t test, the difference between mean SOD values of ischemic stroke and controls was found to be statistically significant ($p<0.01$). Also on comparison between hemorrhagic stroke and control the difference in mean MDA and SOD values was found to be statistically significant ($p<0.01$). InimioaraM et al [21] Sarkar et al [22], Beg Met al [23] observed significantly higher concentration of MDA in stroke patients compared with controls, similar to our study and suggested that increased level of lipid peroxides may be due to oxidation of blood or neural lipids by ischemia. They suggested that increased level of lipid peroxide may be due to oxidation of blood or neural lipids by ischemia and rise in lipid peroxide in hemorrhagic stroke was due the compressive effects producing ischemia. These studies match with findings of our study, that serum MDA levels are increased after stroke suggesting involvement of lipid peroxidation in the pathophysiology of ischemic as well as hemorrhagic stroke. Hence, increasing the anti-oxidative capacity in serum within the first day after the onset of symptoms might be a therapeutic option to minimize the oxidative injury caused by oxygen free radicals until the endogenous free radical scavenging systems recovers.

Conclusion

The difference in lipid profile between ischemic and hemorrhagic stroke should be taken into consideration while starting statin therapy as primary preventive measure to reduce incidence of first stroke in high risk patients, as well as during secondary prevention in case of ischemic strokes. Antioxidants are depleted as a consequence of an excessive production of oxygen free radicals very early after the onset of stroke. Antioxidant therapy in addition to conventional treatment strategies could be a therapeutic option to reduce injury caused by oxidative stress.

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