Effect of Lipid Profile Upon Prognosis in Ischemic and Haemorrhagic Cerebrovascular Stroke

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Abstract Stroke is the third major cause of death worldwide. Elevated plasma concentration of low density lipoproteins and low plasma concentration of high density lipoprotein concentration are associated with an increased risk of atherosclerosis and coronary heart disease but the relation between serum lipids, and cerebrovascular disease is less clear. The aim of this study was to investigate the reliability and accuracy of serum lipid profile in assessing the prognosis/neurological worsening in patients with ischemic and hemorrhagic cerebrovascular stroke. The subjects in the present study comprised of 101 healthy controls and 150 cerebrovascular stroke patients (including 90 with ischemic stroke and 60 with intracerebral hemorrhagic stroke). In both the groups fasting lipid profile was

determined within 72 h of the stroke. A statistically significant association was observed ($p < 0.001$) between the parameters of lipid profile of cases and healthy controls, and also with the prognosis of the stroke.

Keywords Stroke · Total cholesterol (TC) · High density lipoprotein-cholesterol (HDL-C) · Low density lipoprotein-cholesterol (LDL-C) · Triglycerides (TG) · National Institute of Health Stroke Scale (NIHSS)

Introduction

Stroke is the commonest cause of death in China and Japan and is the third most common cause of death, in the developed countries [1] with more than two million reported cases every year. Stroke describes a clinical event caused either by hemorrhage or occlusion in the blood supply to the central nervous system resulting in tissue infarction. Worsening of neurological symptoms after a stroke has always interested clinicians and was formally reported by Millikan and Siekert [2, 3] more than 40 years ago. In a clinical setting, attempts to find predictors of neurological worsening showed controversial results [4–7]. Although vascular disease is the prime contributor to its pathogenesis, dyslipidaemia is not undoubtedly established as a risk factor for stroke in the same way that it is for coronary artery disease [8, 9].

Evidence of a causal relation between lipid profile and stroke is inconsistent and most large-scale studies on cholesterol and stroke risk have not differentiated between ischemic and hemorrhagic stroke, nor did they differentiate among various subtypes of ischemic stroke [10–13]. Studies of cholesterol levels in stroke patients have

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revealed results varying from insignificant changes to a moderate elevation [14]. There are several studies which have not found any association between lipid profile and incident ischemic stroke [15, 16]. The aim of this study was to delineate the reliability and accuracy of serum lipid profile in assessing the prognosis/neurological worsening in patients with ischemic and hemorrhagic cerebrovascular stroke.

Material and Methods

The study was conducted by the Department of Biochemistry in collaboration with the Department of Neurology at Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, between January 2011 and July 2012. The study protocol was approved by the Institutional Ethics Committee; Informed consent was given by all subjects themselves, or by their guardians as applicable.

The subjects were divided into two groups, the first group consisted of 101 controls selected mostly from the patient's attendants and a few from among the hospital staff, of comparable age and sex. These subjects were healthy and did not have any history suggestive of cerebrovascular stroke events.

Second group consisted of 150 patients with cerebrovascular stroke, amongst patients admitted in intensive care unit (ICU) and Neurology/Medicine wards. In this group 90 cases presented with ischemic stroke and 60 cases presented with intracerebral hemorrhagic stroke based on CT Scan brain/MRI brain findings. Patients with stroke, but having doubtful diagnosis were excluded from the study.

Detailed history was taken from the selected subjects, themselves or from their close relatives. The detailed neurological examination using the National Institute of Health Stroke Scale (NIHSS) was performed. Neurological worsening has been monitored by National institute of health stroke scale (NIHSS) which is a well validated and commonly used stroke impairment scale that sums the scores from individual elements of the neurological examination to provide an overall stroke impairment score. The disability was assessed by National Institute of Health Stroke Scale at the time of admission (within 72 h from the onset of stroke) and on 7th day after admission. Depending on the disability score, cases were categorized into mild, moderate and severe disability. Early neurological worsening was diagnosed as an increase in National Institute of Health Stroke Score (NIHSS) by two or more points (or stroke-related death) between admission and day 7 and who remained stable or improved in the same period was classified as "no worsening".

5 ml venous blood sample was collected from all subjects in a plain serum separator tube. For control subjects,

early morning fasting blood sample was collected. For patients with stroke, the venous blood samples were drawn within 72 h from the onset of symptoms. The samples were processed as per the laboratory protocol, and the lipid profile parameters, namely total cholesterol (TC), high density lipoprotein (HDL) and serum triglyceride (TG) were assayed on the same day, using the ERBA Chem 5 semiautoanalyser.

Total cholesterol estimation was done using cholesterol oxidase method, with kits from Accurex Biomedical Private Ltd, Mumbai, India.

HDL—cholesterol estimation was done using polyethylene glycol (PEG) precipitation followed by cholesterol oxidase method, with kits from Crest Biosystems, Goa, India.

Low density lipoprotein-cholesterol (LDL-C) was calculated indirectly using the Friedwald formula.

Triglyceride estimation was done using glycerol phosphate oxidase (GPO) method, using kits from Crest Biosystems, Goa, India.

Results

Out of total of 251 subjects, 150 cases of cerebrovascular stroke were included in the study group and 101 subjects as control.

Table 1 depicts that the maximum number of patients (58.66 %) in the study group (cases) were in 46–65 years age group and minimum (16.66 %) were in 30–45 years age group. In the control group also most of the patients (82.17 %) belonged to 46–65 years age group and the least (5.9 %) were above 66 years of age. In the study group percentage of males (63.33 %) was more as compared to females (36.66 %). Incidence of hypertension (78.66 %), atrial fibrillation (61.33 %), diabetes mellitus (44 %) were more in the study group as compared to other risk factors.

From Table 2 the difference in values of TC, HDL, LDL, TG in study group and controls was found to be highly significant ($p < 0.001$).

The mean value for serum TC, LDL-C, TG was found to be high and mean value for serum HDL was found to be less in ischemic stroke patients as compared to hemorrhagic stroke (Table 3) and the difference was found to be statistically significant.

In Table 4, serum total cholesterol, serum HDL, serum LDL and serum Triglycerides were found to be significantly higher (≤ 0.001) in cases of neurological worsening in ischemic stroke.

Serum total cholesterol and serum triglycerides were found to be significantly lower (< 0.05) in patients with hemorrhagic stroke who had neurological worsening, compared to those who did not have neurological worsening as shown in Tables 5 and 6.

Table 1 Demographic profile of study group (cases) and controls

Demographical variables	Subjects n = 251	
	Cases n = 150	Control n = 101
Age category (years)		
30–45	25	45
46–65	88	50
66–85	37	6
Sex		
Female	55	23
Male	95	44
Hypertensive		
No	32	44
Yes	118	26
Smokers		
No	108	9
Yes	42	25
Atrial fibrillation		
No	58	88
Yes	92	13
Diabetes mellitus		
No	84	75
Yes	66	26
Alcohol		
No	96	79
Yes	54	22

Table 2 Lipid profile in study group (cases) and controls

Variables	SUBJECTS		<i>p</i> value
	Controls Mean ± SD	Study group Mean ± SD	
Statistics			
Total cholesterol (mg/dl)	171.49 ± 18.99	225.83 ± 41.89	<0.001
HDL (mg/dl)	43.27 ± 9.81	32.49 ± 5.96	<0.001
LDL (mg/dl)	103.76 ± 10.85	156.43 ± 38.01	<0.001
Triglycerides (mg/dl)	122.28 ± 24.98	183.80 ± 40.29	<0.001

Table 3 Comparison of lipid profile in ischemic and haemorrhagic stroke

Variables	Type of stroke	n	Mean ± SD	<i>p</i> value
Total cholesterol (mg/dl)	Ischemic	90	246.89 ± 31.22	0.000
	Intra cerebral hemorrhage	60	194.23 ± 35.62	
HDL (mg/dl)	Ischemic	90	31.56 ± 5.23	0.025
	Intra cerebral hemorrhage	60	33.90 ± 6.72	
LDL (mg/dl)	Ischemic	90	175.33 ± 29.49	0.000
	Intra cerebral hemorrhage	60	128.08 ± 31.22	
Triglycerides (mg/dl)	Ischemic	90	194.67 ± 34.19	0.000
	Intra cerebral hemorrhage	60	167.50 ± 43.42	

Discussion

The impact of cerebrovascular stroke on individual patients, their families and society as a whole is immense. Therefore it is imperative to acquire a clear understanding of its pathogenesis, to identify the predisposing factors and also to determine their individual risks.

Several studies have been conducted to investigate the association between atherosclerosis, coronary artery disease, peripheral vascular disease and serum lipids, but attempts to relate the various parameters of lipid profile with the risk or the incidence or the outcome/prognosis of cerebrovascular diseases by some workers, have been inconclusive [8, 9].

In this study, we found that the study group (individuals with ischemic or hemorrhagic stroke) have been found to have a significantly deranged lipid profile, in comparison to the control group (individuals without stroke).

Shahar et al. [15], Bowman et al. [16] reported the lack of association between lipids and stroke. Study conducted by Bowman et al., of 296 stroke patients and the same number of controls, found that levels neither of total cholesterol, triglycerides nor HDL were associated with risk of ischemic stroke, although a high total cholesterol/HDL ratio was found to increase the risk. However in their study, due to inability to differentiate between hemorrhagic and ischemic stroke, serum cholesterol's positive association with ischemic stroke may have been concealed by a negative relationship with hemorrhagic stroke.

In the present study, perhaps the confounding effect of lipids in hemorrhagic stroke was balanced by an increase in serum lipid profile in ischemic stroke accounting for raised levels in cerebrovascular stroke.

We found a significantly raised ($p \leq 0.001$) lipid profile in cases with neurological worsening as compared to no worsening in ischemic stroke while serum Total Cholesterol and serum Triglycerides were found to be significantly lowered ($p < 0.05$) in cases with neurological worsening in hemorrhagic stroke.

Okumara et al. [17], Irribarren [18], Tirschwell [19], in their studies observed that hypercholesterolemia is a protective factor against ICH and that low blood cholesterol

Table 4 Neurological worsening with lipid profile in ischemic stroke

Neurological worsening	n	Variables	Mean $\pm$ SD	<i>p</i> value
No	76	Total cholesterol	242.05 $\pm$ 31.15	0.001
Yes	14	(mg/dl)	273.14 $\pm$ 14.03	
No	76	HDL (mg/dl)	32.63 $\pm$ 4.58	0.000
Yes	14		25.71 $\pm$ 4.74	
No	76	LDL (mg/dl)	171.18 $\pm$ 30.02	0.002
Yes	14		197.86 $\pm$ 10.51	
No	76	Triglycerides	187.37 $\pm$ 30.91	0.001
Yes	14	(mg/dl)	234.29 $\pm$ 22.09	

Table 5 Neurological worsening with lipid profile in hemorrhagic stroke

Neurological worsening	N	Variables	Mean $\pm$ S D	<i>p</i> value
No	11	Total cholesterol	197.12 $\pm$ 38.38	0.027
Yes	49	(mg/dl)	181.36 $\pm$ 13.80	
No	11	HDL (mg/dl)	35.55 $\pm$ 7.08	0.288
Yes	49		33.45 $\pm$ 4.72	
No	11	LDL (mg/dl)	129.48 $\pm$ 33.85	0.239
Yes	49		121.81 $\pm$ 14.01	
No	11	Triglycerides	173.97 $\pm$ 42.58	0.011
Yes	49	(mg/dl)	138.63 $\pm$ 35.99	

Table 6 Dyslipidemia with neurological worsening in ICH and Ischemic stroke

Total cholesterol	Neurological worsening in ich		Neurological worsening in is	
	Yes	No	Yes	No
<200	31	10	0	13
200–239	13	1	1	17
>240	5	0	13	46
HDL				
<40	37	6	14	64
>40	12	5	0	12
LDL				
<100	4	1	0	0
100–159	38	10	0	22
>160	7	0	14	54
TG				
<200	33	9	0	8
200–499	16	2	14	68

increases risk for ICH with an inverse relationship existing between serum cholesterol and incidence of ICH.

Bang et al. [20], postulated that Cholesterol is known to have effects on the vasculature and is essential for normal membrane fluidity, and adequate cholesterol levels may be important for maintaining the integrity of vessels and their resistance to rupture.

Variation in lipid profile with respect to ischemic and hemorrhagic stroke and as a risk factor for determining prognosis in the above two types of stroke arises by the fact that cerebral ischemic patients have a more atherogenic lipid profile whereas in intracerebral hemorrhage, lipids apparently play a protective role.

The difference in serum lipids behavior between patients with ischemic and hemorrhagic stroke addresses the controversy surrounding the role of blood lipid levels in risk of cerebrovascular accidents (CVA). Many studies conducted thus far have compared a group of CVA patients with the general population, without distinguishing the type of stroke under consideration.

Conclusion

Increased Serum levels of total cholesterol, Triglycerides, Low density lipoprotein and low serum levels of High density lipoprotein were associated with increased risk of ischemic stroke and also poorer prognosis whereas low levels of serum cholesterol, serum Triglycerides were associated with increased risks of hemorrhagic stroke and neurological worsening.

Stroke patients with dyslipidemia need a comprehensive health care approach involving dietician, physician and good biochemical investigative support. This study points to the need to stratify cerebral vascular accidents based on their type (ischemic or hemorrhagic) in order to determine the real association between lipid alterations and occurrence of these neurological events. This study may also help guide future trials attempting to relate lipid alterations with occurrence of vascular events.

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