

Comparison of Serum Lipid Profile in Ischaemic and Haemorrhagic Stroke

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ABSTRACT

Objective: To compare serum lipid profile between patients of ischaemic and haemorrhagic strokes.

Study Design: Cross sectional, comparative study.

Place and Duration of Study: Military Hospital, Rawalpindi, from August 2004 to February 2005.

Methodology: Patients with diagnosis of stroke comprising 100 consecutive patients each of ischaemic and haemorrhagic strokes were included in the study while patients on lipid lowering therapy were excluded from study. To determine the subtype of stroke, clinical examination followed by CT scan of brain was done. A serum sample after 8 hours of overnight fasting was taken on the next day of admission for both groups of patients. Total serum cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol and HDL-cholesterol was determined, using enzymatic colorimetric method. Statistical analysis was done by comparison of lipid profile in two subgroups, using proportion test for any significant difference.

Results: The mean age at presentation of patients with stroke was 64.2±12 years with a male to female ratio of 3.6:1. In 100 ischaemic stroke patients, raised serum total cholesterol was seen in 42, triglyceride in 04, LDL-cholesterol in 05 and VLDL-cholesterol in 07 patients. Serum HDL-cholesterol was below the normal reference in 31 cases. On the other hand, serum total cholesterol and triglycerides was raised in 05 patients each, LDL-cholesterol in 09 and VLDL-cholesterol in 03 patients of haemorrhagic stroke. Serum HDL-cholesterol was below normal in 04 patients of haemorrhagic stroke. On comparison, there were significantly greater number of patients with raised serum cholesterol and low HDL-cholesterol in ischaemic stroke than haemorrhagic stroke ($p < 0.05$). No statistical significance was found on comparing serum values of ischaemic and haemorrhagic stroke for triglycerides, LDL-cholesterol and VLDL-cholesterol.

Conclusion: Ischaemic stroke patients had high serum total cholesterol and lower HDL-cholesterol levels as compared to haemorrhagic stroke. High risk patients of stroke may be screened using serum lipid profile and further studies are suggested to evaluate the effect of lipid lowering therapy in terms of morbidity and mortality in ischaemic stroke patients.

Key words: Cholesterol. Stroke. Ischaemic stroke. Haemorrhagic stroke.

INTRODUCTION

Stroke is a global health problem. It is the leading cause of adult disability and the second leading cause of mortality worldwide. Mortality from strokes is the second leading cause worldwide.¹ About 15 million people suffer from non-fatal strokes leading to disability in about a third of patients. It is a leading cause of functional impairments, with 20% of survivors requiring institutional care after three months and 15-30% being permanently disabled.²

The incidence and mortality of stroke vary greatly among different populations and has declined considerably in several foreign studies probably due to better preventive measures.³ There are various risk factors such as age, gender, familial trends, race and ethnic groups and modifiable factors such as

hypertension, cardiac disease, diabetes mellitus, dyslipidaemia, smoking, alcohol abuse, physical inactivity, asymptomatic carotid stenosis and transient ischaemic attacks.³ Risk factors for strokes have been studied locally.^{4,5} The relationship of serum lipids and lipoproteins with cerebrovascular disease are being studied along with many other risk factors as in coronary heart disease.^{2,6} Several clinical trials showed an association between high concentrations of serum cholesterol and ischaemic stroke.^{2,7} 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.⁸⁻¹⁰ Some demonstrated an inverse relation between total cholesterol and death from haemorrhagic stroke.¹¹ Therefore, the association between cholesterol and stroke may not be as straight forward as for coronary heart disease.

Serum lipid levels have an established effect on short-term mortality due to strokes.¹² It is important to evaluate the difference in serum lipid levels in subtypes of strokes to guide lipid-lowering therapy which can reduce incidence of stroke and related mortality by adapting primary and secondary preventive measures.^{13,14}

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No study is available locally to compare all the components of serum lipid profiles in ischaemic and haemorrhagic strokes. Therefore, this study was carried out to compare serum lipid profiles in patients with ischaemic and haemorrhagic cerebrovascular accidents to validate and develop guidelines in local patients.

METHODOLOGY

This comparative cross sectional study was conducted at Military Hospital, Rawalpindi, from August 2004 to February 2005. Patients with a diagnosis of stroke comprising 100 consecutive patients each of ischaemic and haemorrhagic strokes were included in the study by non-probability consecutive sampling.

Stroke was defined according to WHO definition as, rapid onset of a neurological deficit attributed to obstruction or rupture in the cerebral arterial system. Clinical diagnosis was established and CT scan brain without contrast injection was performed to stratify the patient into each category. Past medical and personal history for cigarette smoking, arterial hypertension, diabetes mellitus, high altitude and ischaemic heart disease was also sought and patients on lipid lowering therapy were excluded from study.

Serum samples were obtained after 8 hours of overnight fasting, on the next morning after admission. Venous blood samples were collected into plain tubes. Samples were centrifuged at 4°C for 15 minutes after incubation of 20 minutes for extraction of serum. The sera were analyzed for serum lipid profile including total cholesterol, triglyceride, LDL-cholesterol, VLDL-cholesterol and HDL-cholesterol by enzymatic colorimetric method using chemistry auto-analyser.

The data was analysed using SPSS version 11.0. Rational descriptive statistics; frequencies and percentages were computed for presentation of qualitative variables like gender, age, CT scan brain findings and quantitative variables as lipid profile. Mean values of the cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol and VLDL-cholesterol were determined. Frequency percentage of abnormal lipid profile in both groups of patients of ischaemic and haemorrhagic stroke, were determined and compared using proportion test for any significant difference taking p-value of < 0.05 as significant.

RESULTS

The mean age of presentation of patients with stroke was 64.2±12 years. The age range was 19-97 years with a male to female ratio of 3.6:1. The mean age of male patients with stroke was 61±14 years, while it was 67±9 years in female patients.

Fasting serum lipid profile of 100 ischaemic stroke patients showed raised serum total cholesterol in 42 patients with mean serum total cholesterol of 5.08±1.48

mmol/L. Serum triglyceride was above normal reference range in 4 cases having a mean value of 1.22±0.30 mmol/L. Similarly, serum LDL-cholesterol was raised in 5 patients having a mean value of 4.46±0.36 mmol/L and VLDL-cholesterol was high in 7 cases with mean value of 0.74±0.36 mmol/L. On the contrary, serum HDL-cholesterol was below the normal reference range in 31 cases with a mean value of 0.86±0.30 mmol/L (Table I).

Table I: Comparison of serum lipid profile in ischemic and haemorrhagic strokes.

Lipid profile	Stroke type	Mean ± SD
Total cholesterol (< 5.2 mmol/L)	ischaemic	5.08±1.48
	haemorrhagic	3.92±0.79
Triglyceride (0.4-2.3 mmol/L)	ischaemic	1.22±0.30
	haemorrhagic	1.27±0.31
HDL-cholesterol (> 0.9 mmol/L)	ischaemic	0.86±0.30
	haemorrhagic	1.03±0.16
LDL-cholesterol (< 3.4 mmol/L)	ischaemic	4.46±0.33
	haemorrhagic	4.46±0.36
VLDL-cholesterol (0.26-1.03 mmol/L)	ischaemic	0.74±0.36
	haemorrhagic	0.73±0.31

LDL: Low density lipo-protein; VLDL: Very low density lipo-protein; HDL: High density lipo-protein.

The 100 patients of haemorrhagic stroke showed a high serum total cholesterol and serum triglyceride in 5 patients each with a mean value of 3.92±0.79 mmol/L and 1.27±0.31 mmol/L respectively. Serum LDL-cholesterol was increased in 9 patients with mean level of 4.46±0.36 mmol/L. Serum VLDL-cholesterol was also raised in 3 patients with a mean value of 0.73±0.31 mmol/L while, serum HDL-cholesterol was below the normal reference range in 4 patients with haemorrhagic stroke having a mean value of 1.03±0.16 mmol/L (Table I).

Comparison of serum lipid profile of two categories of stroke showed a raised serum total cholesterol in 42% patients of ischaemic stroke in contrast to 5% patients with haemorrhagic stroke which is significant at a p-value of < 0.001. Similarly, serum HDL-cholesterol was below the normal reference range in 31% patients of ischaemic stroke as compared to 4% patients with haemorrhagic stroke having a significant p-value of < 0.001. No statistical significance was found on comparing serum values of triglycerides, LDL-cholesterol and VLDL-cholesterol in ischaemic and haemorrhagic stroke patients (Table II).

Table II: Comparison of abnormal lipid profile in ischemic and haemorrhagic stroke patients (n=200).

	% of cases with abnormal values		p-value
	Ischemic stroke (n=100)	Haemorrhagic stroke (n=100)	
Serum cholesterol	42	5	0.0001
Serum Triglyceride	4	5	0.366
Serum LDL-cholesterol	7	3	0.097
Serum VLDL-cholesterol	5	9	0.133
Serum HDL-cholesterol	31	4	0.0001

LDL: Low density lipo-protein; VLDL: Very low density lipo-protein; HDL: High density lipo-protein.

DISCUSSION

Stroke is a clinical syndrome characterized by rapidly developing symptoms and/or signs of focal and at times global loss of cerebral functions, with symptoms lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.¹⁵ According to World Health Organization report for 2002, total mortalities due to stroke in Pakistan were 78512.¹⁶

The most vulnerable age for stroke is between 61-70 years for males and 51-60 years for females.³ This was also seen in this study along with the gender ratio of 3.6:1 for male to female as in other local studies.³

Cerebral atherosclerosis with atheroma formation is the basic underlying patho-physiologic mechanism in ischaemic stroke.³ Conflicting results exist in the literature about the correlation between the total plasma cholesterol of patients and the risk of stroke. Qizilbash *et al.* in a review of 10 studies examining the relationship between serum total cholesterol and subsequent stroke concluded that there was a significant association however, other studies were less conclusive.^{17,18} Hyperlipidemia was present in 16% patients of stroke and was the 3rd most common risk factor for stroke in the study by Khan *et al.* and Tanveer *et al.*, while, the present study showed hyperlipidemia in 21% of all 200 patients of stroke.^{19,20}

There is no established biological mechanism that explains these results, but cholesterol is known to have effects on the vasculature and is essential for normal membrane fluidity. Rabbits fed a high cholesterol diet have larger experimentally induced infarcts associated with an increase in platelet deposition in the thrombus at the infarct. All of these effects suggest that, a higher serum cholesterol concentration would predispose to stroke with a poor outcome.²¹ It has now been established that, the serum cholesterol measurements within the first 48 hours are identical to those after three months, although a fall in concentration does occur between these times.²² Earlier studies showed a positive relation between serum total cholesterol and non-haemorrhagic strokes with an inverse association to intracranial haemorrhage.²³ The present study also showed a positive association with ischaemic stroke while, no association was seen with haemorrhagic stroke.

Association between concentrations of serum triglycerides and the risk of stroke is also overshadowed. Some studies led to negative results whereas others showed a positive association with high serum triglyceride concentrations.²⁴ Copenhagen City Heart Study showed a log linear association between serum triglyceride concentrations and non-haemorrhagic stroke while no association was found of high plasma triglyceride concentration as a risk factor for both types of stroke in this study.²⁵

Serum HDL-cholesterol has anti-atherogenic properties with ability to trigger the flux of cholesterol from peripheral cells to the liver and thus having a protective effect.²⁶ There is an inverse association between HDL-cholesterol and ischaemic stroke in the present study as 31% patients of ischaemic stroke had below than normal serum HDL-cholesterol. However, recently it has been observed that serum HDL-cholesterol levels decrease significantly at the time of acute ischaemic stroke and it may be an acute phase reactant or nascent biomarker of acute stroke susceptibility.²⁷

A positive relationship between high serum LDL-cholesterol levels and the risk of ischaemic stroke has been seen as well. However, no such association was seen in this study.

These counter-intuitive effects of serum lipids cannot be taken at face value without considering possible sources of bias in this study. A hospital population was examined and referrals were admitted selectively for severity of the symptoms and requiring immediate nursing and hospital care. On the other hand, a community study is likely to miss those patients who die within 24 hours of the onset of stroke. Moreover, the serum concentrations may reflect the severity of stroke, rather than the premorbid concentration. In this study, blood samples were collected within 24 hours and there was no follow-up data on those patients to indicate the effect of stress or nutrition, but studies have shown that serum cholesterol measurements within the first 48 hours remain identical to those after three months.²²

This study, despite its shortcomings, suggests the presence of significant difference between the values of serum total cholesterol and serum HDL-cholesterol in ischaemic and haemorrhagic strokes while no significant difference is seen between ischaemic and haemorrhagic strokes as far as serum values of triglycerides, LDL-cholesterol and VLDL-cholesterol are concerned.

In the light of the above, screening should be done for lipid abnormalities so that lipid lowering agents can be used as a primary preventive measure in selected high-risk patients for stroke while, lipid lowering therapy should be initiated as secondary preventive measure especially in ischaemic strokes. Meta-analyses estimate that statin therapy results in a 24-29% reduction in stroke related mortality especially ischaemic subtype over a wide range of lipid values.²⁸

CONCLUSION

Ischaemic stroke patients had higher serum total cholesterol and lower HDL-cholesterol levels in comparison to haemorrhagic stroke. High risk patients of stroke may be screened using serum lipid profile and further studies are suggested to evaluate the effect of lipid lowering therapy in terms of morbidity and mortality in ischaemic stroke patients.

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