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Research Article

Role of dyslipidemia in stroke and comparison of lipid profile in ischemic and hemorrhagic stroke -a case control study

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ABSTRACT

Background: The role of dyslipidemia as a risk factor for stroke is questionable. One of the reasons could be that most studies club together ischemic and hemorrhagic stroke. In India, now there is an increase in the burden of cerebrovascular disease. Hence it is very important that we should have a thorough knowledge of the risk factors for stroke and the ways of preventing its occurrence. Objective of the study was to know whether there is a role for dyslipidemia in the occurrence of stroke and if there is any difference in the lipid profile of patients with ischemic and hemorrhagic stroke.
Methods: Case control study with 60 patients having hemorrhage and 60 patients with infarct and 73 controls. The patients in both the groups did not have diabetes and were not taking statins.
Results: Of the 120 patients with stroke 51 (42.5%) had cholesterol levels >200mg% OR 3.75 (1.83-7.7) p <0.001 and 77 (64.2%) had LDL cholesterol >100 mg% OR 2.29 (1.27-4.15) p 0.009. In the HDL-C category 32 (26.7%) had HDL less than 40 mg% while in the control group 30 (41.1%) had low HDL cholesterol OR 0.52 (0.28-0.96) p 0.05 . There was no difference in the lipid profile of ischemia and hemorrhage.
Conclusions: High total and LDL cholesterol are important risk factors in the development of stroke be it infarct or hemorrhage. HDL levels influence the development of hemorrhagic stroke but not infarct. There was no difference in the lipid profile of the two categories of stroke. Low HDL cholesterol is protective in hemorrhagic stroke.

Keywords: Ischemic stroke, Cerebral hemorrhage, Lipid profile, Cholesterol, HDL cholesterol, LDL cholesterol, Triglyceride

INTRODUCTION

The traditional risk factors for coronary artery disease and stroke are smoking, diabetes, hypertension and dyslipidemia.[1] But unlike in coronary artery disease the evidence for the role of these risk factors in stroke is less convincing. Among the risk factor smoking and hypertension are said to be the most important ones. The influence of diabetes on the burden of stroke is more controversial.[2] The term atherogenic dyslipidemia was first described by Austin et al. It includes the spectrum of high LDL-cholesterol, high triglyceride and low HDL-cholesterol.[3] It is well proven by epidemiological studies that high LDL –C and low HDL-C are associated with cardiovascular disease.[4] Whether dyslipidemia is a risk factor for stroke is questionable. One of the reasons why the role of lipids is controversial might be because most studies club together ischemic and hemorrhagic stroke.

The combination of positive association with ischemic stroke and negative association with hemorrhagic stroke might mask the positive influence when considering stroke as one entity.[5] Studies assessing the lipids in relation to stroke subtypes show contradictory results. MRFIT (Multiple Risk Factor Intervention Trial) showed high cholesterol level to be associated with increased

mortality while there was reciprocal relation between cholesterol level less than 200mg /dl and hemorrhagic stroke.[6] An Iranian study found significant association between dyslipidemia and ischemic stroke.[5] Despite the controversies the use of statins has been found to be associated with a decrease in the relative risk of all types of stroke.[7,8]

There is increasing prevalence of conditions like diabetes, hypertension, obesity and dyslipidemia in India. This has also led to an increase in the burden of coronary artery disease and cerebrovascular disease.[9] This has tremendous social impact in a country like India as it has been seen that stroke affects younger individuals in the Indian population.[10]

And the sickness and residual disability of the sole earning members drains the resources of many families. Hence it is very important that we should have a thorough knowledge of the risk factors for stroke and the ways of preventing the occurrence of this devastating condition.

We did this study in the background of such conflicting information. The objectives were to know whether there is a role for dyslipidemia in the occurrence of stroke and to find out if there is any difference in the lipid profile of patients having the two subtypes of stroke namely ischemia and hemorrhage.

METHODS

Case control study on 60 consecutive patients admitted with a diagnosis of hemorrhagic stroke and 60 consecutive patients with ischemic stroke and 73 control subjects, was done The participants included patients who were admitted in the medicine wards of Government Medical College Thrissur, which is a tertiary care centre in Kerala, India. The control subjects were age and sex matched and admitted to the hospital for illnesses other than stroke nor did they have previous episode of stroke. The diagnosis of stroke was confirmed by taking CT scan of brain.

The patients in both the groups did not have diabetes nor were they taking statins. Those who had secondary causes for intracerebral hemorrhage, who were admitted more than 24hours after stroke, with familial hypercholesterolemia, with associated significant co morbidities like hypothyroidism were excluded from the study.

Lipid profile was taken following a 12 hour fasting on the next day of admission. Serum total cholesterol less than200mg/dl, LDL cholesterol<100 mg/dl, triglyceride less than150mg/dl, and HDL more than 40 mg/dl was taken as normal. Data was analyzed using SPSS software. Quantitative data were expressed as mean and standard deviation. Qualitative data were expressed as percentage. Chi square test was used as test of significance, with p value less than 0.05 taken to be significant.

RESULTS

We studied 60 consecutive patients with ischemic stroke and 60 consecutive patients with hemorrhagic stroke and 73 control subjects after getting informed consent.

The epidemiological data is presented in Table 1 and 2.

Table 1: Age wise distribution of the two subtypes of stroke and control.

Age group years	Hemorrhagic stroke number (%)	Ischemic stroke number (%)	Control number (%)
18-44	5 (8.3)	11 (18.3)	10 (13.7)
45-64	13 (21.6)	18 (30)	22 (30.1)
>65	42 (70)	31 (51.7)	41 (56.2)
Total	60 (100)	60 (100)	73 (100)

Table 2: Sex distribution of two subtypes of stroke and control.

Sex	Hemorrhagic stroke Number (%)	Ischemic stroke Number (%)	Control Number (%)
Male	35(58.3)	37(61.7)	45(61.6)
Female	25(41.7)	23(38.3)	28(38.4)
Total	60(100)	60(100)	73(100)

The mean age of patients with stroke was 65.6±15 years, while that for hemorrhagic stroke was 68.5±14 years and that for ischemic stroke was 62.6±15.4 years. The mean age of male patients with hemorrhagic and ischemic stroke was 67.2±13 years and 58.8±16 years respectively. The mean age of females with hemorrhagic and ischemic stroke was 70.4±15 years and 68.7±12 years respectively.

Table 3: Mean value of lipids in hemorrhagic and ischemic stroke and control.

Lipid profile	Stroke type	Mean±Std deviation mg %
Total cholesterol	Hemorrhagic	188±36
	Ischemic	189±46
	Control	160±5.9
LDL cholesterol	Hemorrhagic	114 ±34
	Ischemic	119 ± 42.5
	Control	97.8 ±33.3
HDL cholesterol	Hemorrhagic	49.9 ±14
	Ischemic	44.1 ± 10.3
	Control	44.1 ± 10.3
Triglyceride	Hemorrhagic	116.9 ± 39
	Ischemic	126.5± 45
	Control	126.5± 45

Of the 120 patients with stroke 51 (42.5%) had cholesterol levels >200mg% OR 3.75 (1.83-7.7) p <0.001 and 77 (64.2%) had LDL cholesterol >100 mg% OR 2.29

(1.27-4.15) p 0.009. There was no difference between the stroke and control patients with respect to triglyceride levels. In the HDL-C category 32 (26.7%) had low levels of HDL (less than 40 mg%) while in the control group 30 (41.1%) had low HDL cholesterol OR 0.52 (0.28-0.96) p 0.05.

Table 4: Comparison of lipid profile of patients with stroke and control subjects.

Lipid	Stroke N (%)	Control n (%)	P value	OR	95% CI
Cholesterol >200mg%	51 (42.5%)	12 (16.4%)	<0.001	3.75	1.83-7.7
LDL-C >100 mg%	77 (64.2%)	32 (43.8%)	0.009	2.29	1.27-4.15
Triglyceride >150 mg%	23 (19.2%)	10 (13.7%)	0.43	1.49	0.66-3.3
HDL-C <40mg%	32 (26.7%)	30 (41.1%)	0.05	0.52	0.28-0.96

Table 5: Comparison of lipid profile of patients with hemorrhagic stroke and control subjects.

Lipid	Hemorrhagic stroke N (%)	Control subjects N (%)	P value	OR	95%CI
Cholesterol >200mg%	28(46.7%)	12(16.4%)	<0.001	4.44	1.99-9.9
LDL-C >100 mg%	39 (65%)	32(43.8%)	0.02	2.3	1.1-4.8
Triglyceride >150 mg%	10(16.7%)	10(13.7%)	0.8	0.48	3.2
HDL-C <40mg%	12(20%)	30(41.1%)	0.01	0.35	0.16-0.78

The patients who had bleed had abnormal total cholesterol and LDL cholesterol when compared to control subjects OR 4.44(1.99-9.9) p <0.001 and OR 2.3 (1.1-4.8) p 0.02 respectively.

HDL cholesterol below 40mg% was obtained in 41.1% of control subjects in comparison with 20% of patients who were suffering from hemorrhagic stroke.

OR 0.35 (0.16-0.78) p 0.01. There was no difference in the triglyceride levels among patients with bleed and control subjects. Comparison of the lipid profile of patients with cerebral infarct and control revealed that patients with infarct had abnormal total cholesterol and LDL cholesterol OR 3.16(1.4-7.09) p 0.008 and OR 2.2 (1.09-4.45) p 0.03 respectively.

While the observing the HDL cholesterol level in patients with ischemia and control subjects 66.7% (n=40) of the patients with infarct and 58.9% (n= 43) of controls had HDL cholesterol more than 40 mg %. p 0.45.

There was no difference in the triglyceride levels among patients with infarct and control subjects.

Table 6: Comparison of lipid profile of patients with ischemic stroke and control subjects.

Lipid	Ischemic stroke N (%)	Control subjects N (%)	P value	OR	95% CI
Cholesterol >200mg%	23 (38.3%)	12 (16.4%)	0.008	3.16	1.4-7.09
LDL-C >100 mg%	38 (63.3%)	32 (43.8%)	0.03	2.2	1.09-4.45
Triglyceride >150 mg%	13 (21.7%)	10 (13.7%)	0.32	1.7	0.7-4.3
HDL-C <40mg%	20 (33.3%)	30 (41.1%)	0.45	0.71	0.35-1.4

Table 7: Comparison of lipid profile of hemorrhagic and ischemic stroke.

Lipid	% of stroke with abnormal values		pvalue
	Hemorrhagic	Ischemic	
Serum cholesterol >200 mg%	46.7%(n=28)	38.3% (23)	0.35
LDL cholesterol >100 mg%	65%(n=39)	63%(n=38)	0.8
HDL cholesterol <40 mg%	20%(n=12)	33.3%(n=20)	0.14
Triglyceride >150 mg%	16.7%(n=10)	21.7%(n=13)	0.4

On comparing the lipid profile of the two categories of stroke there was no difference between the two groups. On doing regression analysis in comparing ischemic and hemorrhagic strokes with control patients with bleed had higher total cholesterol and lower HDL while patients with infarct had higher total cholesterol levels.

Table 8: Logistic regression showing lipid in each stroke subtype compared with the control group.

	Hemorrhage vs control			Ischemia vs control		
	OR	CI	p	OR	CI	p
Cholesterol	0.27	0.11-.69	0.006	0.41	0.2-1.1	0.06
LDL-C	0.73	0.32-1.6	0.45	0.65	0.3-1.4	0.28
HDL-C	2.3	1.1-5.3	0.03	1.19	0.6-2.5	0.63
Triglyceride	1.39	0.49-3.9	0.52	0.83	0.3-2.1	0.7

DISCUSSION

Atherosclerosis is the main pathology responsible for cerebrovascular disease and coronary artery disease. The fact that dyslipidemia is a risk factor for developing coronary artery disease is undisputed. But such confidence is lacking regarding association between dyslipidemia and stroke. In this study we could demonstrate that dyslipidemia is indeed a risk factor in stroke, both ischemia and hemorrhage but there is difference between the two subtypes.

Togha et al observed that the risk of developing ischemic stroke increases as the total cholesterol and LDL values rise.[11] MRFIT study showed an inverse relation between cholesterol level and hemorrhagic stroke, while the risk increased for ischemic stroke with cholesterol levels more than 200mg/dl, and more than doubled when serum cholesterol values rose above 280 mg/dl.[6]

The observation that high cholesterol levels are protective in hemorrhagic stroke is supported by a Japanese study.[12] and a study by Jayachandran et al.[13] On the other hand there is also evidence to show that serum cholesterol does not have an influence on occurrence of stroke.[14] High levels of LDL cholesterol has been uniformly linked to a higher occurrence of ischemic and hemorrhagic stroke.[5,15]

We observed that the abnormal lipids associated with bleed are total cholesterol, LDL cholesterol and HDL cholesterol while only total cholesterol and LDL cholesterol are associated with infarct. Triglycerides did not have an association with either stroke type.

HDL cholesterol is conventionally considered as the "good cholesterol". But now the seeds of doubt have been sowed-is HDL cholesterol really "good" at all levels. Too much of even good things are not good. Recent studies are of the opinion that values of HDL cholesterol more than 58mg% may in fact be more harmful than good.[16] An Iranian study did not find any influence for HDL cholesterol on stroke.[5]

In this study we also observed that majority of the people who had hemorrhagic stroke (80%) had high HDL cholesterol that is above 40 mg%, which is traditionally considered as protective level. This surprising effect of HDL cholesterol, which was quite contrary to our already existing knowledge, was observed especially in hemorrhagic stroke and to a lesser extent in ischemic stroke.

On doing regression analysis in comparing ischemic and hemorrhagic strokes with control there was difference between the cholesterol and HDL cholesterol levels in patients with bleed, while patients with infarct had higher total cholesterol levels. Another important aim of our study was to find out if there is any difference in the lipid profile between the two categories of stroke. We did not observe any difference between the two.

CONCLUSION

Dyslipidemia in the form of high total and LDL cholesterol is an important risk factor in the development of stroke be it infarct or hemorrhage. HDL levels influence the development of hemorrhagic stroke but not infarct. There was no difference in the lipid profile of the two categories of stroke. Contrary to the prevailing knowledge there was no inverse relation between HDL cholesterol and stroke especially in bleed. The role of high HDL in stroke is not found to be protective.

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