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Study of lipid profile in cases of non-diabetic stroke

Ayaskanta Kar, Chinmayananda Dash*, Malati Murmu, Karun Mahesh K. P.

Department of Medicine, VSS Institute of Medical Sciences and Research, Burla (Sambalpur), Odisha, India

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*Correspondence:

Dr. Chinmayananda Dash,

E-mail: chinuwaitin4u@gmail.com

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ABSTRACT

Background: To study serum lipid profile in non-diabetic patients with stroke and to determine whether there is any significant correlation between them and to compare the serum lipid profile between ischaemic and haemorrhagic group. Design: Case control study.

Methods: The current study was done in the Department of Medicine VIMSAR, Burla, Odisha. Total 100 patients of completed stroke (Ischaemic63 and haemorrhagic37) and 30 controls were included in the study. All cases were adult (more than 14 years of age). Patients with suspected embolic stroke, diabetes (Type 1 and 2) and patients on lipid lowering drugs were excluded from the study. Routine investigations and fasting serum lipid profile was done.

Results: 45 patients had elevated serum total cholesterol levels out of which 75.56% had Ischaemic stroke and 24.49% had haemorrhagic stroke. 24 cases had elevated serum Triglyceride levels of which 66.67% had Ischaemic stroke and 29.17% had haemorrhagic stroke. 76.47% of cases having elevated serum LDL cholesterol suffered from Ischaemic stroke where as 20.59% had haemorrhagic stroke.

Conclusions: A statistically positive correlation was found between serum total cholesterol, Triglyceride, LDL levels and the risk of stroke.

Keywords: Dyslipidemia, Lipid Profile, Stroke

INTRODUCTION

Stroke or cerebrovascular accident is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause. Stroke is the second leading cause of death worldwide causing 6.2 million deaths in 2011. Stroke is a common medical emergency. It is also a major cause of long term disability.

Stroke is difficult to treat and the treatment is still not effective. Prevention is the best option but ability to forecast the stroke is challenging making the detailed study of risk factors essential.² The risk factors of stroke include various fixed and modifiable risk factors, notable among them are age, gender, heredity, diabetes mellitus, hypertension, dyslipidemia, smoking, atherosclerosis,

excessive intake of alcohol and other rare causes.² There is good evidence that modification of risk factors will reduce the risk of stroke.^{2,3}

Studies have shown that elevated levels of serum lipids are important risk factors for the development of atherosclerosis which is the precursor of stroke. Elevated plasma concentration of low density lipoproteins (LDL) and low levels of high density lipoprotein (HDL) concentrations are associated with an increased risk of atherosclerosis. The relationship between atherosclerosis and elevated serum lipids is well established and aggressive treatment of dyslipidemia decreases the risk of stroke. Numerous clinical trials have shown a marked reduction in stroke incidence with use of cholesterol lowering drugs as in case of coronary artery disease, the level of low density lipoprotein (LDL) cholesterol has the

most impact on incidence of stroke but elevated triglyceride (TG) may also confer risk.⁵

Studies of cholesterol levels in stroke patients have revealed results varying from insignificant changes to a moderate elevation. The amount of evidence relating to relation between serum lipids, lipoproteins and cerebrovascular accident is not adequate. The incidence rises steeply with age, and in many lower and middle income countries it is rising in association with less healthy lifestyles, prompted us to undertake this study. Hence the study has been taken up to study lipid abnormalities in non diabetic stroke patients in our setup.

METHODS

The objective of the study was to observe the serum lipid profile in non-diabetic patient with stroke and to determine any significant correlation between abnormal lipid profile and stroke in non-diabetic patients and to compare serum lipid profile between patient of ischaemic and haemorrhagic stroke.

Study design

The present study was conducted on non-diabetic stroke patients admitted to the Department of General Medicine, VIMSAR, Burla, Sambalpur, Odisha, from November 2014 to October 2016 with normal individuals of comparable age and sex served as controls. The type of study is of case-control.

Inclusion criteria

The study included a total of 100 adult cases (more than 14 years of age) of completed stroke. They were divided into two categories: 1. Patients with ischaemic stroke, 2. Patients with haemorrhagic stroke. 30 (Thirty) normal individuals of comparable age and sex served as controls for the study.

Exclusion criteria

Diabetic stroke patients, cerebrovascular accidents associated with head injury or brain tumour, pregnancy, puerperium, patients who were on lipid lowering drugs, patients with suspected emboli of cardiac origin and patients with subarachnoid hemorrhage were excluded from the study.

Data collection

Data was collected with meticulous history, clinical examination with detailed neurological examinations along with appropriate investigations. A structured questionnaire was used to obtain data on family history of diabetes mellitus, history of hypertension, past and present illness, dietary pattern, addiction and medication.

Blood samples are collected for CBC, fasting and post prandial blood sugars, HbA1c, blood urea, serum creatinine, fasting lipid profile (Serum total cholesterol, serum Triglycerides, Serum high density Lipoproteins, Serum low density Lipoproteins), serum Electrolytes, ECG, CT scan of brain/MRI of brain.

RESULTS

In the present study, a total of 100 patients with complete stroke were included and 30 cases as control. Among males, the age group 60-69 was mostly affected by ischaemic stroke, and the patients in the age group 40-49 were largely affected by haemorrhagic stroke. Among females, the age group 60-69 was largely affected by ischemic as well as hemorrhagic stroke, which was two decade later than the males.

Table 1: Sex distribution in study population.

Groups	Male	Female
Control	20	10
Ischaemic	41	22
Haemorrhagic	27	10

Table 2: Age and sex distribution of study population.

Age	Control		Ischa	aemic	Hae	Haemorrhagic	
group	M	F	M	F	M	F	
20-29	2	0	2	0	0	0	
30-39	3	2	3	0	2	0	
40-49	4	2	8	3	8	0	
50-59	5	3	11	6	7	3	
60-69	4	3	12	8	6	6	
70-80	2	0	5	5	4	1	
Total	20	10	41	22	27	10	

Out of 100 cases, 63 cases were of ischaemic stroke, of which 41 were male and 22 were female. 37 cases were of haemorrhagic stroke, of which 27 were male and 10 were female and out of 30 control 20 were male and 10 were female (Table 1). The maximum numbers of patients were in the age group 60-69 (Table 2).

Analyzing the distribution of total cholesterol in study population (Table 3) it was found that, 75.56% of patients having elevated serum cholesterol levels (total cholesterol >240 mg% according to Adult Treatment Panel (ATP) – III guidelines6) fall in ischaemic category whereas 24.44% fall in haemorrhagic stroke category. The differences across the groups on the basis of their total cholesterol level was found to be significant ($\chi 2$ -27.514; p<0.0001).

Analyzing serum triglyceride in study population it is observed that 66.67% of patients among elevated serum triglyceride (serum triglyceride >200 mg% according to ATP – III guidelines) had ischaemic stroke and 29.17%

had haemorrhagic stroke. The differences across the groups on the basis of their total serum triglyceride level

was found to be significant (χ 2 -10.691; p -0.0303). (Table 4).

Table 3: Distribution of total cholesterol in study population and their statistical analysis.

			Total ch	olester	ol		■ Total
			<200		200-240	>240	Total
		Count	19		11	0	30
	Control	% within group	63.33		36.67	0.00	100.00
		% within Total cholesterol	32.76		40.74	0.00	23.08
		Count	20		9	34	63
Group	Ischaemic	% within group	31.75		14.29	53.97	100.00
_		% within Total cholesterol	34.48		33.33	75.56	48.46
		Count	19		7	11	37
	Haemorrhagic	% within group	51.35		18.92	29.73	100.00
		% within Total cholesterol	32.76		25.93	24.44	28.46
		Count	58		27	45	130
Total		% within group	44.62		20.77	34.62	100.00
		% within Total cholesterol	100.00		100.00	100.00	100.00
Chi-Sq	uare test						
		Value		df	Asymp.	Sig. (2-sided)	
Pearson	Chi-Square	27.514		4	< 0.0001		
No. of v	valid cases	130					

Table 4: Distribution of serum triglyceride in study population and their statistical analysis.

			Serum tri	Serum triglyceride					
			<150	150-199	200-499	Total			
		Count	15	14	1	30			
	Control	% within group	50.00	46.67	3.33	100.00			
		% within triglycerides	27.27	27.45	4.17	23.08			
	Group Ischaemic	Count	20	27	16	63			
Group		% within group	31.75	42.86	25.40	100.00			
		% within triglycerides	36.36	52.94	66.67	48.46			
		Count		10	7	37			
	Haemorrhagic	% within group	54.05	27.03	18.92	100.00			
		% within triglycerides	36.36	19.60	29.17	28.46			
		Count	55	51	24	130			
Total		% within group	42.31	39.23	18.46	100.00			
		% within triglycerides	100.00	100.00	100.00	100.00			
Chi-Squa	are test								
		Value		df	Asymp. Sig. (2-	sided)			
Pearson (Chi-Square	10.691		4	0.0303				
No. of va	llid cases	130							

Analyzing serum LDL cholesterol within study population (Table 5) it is found that 76.47% of patients having elevated serum LDL cholesterol (serum LDL cholesterol >160 mg% according to ATP – III guidelines) suffered from ischaemic stroke whereas 20.59% had haemorrhagic stroke. The differences across the groups on the basis of their total serum LDL level was found to be significant ($\chi 2$ -22.878; p -0.0008). Analysis of serum HDL shows, 29 cases have low HDL cholesterol levels (serum HDL Cholesterol levels < 40 mg% according to

ATP III guidelines). 21.62% of haemorrhagic stroke patients had low HDL levels as compared to 17.46% of ischaemic stroke patients indicating greater abnormality levels in haemorrhagic stroke patients. The differences across the groups on the basis of their total serum HDL cholesterol level was found to be insignificant (χ 2 -2.968; p -0.2267). (Table 6).

Analyzing the distribution of VLDL cholesterol in the study population, it was found that, 73 cases had high

VLDL cholesterol levels (serum VLDL Cholesterol levels >30 mg% according to ATP III guidelines). 51.35% of haemorrhagic stroke patients had high VLDL levels as compared to 61.90% of ischaemic stroke

patients and among controls 50.00% had high VLDL levels. The differences across the groups on the basis of their total serum VLDL cholesterol level was found to be insignificant ($\chi 2$ -1.654; p -0.4373) (Table 7).

Table 5: Distribution of serum LDL cholesterol in study population and their statistical analysis.

		LDL Cholesterol						
			<100	100-130	131-160	>160	Total	
		Count	13	12	4	1	30	
	Control	% within group	43.33	40.00	13.33	3.33	100.00	
		% within LDL	31.71	40.00	16.00	2.94	23.08	
		Count	13	10	14	26	63	
Group	Ischaemic	% within group	20.63	15.87	22.22	41.27	100.00	
		% within LDL	31.71	33.33	56.00	76.47	48.46	
	Hemorrhagic	Count	15	8	7	7	37	
		% within group	40.54	21.62	18.92	18.92	100.00	
		% within LDL	36.58	26.67	28.00	20.59	28.46	
		Count	41	30	25	34	130	
Total		% within group	31.54	23.07	19.23	26.15	100.00	
		% within LDL	100.00	100.00	100.00	100.00	100.00	
Chi-Squ	are test							
		Value	df	Asymp.	Sig. (2-sided)			
Pearson	Chi-Square	22.878	6	0.0008				
No. of va	alid cases	130						

Table 6: Distribution of serum HDL cholesterol in study population and their statistical analysis.

			HDL cholest	erol	Total
			<40	≥ 40	Total
		Count	10	20	30
	Control	% within group	33.33	66.67	100.00
		% within HDL	34.48	19.80	23.08
		Count	11	52	63
Group	Ischaemic	% within group	17.46	82.54	100.00
		% within HDL	37.93	51.48	48.46
		Count	8	29	37
	Haemorrhagic	% within group	21.62	78.38	100.00
		% within HDL	27.59	28.71	28.46
		Count	29	101	130
Total		% within group	22.31	77.69	100.00
		% within HDL	100.00	100.00	100.00
Chi-Squar	re test				
		Value	df	Asymp. Sig. ((2-sided)
Pearson Cl	hi-Square	2.968	2 0.2267		
No. of vali	id cases	130			

Lipid profile among female controls and female patients revealed no significant difference except the level of total cholesterol and LDL in patients affected with ischaemic stroke. No significant difference was found among female patient suffering from haemorrhagic stroke and female controls (Table 8).

The comparison of lipid profiles among male controls and male patients suffering from haemorrhagic stroke showed no significant difference. Except for the level of total triglyceride and VLDL in patients affected with ischaemic stroke, significant difference was found while comparing among male patient and male controls (Table 9).

Table 7: Distribution of serum VLDL cholesterol in study population and their statistical analysis.

				VLDL Cho	lesterol	Total
				≤30	>30	Total
		Count		15.00	15.00	30.00
Control	% within group		50.00	50.00	100.00	
	% within VLDL		26.32	20.55	23.08	
	Count		24.00	39.00	63.00	
Group	Group Ischaemic	% within group	% within group			100.00
		% within VLDL		42.10	53.42	48.46
		Count	Count			37.00
	Haemorrhagic	% within group	48.65	51.35	100.00	
		% within VLDL		31.57	26.02	28.46
		Count		57.00	73.00	130.00
Total		% within group		43.84	56.15	100.00
		% within VLDL		100.00	100.00	100.00
Chi-Squar	re test					
		Value	df	Asymp. S	sig. (2-sided)	
Pearson Chi-Square		1.654	2	0.4373		
No. of valid cases		130				

Table 8: Showing comparison of lipid profile between female controls and patients.

Dependent Variable	Cases (K)	Mean value of K	Mean value of control (L)	Mean Difference (K-L)	P-value
Total cholesterol	Ischaemic	229.95	168.10	61.85	0.0064
Total cholesterol	Haemorrhagic	205.40	168.10	37.30	0.2408
samum tui altraani da	Ischaemic	167.55	119.00	48.55	0.1082
serum triglyceride	Haemorrhagic	138.60	119.00	19.60	0.7335
HDL	Ischaemic	46.09	41.11	4.98	0.2302
ПDL	Haemorrhagic	45.11	41.11	4.00	0.2406
I DI	Ischaemic	147.25	104.19	43.06	0.0241
LDL	Haemorrhagic	132.23	104.19	28.04	0.3252
MIDI	Ischaemic	33.73	23.60	10.13	0.1175
VLDL	Haemorrhagic	27.68	23.60	4.08	0.7335

Table 9: Showing comparison of lipid profile between male controls and patients.

Dependent Variable	Cases (K)	Mean value of K	Mean value of control (L)	Mean Difference (K-L)	P-value
Total cholesterol	Ischaemic	235.93	185.50	50.43	0.0014
Total cholesterol	Haemorrhagic	199.04	185.50	13.54	0.659
	Ischaemic	173.00	137.45	35.55	0.1598
serum triglyceride	Haemorrhagic	144.11	137.45	6.66	> 0.9999
HDL	Ischaemic	52.98	44.26	8.72	0.0115
HDL	Haemorrhagic	49.04	44.26	4.79	0.2494
I DI	Ischaemic	146.80	110.12	36.68	0.0075
LDL	Haemorrhagic	120.87	110.12	10.75	0.5467
VI DI	Ischaemic	34.72	27.44	7.28	0.1553
VLDL	Haemorrhagic	28.95	27.44	1.51	> 0.9999

Comparison of serum lipid profile between males and females in control group (Table 10), ischaemic group (Table 11) and haemorrhagic group (Table 12) were studied. In all three groups, the mean levels of serum total

cholesterol, triglycerides, HDL, LDL and VLDL were higher in males than in females. There is a trend of increasing cholesterol, triglycerides, HDL, LDL and VLDL in males than that in females.

Table 10: Showing comparison of lipid profile between males and females in control group.

Dependent variable	Sex	N	Mean	Standard deviation	Std. error of mean	P-value
Total abalastanal	M	20	185.50	37.126	8.302	0.1793
Total cholesterol	F	10	168.10	35.670	11.280	0.1793
Serum triglyceride	M	20	137.45	51.256	11.461	0.4030
	F	10	119.00	51.489	16.282	0.4030
HDL	M	20	43.26	10.619	2.374	0.7747
прь	F	10	41.11	8.717	2.757	0.7747
LDL	M	20	110.12	31.739	7.097	0.7580
LDL	F	10	104.49	30.549	9.660	0.7380
VLDL	M	20	27.44	10.402	2.326	0.4030
	F	10	23.60	10.429	3.298	0.4030

Table 11: Showing comparison of lipid profile between males and females in ischemic stroke group.

Dependent variable	Sex	N	Mean	Standard deviation	Std. error of mean	P-value
Total cholesterol	M	41	235.93	64.940	10.142	0.5352
	F	22	229.95	62.376	13.299	0.3332
Comum tuialreamida	M	41	173.00	73.224	11.436	0.7511
Serum triglyceride	F	22	167.55	72.326	15.420	0.7311
HDL	M	41	52.98	12.864	2.009	0.0252
ПDL	F	22	46.09	10.014	2.135	0.0353
I DI	M	41	146.80	56.229	8.782	0.9244
LDL	F	22	147.25	56.512	12.048	0.8344
VLDL	M	41	34.72	14.583	2.278	0.7401
	F	22	33.73	14.363	3.062	0.7401

Table 12: Showing comparison of lipid profile between males and females in haemorrhagic stroke group.

Dependent Variable	Sex	N	Mean	Standard deviation	Std. error of mean	P-value
Total cholesterol	M	27	199.04	63.958	12.309	0.9727
Total cholesterol	F	10	205.40	76.715	24.259	0.9727
comm trialyzarida	M	27	145.11	74.733	14.382	0.7975
serum triglyceride	F	10	138.60	72.554	22.944	0.1913
HDL	M	27	49.04	13.621	2.621	0.6565
HDL	F	10	45.11	8.596	2.718	0.0303
LDL	M	27	120.87	46.448	8.939	0.7194
LDL	F	10	132.23	65.123	20.594	0.7194
VLDL	M	27	28.95	15.005	2.888	0.7843
	F	10	27.73	14.481	4.579	0.7643

The mean levels of serum total cholesterol, triglycerides, HDL, LDL and VLDL were higher in male controls as compared to female controls, but was not statistically significant (Table 10).

Comparing the lipid profile in males and females in ischaemic stroke group, it was observed that, the mean levels of serum total cholesterol, triglycerides, HDL, and VLDL were higher in males as compared to females.

The mean of level of LDL in female was found to be higher compared to males. None of the parameters of

lipid profile shows statistical significance except for serum HDL, which was found to be higher in males as compared to females. (Table 11).

Comparing the lipid profile in males and females in haemorrhagic stroke group it was observed that, the mean levels of serum triglycerides, HDL, and VLDL were higher in males as compared to females. The mean of level of LDL and total cholesterol in female was found to be higher as compared to males.

All the differences among males and females have not reached to a level of statistical significance (Table-12).

DISCUSSION

Stroke is a common clinical problem. Current treatment for patients with established stroke is relatively ineffective. Approximately 50% of patients are left with permanent disability. Effective risk factor interventions offer a real hope of reducing stroke morbidity and mortality. Certain risk factors have been consistently identified as significant predictor of stroke outcome, while some are less consistent.

Diabetes Mellitus, because of its common association with dyslipidemia is a common cause of stroke.⁷ However, little is known regarding the clinical pattern, outcome and predictors of early mortality after stroke in patients without diabetes. Dyslipidemia is also one of the major risk factor noted in patients of stroke without diabetes.⁸ In our study thirty controls were normal individuals.

The present study consisted of 100 patients who were admitted to VIMSAR, Burla of which 63 patients were ischemic stroke, 37 patients were of haemorrhagic stroke and 30 individuals were age and sex matched controls.

The relationship between serum cholesterol levels and the risk of stroke is not clear. A U-shaped relation between the level of serum total cholesterol and the risk of stroke of all types has been proposed, derived from an inverse association with haemorrhagic stroke and a direct association with ischaemic stroke. Possible differences in the effects of cholesterol at different vascular sites could lead to the complex association between serum cholesterol levels and stroke. The origin of the Internal Carotid Artery is probably the most common site of atherosclerosis that leads to Transient Ischemic Attack (TIA) or stroke. Or stroke.

The patients in our study group were aged between 25 to 80 years. Amongst the males, the age group of 60-69 were most commonly affected by ischaemic stroke whereas age group of 40-49 were most commonly affected by haemorrhagic stroke. In females, the age group 60-69 was largely affected by ischaemic as well as haemorrhagic stroke. In a study by Khan and Rehman. out of 100 patients 71 were males and rest females.¹¹ Fifty nine of these patients were above 60 years and 25 between 40-50 years. In another study of 80 patients by Sreedhar K, Srikant B, Joshi L, Usha G,² 56 were males and rest were females and Males in the age group 50-59 were most commonly affected by ischaemic stroke, whereas male patients in the age group 40-49 were most commonly affected by haemorrhagic stroke. In females the age group remains the same as in our study i.e. 60-69 for both ischaemic and haemorrhagic stroke. The incidence of stroke in females was two decades later than in males in our study but in the study by Sreedhar K, Srikant B, Joshi L, Usha G, it was one decade later.² This could be due to selection bias at a tertiary care centre and hence further epidemiological studies will be needed to prove this hypothesis. This finding was similar to study by Roquer *et al.*¹² where they found that the mean age of affected patients was higher in women.

The serum total cholesterol levels in 45 patients having either ischaemic or haemorrhagic stroke were high (Total cholesterol >240 mg% according to the Adult Treatment Panel (ATP) – III guidelines of National Cholesterol Education Program (NCEP)). Among the individuals in control group, not a single person had high serum cholesterol. Applying the Chi-square test, it is conclude that the study group is largely affected by abnormal serum total cholesterol levels than that of control group. Benfante et al and Di Mascio et al have found a positive association between serum cholesterol and risk of stroke. 13,14 Iso et al found an inverse relation between cholesterol level and haemorrhagic stroke but a positive association with non haemorrhagic stroke. 15 There was no correlation between serum cholesterol and risk of stroke in a study by Harmsen et al Rastenyte et al and Hart CL et al. 16-18 found that serum cholesterol levels are not related to risk of death from stroke. The Atherosclerosis Risk in Communities (ARIC) study has concluded that the relation of circulating cholesterol to ischaemic stroke does not resemble its well known relation to coronary artery disease.19

Among patients having ischaemic and haemorrhagic stroke, serum triglycerides were high in 24 patients (>200 mg% according to ATP – III guidelines), which is significant as p value is < 0.05 by Chi-square test. So, our study finds out a positive relation between triglyceride levels and risk of stroke as compared to control group. Hachinski *et al.* observed a positive correlation of serum triglyceride levels with patients suffering from atherothrombotic strokes and Transient Ischemic attacks (TIA) as compared to control subjects.²⁰ But this type of correlation was not found in the study conducted by Sridharan R et al.²¹

Male patients in the age group of 50-59 yrs and female patients in the age group of 60-69 yrs of age suffering from ischaemic stroke had raised levels of serum LDL cholesterol (>160mg% according to ATP - III guidelines). Among haemorrhagic stroke patients, serum LDL cholesterol levels were high in the age group of 40-49 yrs and 50-59 yrs in males and 60-69 yrs among females. Among individuals in control group only a single person had high serum LDL cholesterol levels. Applying the Chi square test the value obtained was statistically significant (p < 0.05). Hence, we conclude that the study group was largely affected by abnormal LDL levels than that of control group. Botet et al and Hachinski et al in their studies have found positive correlation between LDL Cholesterol levels and risk of ischaemic stroke.^{20,22}

Male patients in the age group of 50-59 yrs and female patients in the age group of 50-59 and 60-69 yrs suffering from ischaemic stroke had low serum HDL cholesterol

levels (<40mg% according to ATP - III guidelines). Among haemorrhagic stroke patients serum HDL cholesterol was low in the age group of 40-49 and 50-59 yrs in males. In our study of HDL cholesterol in stroke patients, we found that the haemorrhagic group patients had greater abnormal levels than ischemic group patients which was greater than the control group. On statistical analysis, the Chi-Square value of 2.968 was greater than the significant value of 0.2267, but the p value > 0.05, which is insignificant and thus we conclude that the experimental group is not largely affected by abnormal HDL levels. Simons et al in their study observed that increase in HDL cholesterol is protective in ischemic stroke.²³ The Northern Manhattan Stroke Study group concluded that increased HDL - C levels is associated with reduced risk of ischaemic stroke.²⁴

In patients of ischaemic stroke, serum VLDL levels was high (>30 mg% according to ATP – III guidelines) among males and females in 50-59 yrs age group. Among patients of haemorrhagic stroke, the serum VLDL levels were high in age group of 40-49 in males and 60-69 in females. The study group had higher levels of serum VLDL cholesterol than control group but was not found to be statistically significant (p>0.05).

CONCLUSION

Our study concluded a positive correlation between serum total cholesterol, triglyceride, LDL level and risk of stroke. But it could not establish correlation between serum HDL, VLDL level with the risk of stroke. Dyslipidemia is one of the major risk factors in non diabetic stroke patients. Thus early detection of dyslipidemia and treatment with drugs along with dietary modifications & lifestyle changes can reduce the risk of stroke.

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