Original article

A study on the distribution of the study population with or without cerebral infarct in relation to the lipid profile parameters

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ABSTRACT

BACKGROUND: Carotid atherosclerosis is a reasonable risk factor for cerebral ischemic stroke. Deranged lipid metabolism due to various modifiable and non-modifiable risk factors leads to the pathogenesis of atherosclerosis.

METHODS: This observational study was done with the aim of finding the distribution of the study population with or without infarction and their correlation with lipid profile. After Ethical clearance 50 elderly (age group 50-70) ischemic stroke patients clinically diagnosed as per WHO definition76 and CT Scan (Computed Tomography) suggestive of cerebral infarction were randomly selected from the Department of Medicine. Age sex matched 50 apparently healthy individuals were taken as "control group".

RESULTS: The distribution of the study population (with / without infarct) according to the cut off values of Cholesterol, LDL : HDL & Triglyceride. In one group where lipid profile was altered 72% subjects having cholesterol above the cut off value had infarction whereas 90.24% subjects having abnormal LDL: HDL & 90.48% subjects having abnormal triglyceride had infarction. 82% , 86.44% & 87.9% of the subjects having normal (below cut off value) cholesterol, LDL:HDL and triglyceride respectively did not have any infarction.

CONCLUSION: It was evident from the above study that subjects having altered lipid profile (Cholesterol, LDL:HDL and Triglyceride) more than cut off values are more prone to cerebral infarction. There is a highly significant difference($p<0.0001$) between the two groups with and without infarct with alteration of lipid profile.

KEYWORDS: Carotid atherosclerosis, Cerebral infarction, Lipid profile

BACKGROUND:

WHO in 1978, coined the term stroke for those cases where certain neurological deficit of local & general distribution develops due to disturbances of cerebral function lasting for more than 24 hr or leads to death with no apparent cause other than the vascular one. Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed. It accounts for about 87 percent of all strokes. The relationship between lipids and stroke is complex. Carotid atherosclerosis is a reasonable risk factor for cerebral ischemic stroke. Deranged lipid metabolism due to various modifiable and non-modifiable risk factors leads to the pathogenesis of atherosclerosis. Gradual deposition of lipoproteins in the carotid arteries leads to increased carotid artery Intima Media Thickness (IMT) and gradually plaque formation occurs. Rupture and dislodgement of a plaque leads to embolism and subsequent ischemic stroke.

While there is an overwhelming amount of evidence relating high levels of serum total and LDL cholesterol and low levels of HDL cholesterol with coronary atherosclerosis, the relation between serum lipids, lipoproteins and cerebrovascular atherosclerosis is less clear. Studies of cholesterol levels in stroke patients have revealed results varying

from insignificant changes to a moderate elevation. The merger reports available in Indian patients who have different social, living and dietary habits compared to western population, prompted us to undertake this study.

MATERIALS AND METHODS:

An observational, case cross-sectional type of study1 was conducted in the Department of Physiology in collaboration with Department of Medicine, Radiology and Biochemistry at R.G.Kar Medical College,Kolkata- 700004. After Ethical clearance selection of cases and controls were done by simple random sampling. Study population included 50 stroke patients diagnosed as per WHO definition2 and CT Scan (Computed Tomography) suggestive of cerebral infarction. Age sex matched 50 apparently healthy individuals were taken as "control group".

Subject exclusion criteria:

1. Severely ill subjects.
2. Patients with cerebral hemorrhage.
3. TIA without any CT Scan features of ischemic stroke.
4. Intracranial neoplasm.
5. Patients suffering from meningitis, neurocysticercosis or any infections.
6. Intracranial aneurysms.
7. AV malformations.
8. Any cardiac source of embolism.
9. H/O intake of any lipid lowering drugs.
10. H/O Smoking.
11. Coronary Heart disease

Subject inclusion criteria :

1. Diagnosed stroke patients as per WHO definition2 as "Rapidly developing clinical signs of focal or global neurological deficits lasting for 24 hours or longer or resulting in death with no apparent cause other than vascular origin".

2. Patients admitted with cerebrovascular accident confirmed to be ischemic in nature on CT scan.

3. Subjects with first attack of stroke were chosen.

The interest of this study was conducted on elderly age group3 and was aimed at 50-70 yrs age group of subjects. The controls were apparently healthy and age and sex matched with cases.

Study parameters: History and Physical Examination with examination of the Nervous System in details. Plain CT Scan of the Brain of the cases were taken. Biochemical Tests: (1) Lipid Profile (after 12 hrs overnight fasting) for Cholesterol (CHOD/PAP Method), Triglycerides by (GPO/PAP Method) LDL:HDL ratio. (HDL by PEG Precipitation method and LDL by Friedewald's formula (Total Cholesterol)- (Triglycrides/5) -(HDL Cholesterol). Carotid Doppler Study was performed only with appropriate high frequency transducers with patient in supine position. The ROC curve (Receiver Operating Characteristic curve) was used to find out the cut off value of Cholesterol, LDL:HDL, Triglyceride with greatest sensitivity and specificity(lowest 1- specificity) of the population under study(cases and controls).After applying the cut off value we had categorized the study population into two Groups- GroupI & Group II,

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Plan of statistical analysis:

Data were compiled in MS excel worksheet (Office document 2007) and analysis done in SPSS VERSION 17 statistical software (for windows). Results were statistically analyzed using following statistical tests : Chi-square test. Independent Sample "T-test".Multiple Regression Analysis.

Mean and Standard deviation were calculated from the results of individual parameter. P value of <0.05 was considered to be significant and P<0.001 as highly significant. The results were calculated within 95% confidence limits.

RESULTS

Basic characteristics of subjects.

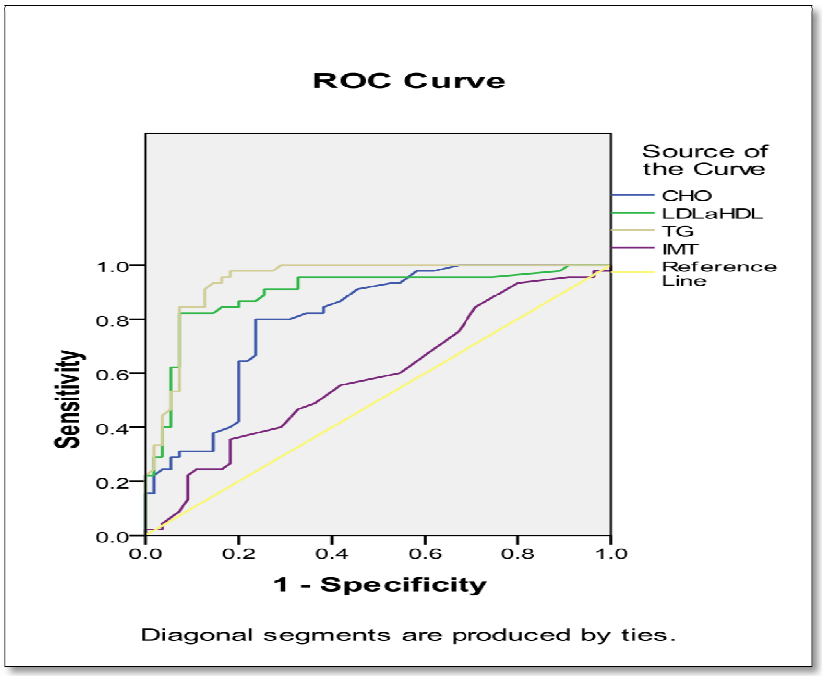
Basic characteristics of case (N=50)(Mean±SD) are , age (yrs) 61.72±6.93 systolic BP (mm of Hg) 154.60±16.13 ,diastolic BP (mmof Hg) 97.72±16.07 fasting Blood Sugar (mg/dl)117.92±33.85 >0.05

and post Prandial Blood Sugar (mg/dl) 134.24±60.62.

The ROC curve was used to find out the cut off value of Cholesterol, LDL: HDL, Triglyceride & Avg. IMT with greatest sensitivity and specificity (lowest 1-specificity) of the studied population (cases and controls).

CUT OFF VALUES OF DIFFERENT PARAMETERS IN THE STUDY POPULATION:

Diagram:1



Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
Cholesterol	133.0000	.800	.273
	135.0000	.800	.255
	136.5000	.800	.236
	138.5000	.778	.236
	141.0000	.733	.236

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
LDL: HDL	1.9600	.822	.145
	1.9750	.822	.127
	1.9900	.822	.073
	2.0600	.756	.073
	2.1500	.733	.073

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
Triglyceride	137.0000	.844	.109
	139.0000	.844	.091
	144.5000	.844	.073
	149.5000	.822	.073
	154.0000	.756	.073

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
Avg. IMT	.0875	.467	.327
	.0925	.400	.291
	.0975	.356	.182
	.1025	.267	.182
	.1100	.244	.164

TABLE 2:

AREA UNDER THE CURVE (AUC)

Test Result Variable(s)	Area	Std. Error
Cholesterol	0.801	0.044
LDL:HDL	0.896	0.035
Triglyceride	0.941	0.024

CUT OFF VALUES OF DIFFERENT PARAMETERS IN THE STUDY POPULATION:

TABLE 3:

After applying the cut off value we categorized the study population into two groups, above and below the cut off value. Two sub groups of each- with or without infarction are again created in the following table and the significance of their association is calculated by the Chi-Square test.

Parameters	Cut Off Value
Cholesterol(mg/dl)	136.5
LDL:HDL	1.99
Triglyceride (mg/dl)	144.5

DISTRIBUTION OF THE STUDY POPULATION (WITH / WITHOUT INFARCT) ACCORDING TO THE CUT OFF VALUES OF CHOLESTEROL, LDL : HDL & TRIGLYCERIDE :

TABLE :4

Parameters (Cut-off values)	**GROUP IA (Below cut off values)**			**GROUP IB (Above cut off values)**			χ^2	**Significance**
	Total (n)	With Infarct	Without Infarct	Total (n)	With Infarct	Without Infarct	Degree of freedom = 1	
Cholesterol (136 mg/dl)	50	18% (n=9)	82% (n=41)	50	72% (n=36)	28% (n=14)	27.313	p< 0.0001
LDL : HDL (1.99)	59	13.56% (n=8)	86.44% (n=51)	41	90.24% (n=37)	9.76% (n=4)	54.412	p< 0.0001
Triglyceride (144mg/dl)	58	12.1% (n=7)	87.9% (n=51)	42	90.48% (n= 38)	9.52% (n=4)	57.336	p< 0.0001

DISCUSSION:

It is seen that more number of subjects in the study population shows LDL: HDL and triglyceride below the cut off value, where as equal number subjects shows cholesterol above and below the cut off value. More number of subjects in Gr IB (where lipid profile are altered) have got infarct. Among them 72% subjects having cholesterol above the cut off value has got infarct. Whereas 90.24% subjects having abnormal LDL: HDL & 90.48% subjects having abnormal

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triglyceride have got infarct. More number of subjects having normal lipid profile in GROUP IA (below cutoff value) do not have any infarct. Among them 82% ,86.44% & 87.9% subjects having normal (below cut off value) cholesterol, LDL:HDL, triglyceride respectively do not have any infarct.

Previous study showed that Benfante R et al4 and Di Mascio R et al5 have found a positive association between serum cholesterol and risk of stroke. Iso et al 6 found an inverse relation between cholesterol level and hemorrhagic stroke but a positive association with non hemorrhagic stroke. This Multiple Risk Factor Intervention Trial also demonstrated increased mortality among men with high cholesterol levels. The adjusted risk ratio was 1.8 for those with serum cholesterol 240 to 279 mg/dL and 2.6 for those with cholesterol levels ≥280 mg/dL. Harmsen P et al7 found no correlation between serum cholesterol and risk of stroke. Rastenyte D et al8, and Hart CL et al9 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 ischemic stroke does not resemble its well known relation to coronary heart disease.10 Botet PJ et al11 and Hachinski V et al12 in their studies have found positive correlation between LDL Cholesterol levels and risk of ischemic stroke. An inverse relationship between HDL and stroke risk was demonstrated in both the Oxfordshire Community Study and the Northern Manhattan Stroke Study,13,14,15 .

CONCLUSION

From the above study it can be concluded that altered lipid profile is associated with cerebral ischemia and the risk of cerebral infarction by atheromatous plaque formation which may lead to lifelong disability or death.Timely medical intervention with lipid lowering drugs like statins may be life saving here.

Limitations of the study

- Sample size is small.
- Study period was only one year.
- Follow up was not possible.

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