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ASSOCIATION OF HIGH PLASMA HOMOCYSTINE AND TOTAL SERUMCHOLESTEROL LEVELS WITH ACUTE ISCHEMIC STROKE

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Abstract

Background: *Stroke or cerebrovascular accidents ranks first in frequency and emergency among all neurological disorders. Incidence of stroke is coming down in western countries while it is showing an alarming rise in India. Raised homocysteine and serum cholesterol is associated with atherosclerotic vascular events.* ***Aims and Objective:*** *Present study was carried out to find association between high plasma homocystine and total serum cholesterol levels with acute ischemic stroke.* ***Materials and Methods:*** *Study included 30 diagnosed cases of acute ischemic stroke (20 Male and 10 Females) and 30 controls (20 Male and 10 Females) of same age and sex. Blood sample of cases and controls was collected for plasma homocystine and total serum cholesterol levels from venous blood to study the association.* ***Statistical analysis:*** *Data analysis was done using Chi-square test. The outcome of analysis was presented as Chisquare score, df and p value to find out association. The 'p' value of less than 0.05 (*p<0.05) was considered as significant.* ***Results:*** *There was significantly higher level of plasma homocysteine and total serum cholesterol in studied stroke patients than controls.* ***Conclusion:*** *There is significant association between plasma homocysteine and total serum cholesterol and acute ischemic stroke. Hence higher levels of plasma homocysteine and total serum cholesterol may be the risk factor for acute ischemic stroke. Further studies on large population are needed to find whether increased level of these parameters can be used as screening test for ischemic stroke.*

Keywords: *Homocystine, Serum cholesterol, Acute ischemic stroke, Risk factor, Screening test*

INTRODUCTION

Every major hospital in our country has at least few cases of stroke every day. India like other developing countries is in the midst of a stroke epidemic.[1] Incidence of stroke is showing an alarming rise in India compared to western countries. Homocysteine (Hcy) is an amino acid which is formed by demethylation of methionine, an essential amino acid derived from diet. Normal level of plasma homocystineis 15-30 micromole/L. Hyperhomocystenemia has received increased attention due to its role in cerebrovascular and cardiovascular disease. Homocysteine, the sum of homocysteine, homocysteine-cystine mixed sulfide, free and protein bound had been shown to be associated with vascular disease including stroke and peripheral vascular diseases. [2]

Increase in total cholesterol is associated with the atherosclerotic plaque formation leading to emboli formation and ischemic stroke. Serum total cholesterol has been attributed as a risk factor for acute ischemic stroke.[3] One of the studies has shown increased risk of ischemic stroke with a total cholesterol levels 7 mmol/L or greater (≥ 271 mg/dL). [4] Hence it seems that there is a relationship between ischemic stroke and level of plasma homocysteine and total cholesterol.

The objective of this study was to find association of plasma homocysteine and total serum cholesterol levels with acute cerebral ischemic stroke. To find association we compared these levels in diagnosed patients of acute cerebral ischemia and normal subjects of same age and sex. Findings may be useful in assessing plasma homocysteine and total serum cholesterol levels as one of the risk factor for acute ischemic stroke.

MATERIALS AND METHODS

The study was conducted in one of the major general hospital of Mumbai. Study was approved by the institutional ethical committee and written informed consent of participants/attendant of patient was taken. Our study was case-control study consisting 30 diagnosed cases of acute ischemic stroke (20 Male and 10 Females) and 30 controls (20 Male and 10 Females) of same age. Patients admitted in the medicine ward with acute cerebrovascular accident (onset of focal neurological deficit including motor deficits, aphasia – sensory or motor, cranial nerve involvement, cerebellar involvement with or without altered sensorium) within 48 hours of appearance of symptoms and showing cerebral infract

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on CT scan were included as cases in the study. Detail history taking along with the general and systemic examination of each participant was done so as to select them as control.
Blood sample of cases and controls was collected for plasma homocystine and total serum cholesterol levels from venous blood. Plasma was separated within 30 minutes and stored at 20°C. Fluorescence polarization immunoassay (FPIA) was used for plasma homocystine estimation. Total serum cholesterol was estimated using enzymatic method (CE-CO-CAP enzymatic end point).

STATISTICAL ANALYSIS

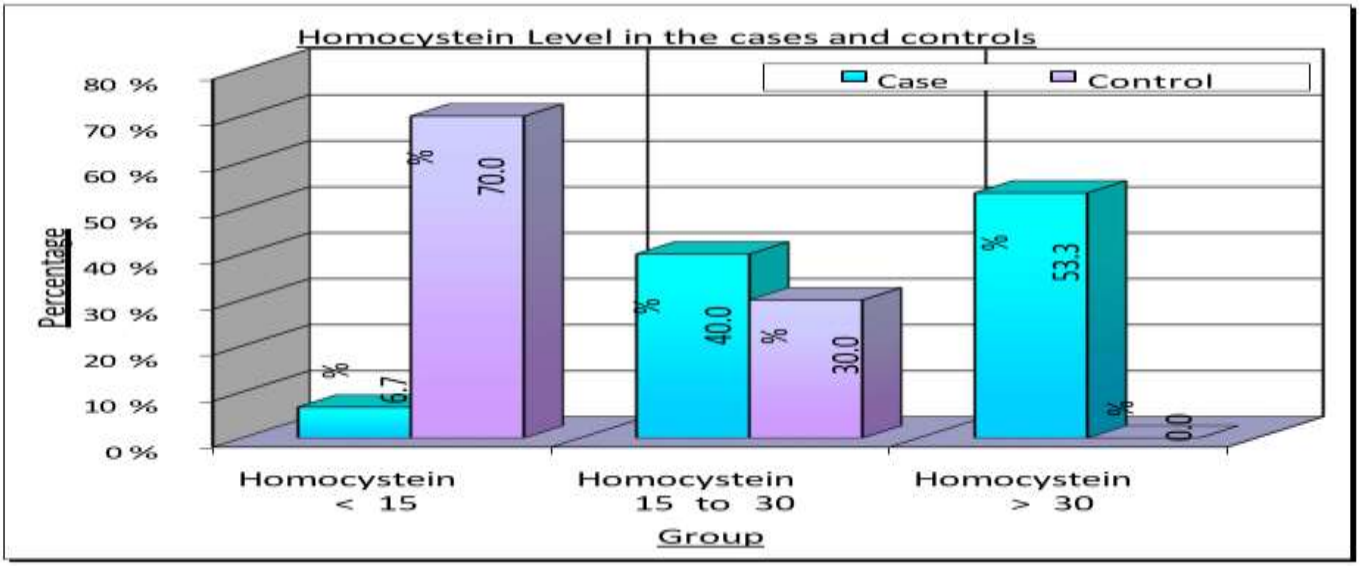
Data analysis of plasma homocystine and total serum cholesterol levels of case and control groupwas done by using SPSS version 16.0 (SPSS Inc, Chicago, USA) software. Chi-square test was applied to find out association of observed values making three groups for plasma homocysteine levels (< 15, 15-30 and > 30 micromole/L) and two groups for total serum cholesterol levels (< = 200 and > 200 mg/dL). The outcome of analysis was presented as Chisquare score, df and p value to find out association. The 'p' value of less than 0.05 (*p<0.05) was considered as significant.

RESULTS

Table No 1 and graph no 1 shows the statistical analysis of plasma homocysteine levels in the cases and controls.

Homocysteine (micromole/L)		Group		Total
		Case	Control	
< 15	No.	2	21	23
	%	6.7%	70.0%	38.3%
15 to 30	No.	12	9	21
	%	40.0%	30.0%	35.0%
> 30	No.	16	0	16
	%	53.3%	0.0%	26.7%
Total	No.	30	30	60
	%	100.0%	100.0%	100.0%
Chi-square Tests	Value	df	p-value	Association is-
Pearson Chi-Square	32.124	2	< .00001	Significant

Table 1: Statistical analysis of plasma homocysteine levels in the cases and controls
Plasma homocysteine levels in 2 cases (6.7 %) was less than 15 micromoles/L; where as in 12(40 %) had plasmahomocysteine between 15-30 micromole/L, while 16 cases (53.3%) had a plasmahomocysteine more than 30 micromole/L. There was a significantly higher level of homocysteine in stroke patients.



Graph 1: Plasma homocysteine level in cases and controls

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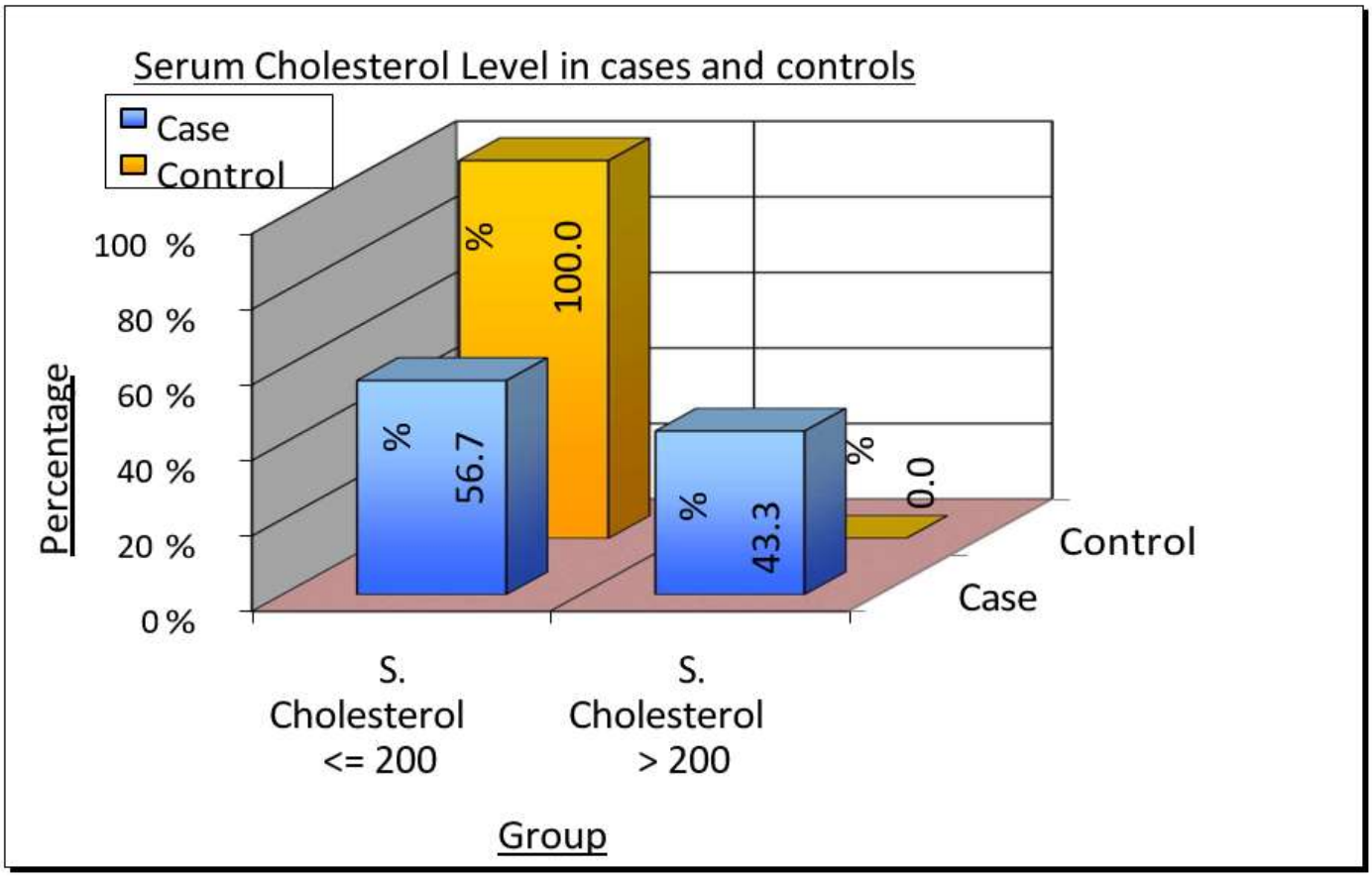
Table No 2 and graph no. 2 shows the statistical analysis of serum total cholesterol levels in the cases and controls

S. Cholesterol		Group		Total
		Case	Control	
<= 200	No.	17	30	47
	%	56.7%	100.0%	78.3%
> 200	No.	13	0	13
	%	43.3%	0.0%	21.7%
Total	No.	30	30	60
	%	100.0%	100.0%	100.0%
Chi-square Tests	Value	df	p-value	Association is-
Pearson Chi-Square	16.596	1	0.000046	Significant
Continuity Correction	14.141	1	0.00017	Significant

Table 2: Statistical analysis of serum total cholestrol levels in cases and controls

Total serum cholesterol levels in 13 cases (43.3 %) was more than 200 mg/dl while 17 cases (56.7%) had serum cholesterol less than 200mg/dl. All the controls had serum cholesterol less than 200 mg/dl. Total serum cholesterol was significantly higher in acute ischemic stroke patients as compared to control



Graph 2: Total serum cholesterol levels in cases and controls

DISCUSSION

Present study was undertaken to evaluate association between plasma homocysteine and total serum cholesterol levels with acute ischemic stroke. In present study level of plasma homocystine was significantly higher in patients of acute ischemic stroke. This finding of our study was consistent with the studies done by Boyson G et al. and Dattaet al. who found raisedhomcystine level in patients with acute ischemic stroke. [5, 6] In a study Zongte Z et al. observed that total homocystine level was significantly higher in patients with stroke (cerebral infarction) [7] and similar result was noted by

Wayne h Gills et al. in both black and white population. [8] However a meta-analysis of observational studies by the Homocystine Studies Collaboration indicated that homocystine levels were less strongly related to stroke risk in healthy populations than that suggested. [9] The role of homocystine in stroke is attributed to it being prothrombotic [10], also hyperhomocysteinemia promotes atherosclerosis and which is commonly caused by B-vitamin deficiencies, especially folic acid, B_6, and B_{12}; genetic disorders; certain drugs; and renal impairment. Atherosclerosis is promoted by increased homocystine through increased oxidant stress, impaired endothelial function, and induction of thrombosis. [11] Association of nutrition related low plasma folate, vitamin B12 with hyperhomocysteinemia (proxy measure for status of vitamin B) was reported in many developing countries. It is also suggested that supplementation with nutrient cofactors is required for optimal functioning of homocysteine metabolic pathways and could be one of the possible way of stroke prevention in these countries. [12]

In present study total serum cholesterol levels in 13 cases (43.3 %) were more than 200 mg/dl while 17 cases (56.7%) had serum cholesterol less than 200mg/dl. All the controls had serum cholesterol less than 200 mg/dl. The finding of our study was consistent with study by Lappela

MJ who studied total cholesterol as risk factor in different subtypes of stroke [4] and also with Togha M from Iran [13]. Analysis of Eurostroke data showed no significant association between total cholesterol and risk of total stroke (ischemic and hemorrhagic) but they attributed it to positive association between increased cholesterol and cerebral infarction being counterbalanced by the inverse association between low cholesterol and cerebral haemorrhage.[14] In a prospective study low total cholesterol level (160 mg/dL) was associated with higher total ischemic stroke mortality after adjustment for clinical risk factors in a Japanese general population cohort. [15] Our study also showed the significant association between total serum cholesterol and acute ischemic stroke so total serum cholesterol is a risk factor for acute ischemic stroke

The limitation of the present study was in its design. This was a small group study carried out in the single institute. Though our study was not vast; it does points towards significant association of hyperhomocysteinemia and high total serum cholesterol with acute ischemic stroke. Larger sample study considering multiple risk factors will definitely be of a great value in predicting the association so that importance of studied parameters can be rule out for screening of the acute ischemic stroke.

CONCLUSION

Present study is based on premise that there is association between high levels of plasma homocysteine and total serum cholesterol levels. Based on results of this study, there is significant association between high levels of studied parameters and acute ischemic stroke. Probable cause for this association is difficult to explain as it has multiple components but there is possible role of increased atherosclerosis due to hyperhomocysteinemia and high total serum cholesterol levels. Our study also suggests that decreasing homocystine and total serum cholesterol levels can be helpful in decreasing the incidence of acute ischemic stroke. Further studies on large population are needed to find whether increased level of these parameters can be used as screening test for ischemic stroke.

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CONFLICTS OF INTEREST: none

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