OBJECTIVES: To determine the relationship of total cholesterol, HDL-C and their ratio among ischemic and hemorrhagic stroke

STUDY DESIGN: An observational prospective comparative study.

PLACE AND DURATION: This research work was carried out from 1st June 2014 to 31st December 2014 at department of medicine Bahawal Victoria Hospital Bahawalpur.

METHODOLOGY: Hundred patients between 30 to 90 years of age, who were admitted by the department of general medicine BVH Bahawalpur with first ever stroke and verified by CT scan brain, were included in the study. Patients who had history of coronary heart disease or lipid lowering drugs, neurological deficits secondary to epilepsy, infective or metastatic disorder, or pre-existing severe cognitive disorder were excluded from this study.

A detailed history and physical examination details along with fasting lipid profile were collected from patient records in the hospital medical department. Mean values of quantitative data were presented as mean SD (standard deviation). Frequency percentage of total cholesterol, high density lipoproteins and triglycerides in both groups of ischemic and hemorrhagic stroke, were determined and compared using proportion test for any significant difference taking p-value of < 0.05 as significant.

RESULTS: Quantitative data of CVA, comprising (50 each of ischemic and hemorrhagic cases) was analyzed. Mean age of presentation was 56 years. In 50 ischemic patients mean total cholesterol was raised above normal reference range. It was 218.30±79mg/dl in ischemic stroke while it was 194±26.7mg/dl in hemorrhagic cases and it was highly significant at P value of < 0.001. The mean HDL concentration was 33.10 -7.33 in patients of ischemic stroke while it was 39.02-4.22 in hemorrhagic cases with p value of o.002 (highly significant). Serum triglycerides levels turned out to be normal in both groups.

CONCLUSION: Hypercholesterolemia and low HDLC was seen significantly in ischemic CVA group as compared to hemorrhagic counterpart.

KEY WORDS: Ischemic stroke, Hemorrhagic stroke, Serum lipid profile.

INTRODUCTION

Most recent international survey has estimated about 15 million people worldwide suffer from nonfatal stroke annually and 33% being permanently disabled.1 Cerebrovascular accident is global health problem. About 80% of all stroke deaths are registered in lower and middle income countries2. An estimated annual incidence of stroke in Pakistan is 250/100,000 which is projected to an estimate of 350,000 new cases every year3. There are limited population-based data regarding the prevalence of established stroke risk factors in Pakistan. The modifiable risk factors of stroke are similar to western population and comprise of hypertension, cardiac disease, diabetes mellitus and dyslipidemia. It is apparent from evidence based data that stroke can be substantially reduced by primary and secondary preventive measure.4 Risk factors of CVA have been studied locally. One of potential risk factor that has gained unique importance in our population is dyslipidemia that leads to cerebral atherosclerosis and it is basic underlying mechanism in ischemic CVA. Meta analysis of some studies show that higher the level of total cholesterol (TC), greater in the risk of CVA and higher the high density lipoprotein cholesterol (HDL-C), lower the risk and each being an independent risk factor5,6. 1mmol/l lowering of TC was associated to 13% reduction of ischemic CVA. Likewise TC to HDL ratio is better predictor of ischemic CVA and it is considered as useful clinical tool7,8. On the other hand some other case control studies have generally failed to show such relationship and have conflicting results. The contribution of various risk factors for stroke may be different in different ethnicities. Previous no data exists in South Punjab to compare the components of lipid profile in subtypes of stroke. It is a neglected iceberg. This recent study didn’t focus to the risk factors but it seeks to assess the levels of total cholesterol and HDL-C in patients with ischemic and hemorrhagic CVA and to assess if these levels confirms or differ with cut off values already known internationally (by NCEP and ADA). Objective of this study was to explore the comparative values of total cholesterol and HDL-C between ischemic and hemorrhagic stroke.

METHODOLOGY

This comparative observational prospective study was carried out from 1st June 2014 to 31st December 2014 at department of medicine Bahawal Victoria Hospital Bahawalpur. One hundred
new onset cases of stroke (comprising equal number of ischemic and hemorrhagic CVA) between ages from 30 to 80 years were selected for the study.

History and clinical examination was recorded on each performa after having a formal consent. CVA was defined according to World Health Organization criteria as syndrome of rapidly developing clinical signs of local or global neurological dysfunction with symptoms lasting more than 24 hours and with no apparent origin other than vascular. Clinical diagnosis was established with CT brain without contrast to stratify patient into each subtype. CT brain was done right twelve hours after onset of stroke. Past medical history for smoking, hypertension, diabetes mellitus and CHD was sought and patients on lipid lowering were excluded from study.

Serum sample was obtained after overnight fast for lipid profile by enzymatic colorimetric methods. The data was analyzed using SPSS version11. Different frequencies were calculated and presented in tabulated form. Mean values of quantitative data were presented as mean SD (standard deviation). Frequency percentage of abnormal lipids in both groups of patients of ischemic and hemorrhagic stroke, were determined and compared using proportion test for any significant difference taking p-value of < 0.05 as significant. To assess the normal or abnormal values of lipids, current National Cholesterol Education Program ATP III guidelines were used to define the cut off values of lipids as according to their recommendations total cholesterol should be < 200mg/dl, HDL-C > 35mg/dl, and TG > 200mg .

RESULTS

Quantitative data of CVA, comprising (50 each of ischemic and hemorrhagic cases) was analyzed. Comparison of demographic data of subjects is shown in Table - I. Both genders were equally divided and most of the males presented in ischemic group. Mean age of presentation was 56.48±5.424. 70% of males and 30% of females presented in ischemic stroke. Table - II shows comparative values of lipoproteins in both subtypes of stroke. In 50 ischemic patients, mean total cholesterol was raised above normal reference range. It was 218.30±79mg/dl in ischemic group while it was 194±26.7mg/dl in hemorrhagic cases and it was highly significant at p value of < 0.001. The mean HDL concentration was 33.10 - 7.33mg/dl in patients of ischemic group and was in high risk category while it was 39.02 - 4.22mg/dl in hemorrhagic cases with p value of 0.002, highly significant. Considering the above mention results the total cholesterol to HDL ratio was 6.6 (normal should be < 5) in ischemic group. The mean triglycerides concentration was 150 ± 48.39mg/dl and 159 ± 26.07mg/dl respectively in both groups with p value of .001.

TABLE - I: DEMOGRAPHIC DATA OF THE SUBJECTS (n=100)

<table>
<thead>
<tr>
<th>Groups</th>
<th>N=100</th>
<th>Mean±SD (years)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic</td>
<td>50</td>
<td>56.44±6.39</td>
<td>35(70%)</td>
<td>15(30%)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>50</td>
<td>56.52±4.31</td>
<td>27(54%)</td>
<td>23(46%)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>56.48±5.424</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

TABLE-II: COMPARATIVE VALUES OF LIPID PROFILE AMONG ISCHEMIC AND HEMORRHAGE STROKE

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Stroke Subtype</th>
<th>Mean Values ± SD (mg/dl)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (normal &lt; 200mg/dl)</td>
<td>Ischemic</td>
<td>218.30±79</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic</td>
<td>194±26.7</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (normal &lt; 150mg/dl)</td>
<td>Ischemic</td>
<td>152.70±48.39</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic</td>
<td>159.04±26.07</td>
<td></td>
</tr>
<tr>
<td>HDL-C (normal &gt; 35mg/dl)</td>
<td>Ischemic</td>
<td>33.10±7.33</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic</td>
<td>39.02±4.22</td>
<td></td>
</tr>
<tr>
<td>TC : HDL-C ratio (normal &lt; 5)</td>
<td>Ischemic</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hemorrhagic</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

The relationships of lipoproteins with CVA are being studied as in coronary heart disease. Some clinical trials show established association of cerebral ischemic with low HDL-C or raised total cholesterol (an evil twin) . This association is independent of other risk factors. On the other hand other prospective studies generally failed to show direct association. Our study does not aims to see the prevalence of risk factors but it evaluates the values of TC, HDL-C and their ratio in type specific CVA (if any) regardless of age, sex and other risk factors. Results had alarmingly paramount importance.

Our findings clearly demonstrate that most of our patients presented in age range of 30-69 years with male to female ratio 3:1. Majority of the patients presented in ischemic group. The results are in accordance to Asghar K et al . Their patients presents in middle and old age group. In their 50 patients, 32 (64%) has cerebral ischemia and 18 (38%) had cerebral
hemorrhage. As far as the frequency of age, subtype of CVA along with lipid profile is concerned, Nazim k et al have shown same findings11. Their most patients of ischemic stroke presented with hypercholesterolemia (serum TC > 200 mg/dl). Frequencies of hypercholesterolemia in Ischemic and hemorrhagic groups were 56 (29.4%) and 32 (17.8%) respectively which was statistically significant (p-value 0.009). Their ischemic group had significantly more frequency (p value 0.005) of low HDL-C than hemorrhagic group.

Blood cholesterol level in patients with ischemic stroke was significantly higher than hemorrhagic stroke. In our present study, there was inverse association between HDL-C and cerebral ischemia.

It is high time to compare our results with a recent large landmark trial among 58235 Finish people. Their pool analysis show significance association of high total cholesterol and low HDL-C with risk of ischemic stroke and inverse association with hemorrhagic stroke14. Our findings are identical to a recent local research conducted by Mehmood etal15. They have reported significantly greater number of patients with raised cholesterol and low HDL-C in ischemic stroke. While only 5 patients of hemorrhagic stroke had raised cholesterol and low HDL-C. Same statistically significant correlation was observed by Sridhar K et al16. In their 50 patients, 32 had hypercholesterolemia, of which 81.3% has cerebral ischemia.

Another Indian investigator Sugata roy etal also seconds these findings17. It was noted in their results that fasting serum lipid profile analysis of 50 ischemic stroke patients revealed raised serum total cholesterol in 21 patients with mean serum cholesterol of 190±35mg/dl where as only 5 patients among hemorrhagic CVA showing raised serum cholesterol with overall mean of 151±29mg/dl. Serum HDL was found to be low in 16 patients i.e. 32% of Ischemic stroke with mean value of 42.4±6mg/dl whereas only 6% of hemorrhagic stroke patients showing low serum HDL with mean value of 45.4±5mg/dl.

Conflicting results exist in large collaborative landmark trial held among the multiple research centers in Europe. Their pool analysis shows no significant association between total cholesterol, HDL-C and subtype of stroke18. Analysis of cerebral haemorrhage and cerebral infarction revealed odd ratio of 0.80 and 1.06 respectively. The possible explanation is that in our study hospital population was examined and referral was admitted selectively for immediate management. On the other hand the community trial is likely to have possibly different criteria.

Serum HDL-C has anti atherogenic properties with ability to clear cholesterol from peripheral cells and they may have unique effect for primary and secondary prevention of stroke19,20. Taking this perspective of low HDL-C, in our patients of ischemic stroke, the same pattern has been recently concluded by Osama A et al and Woodward M et al, showing identical results21,22. Most of the above reported studies have raised the impression that significant difference in lipid parameters exist between cerebral haemorrhage and cerebral ischemia. Despite limitations of our study, based on single ward data, this paradigm is helpful for adapting best preventive plan specially statin therapy as it may result in a 24 – 29 % reduction in mortality especially ischemic subtype. High risk patients should be screened for lipid profile and lipid lowering drugs should be used along with other preventive measures.

**CONCLUSION**

Patients of ischemic stroke had higher total cholesterol and low HDL levels in comparison to hemorrhagic stroke.

**CONFLICT OF INTEREST**

The authors unanimously declare that no conflict of interest exists and we have no intention for financial gain

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**REFERENCES**


