Glucose and Lipid Profile in Patients with Ischemic Cerebrovascular Accidents
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Abstract
Background: Different mechanisms are responsible for the development of Dyslipidemia in individuals with diabetes. Defects in insulin action and hyperglycemia could lead to Dyslipidemia in patients with diabetes. Methods: Cross sectional study carried out in patients presenting with ischemic stroke to medicine emergency unit of the LLRH Hospital from January 2018 to October 2019. Patient of age group 40-80 years. The subjects in the present study were 450 patient comprised of 235 cases with ischemic stroke of age group of 40-80 years and 215 healthy controls of age group of 40-80 years. Results: It is observed that mean serum level of TC, TG, HDL-C, and LDL-C in controls was 186±36.7 mg/dl, 124.7±58.3, 51.6±15.8 mg/dl, and 112±38.3 mg/dl respectively. In ischemic stroke cases the mean serum level of TC, TG, HDL-C, and LDL-C was 271.2±28.4 mg/dl, 216.0±58.2 mg/dl, 24.3±6.5 mg/dl, and 201.7±32.1 mg/dl respectively. It is observed from the table—-that serum level of TC, TG, HDL-C, and LDL-C was higher in ischemic stroke cases than control population, and the differences was highly significant (p value<0.001). Conclusion: Our study show statistically significant association (p < 0.001) of increased levels of HbA1c and Dyslipidemia (TC, TG, HDL-C, and LDL-C) in patients of ischemic stroke.

Keyword: Dyslipidemia, diabetes, hyperglycemia, HDL-C.

INTRODUCTION
Stroke or cerebrovascular accident (CVA) is defined as an abrupt onset of a neurological deficit attributable to a focal vascular cause. Thus the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. The focal vascular event may include cerebral infarction, intra-cerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH)[1].

Cerebrovascular accident (CVA) is defined as the rapid development of localized or global clinical signs of neurological dysfunction with no apparent cause other than that of vascular origin.

A variety of risk factors have been identified and associated with the occurrence of Ischemic CVA, including glucose and lipid metabolism disturbances. Diabetes mellitus is the commonest metabolic disease affecting mankind. It has been recognized for several decades that diabetes mellitus is an established risk factor for atherosclerotic cardiovascular, cerebrovascular and peripheral vascular morbidity and mortality. Coronary artery disease (CAD) is multifactorial in etiology and has several important risk factors, out of which diabetes is one of the important modifiable risk factor [2].

Dyslipidemia is one of the important diabetic complications which is a classical risk factor for cardiovascular disease. The Adult Treatment Panel III has recognized the important roles of HDL-C and triglycerides (TGs), calling this combination an atherogenic dyslipidemia [3].

Improved glycemic control generally has favorable effects on lipoprotein levels in diabetes, with a reduction in cholesterol and triglyceride levels through decreased circulating very-low-density lipoprotein (VLDL) and by increased catabolism of low-density lipoprotein (LDL) through reduced glycation and up regulation of LDL receptors [4].

MATERIAL AND METHODS

Study design
- This is a cross sectional study Carried out in patients presenting with ischemic stroke to the Medicine Emergency Unit of the LLRH
Hospital (tertiary center) during January 2018 to October 2019. Patient was randomly assigned to case and control group. This study receives approval from ethical committee of this institute.

- Sample size: By calculating minimal sample size, 450 Participants included in the study. 235 were cases and 215 were control.
- Subject characteristics:

**Inclusion Criteria**
- Age group 40-80 years
- Patients with ischemic stroke

**Exclusion Criteria**
- Patients with cardio-embolic stroke, with prior history of MI and of non valvular-atrial fibrillation
- Patients with a neurologic deficit attributable to neoplasm, trauma, or subdural or epidural hematoma,
- Transient Ischemic Attack (TIA)
- Patients with hepatic diseases, renal diseases and
- Those who were on lipid lowering medications or on steroids prior to the onset of stroke were also excluded.
- The subjects in the present study were 450 patients comprised of 235 cases with ischemic stroke of age group of 40-80 years and 215 healthy controls of age group of 40-80 years.

**Clinical and biochemical assessment**
- Interviewer administered questionnaires were used to capture the following data; age, sex, occupation, history of diabetes mellitus (taking OHA), and Dyslipidemia (taking Statins).

The biochemical parameters that were evaluated within 48 hours of admission included plasma glycosylated hemoglobin (HbA1c), fasting total serum cholesterol, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL).
- A confirmed value of HbA1c at or above 48 mmol/mol (6.5%) is used as diagnostic for diabetes mellitus as recommended by the American Diabetes Association.
- The diagnosis of stroke was made clinically and with the aid of computed tomography (CT) scans and magnetic resonance imaging (MRI) for some patients.

**Statistical Analysis**
- Statistical analysis was performed using chi-square for qualitative variables and students t-test for quantitative data.
- P value of 0.05 or less was considered as the level of significance.
- A bivariate analysis correlating the biological aspects with biochemical data was also carried out.
- The analyses were performed using SPSS 16.0 software.

**Results**
- Total 450 patients were selected in our study. 235 were cases and 215 were control.
- Study period was January 2018 to October 2019.
- The total numbers are similar and were chosen to identify the correlation between glycemic control and Dyslipidemia in the normal population as well as patients of ischemic stroke.

<table>
<thead>
<tr>
<th>Age in years</th>
<th>CASE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-50</td>
<td>42 (17.88%)</td>
<td>37 (17.20%)</td>
</tr>
<tr>
<td>50-60</td>
<td>117 (49.79%)</td>
<td>110 (51.26%)</td>
</tr>
<tr>
<td>60-70</td>
<td>51 (21.70%)</td>
<td>47 (21.82%)</td>
</tr>
<tr>
<td>70-80</td>
<td>25 (10.63%)</td>
<td>21 (9.72%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>CASE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>132 (56.55%)</td>
<td>125 (58.11%)</td>
</tr>
<tr>
<td>Female</td>
<td>103 (43.45%)</td>
<td>90 (41.89%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>CASE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>119 (50.63%)</td>
<td>91 (42.33%)</td>
</tr>
</tbody>
</table>

Table-1: Demographic profile, baseline characteristics and risk factors
Majority of patients in both groups are between 50 – 70 years of age, accounting for about two thirds of the study population. The mean age was 59.6±9 years in cases and 58.8±9 years in controls. The number of subject in both groups was similar in each decade of life.

- The gender distribution is similar in both populations.
- The below figure shows the distribution of glycemic status in patients with ischemic stroke, and control. About one half of these patients had diabetic range in cases as compared to control population , as evidenced by HbA1c level, suggesting that diabetes was an independent variable influencing ischemic stroke risk, and it has significant effect on the incidence of ischemic stroke (p value 0.003018).
- The mean value of HbA1c in cases was 6.30% ± 16.02 and in control group was 5.80% ± 14.04.

The relevant biochemical parameters from 235 cases and 215 controls revealed that the Glycosylated hemoglobin levels at presentation in were divided into two categories including 119 in diabetic & pre-diabetic range, and 116 non-diabetics in case group and 91 in diabetic &pre-diabetic range, and 124 non-diabetic ranges in control group as depicted in figure1.

<table>
<thead>
<tr>
<th>LIPID PROFILE</th>
<th>Total cholesterol (TC)</th>
<th>Triglycerides (TGs)</th>
<th>HDL cholesterol (HDL-C)</th>
<th>LDL cholesterol (LDL-C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1C &gt;5.6%</td>
<td>high</td>
<td>high</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>PRESENT</td>
<td>74</td>
<td>18</td>
<td>53</td>
<td>32</td>
</tr>
<tr>
<td>ABSENT</td>
<td>39</td>
<td>3</td>
<td>21</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 2 shows that patient with HbA1C in diabetic range having elevated level of total cholesterol (74 patients), elevated level of LDL cholesterol (32 patients), low level of HDL cholesterol (53 patients) and elevated triglyceride (18 patients).

At the same time we also found that level of TC, LDL-C, TGs, were also elevated in non- diabetic cases but number of cases with elevated level of TC, TGs, LDL-C higher in those cases that have HbA1C in diabetic range.

**DISCUSSION**

Stroke is a major problem in Kanpur. Classically stroke is divided into two major category one is due to ischemia called as ischemic infarct and other is hemorrhagic .patient of stroke were presented in emergency department within 24 hour clinical assessment was done and neurological imaging (CT or MRI) was done.
We study 235 cases and 215 control and we attempted to investigate the correlation between HbA1c and lipid profile in ischemic stroke patient. A study suggested that glycemic control is favorable for lipid profile. Strict glycemic control decrease the total cholesterol level and decreases the LDL cholesterol and increases the HDL cholesterol and decreases triglycerides level which help in prevention of ischemic stroke.

We found that those cases in which glycemic control is not found, we found that total cholesterol level was higher (74 cases) compare to non-diabetic group (39 cases), and the difference was statistically significant (p value <0.0001).chi square was 20.0127. We correlated the HbA1c with total cholesterol levels 235 patients of which 74 had diabetes and dyslipidemia, 45 had diabetes only and 39 had dyslipidemia only, while 77 had neither diabetes nor dyslipidemia. This correlation was statistically highly significant (P<0.0001) suggesting that patients with high HbA1c and total cholesterol levels were more likely to have a stroke.

It was also found that triglyceride level was higher in diabetic patients (18 case) compare to non-diabetic group (3 cases), and the difference was statistically significant (p value<0.001).chi square was14.0196. We correlated the HbA1c with triglyceride levels 235 patients of which 18 had diabetes and dyslipidemia, 101 had diabetes only and 3 had dyslipidemia only, while 113 had neither diabetes nor dyslipidemia. This correlation was statistically significant (P<0.001) suggesting that patients with high HbA1c and triglyceride levels were more likely to have a stroke.

Study also shows that serum level of HDL cholesterol was lower in diabetic group (53 cases), compare to non-diabetic group (21 cases), and the difference is statistically highly significant (p value<0.0001).chi square was 19.026. We correlated the HbA1c with HDL levels 235 patients of which 53 had diabetes and dyslipidemia, 66 had diabetes only and 21 had dyslipidemia only, while 95 had neither diabetes nor dyslipidemia. This correlation was statistically highly significant (P<0.0001) suggesting that patients with high HbA1c and HDL levels were more likely to have a stroke.

Study also shows that the distribution of Dyslipidemia as a function of glycemic control, and forms the bedrock of our investigation. The correlation between these two variable as elicited from data obtained from study and, is significant (p<0.0001). The sensitivity of this correlation in the context of ischemic stroke is 75%, while the specificity is 60%. However, an impressive negative predictive value of 91% suggests a beneficial effect of normal or well controlled diabetes and Dyslipidemia. Conversely, a modest positive predictive value of 29% does not appear to help in utilizing this correlation as a measure of future likelihood of ischemic stroke. P value 0.00005 inference-highly significant.

We find that absence of diabetes mellitus & Dyslipidemia is a strong negative predictor of the occurrence of ischemic stroke. Our initial assessment showed that of the 235 patients there were 132 males and 103 females, between the age group of 40 - 80 years with a mean of 59+/9 years. These demographic determinants did not have any impact on the incidence of ischemic stroke in this patient population. Gender was almost equally distributed and age groups were evenly spread, and comparable with the control population of 215 subjects.

These finding resonates with guidelines which recommend treating diabetes and dyslipidemia to goal to achieve favorable clinical outcomes.

Levels of TC, HDL-C, TGs, and LDL-C, show a statistically significant relationship with HbA1c in the incidence of stroke. This has been studied by other investigators and findings are variable across different studies5. However, the general trend towards dyslipidemia, which means abnormality in any lipid component, appears to be a constant finding and in concurrence with our results as well.

In fact, clinical guidelines like ADA and ATP III have been suggesting the virtues of good glycemic and lipid level control since the 20th century6. A large number of clinical trial and independent investigator data have revealed a lower incidence of macro vascular complications of diabetes with HbA1c levels below 7%. Similarly ATP III guidelines have been propagating LDL levels below 100mg/dl for better prevention of atherosclerosis and its complications.

**LIMITATIONS OF THE STUDY**

- Pilot study only (meant to study correlation as POC).
- Not powered to make any recommendations. But supports current clinical guidelines for treating diabetes mellitus and Dyslipidemia.
- While trends in diagnosis and treatment are discernable, however larger study group are needed to verify these findings statistically.
CONCLUSION
Our study show statistically significant association (p < 0.001) of increased levels of HbA1c and Dyslipidemia (TC, TGs, HDL-C, and LDL-C) in patients of ischemic stroke.

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REFERENCES