The relationship of LDL-C in diabetic and non-diabetic stroke patients in District Swat

Sahibzada Saeed Jan, Jan-i-Alam, Farhat Rahman

ABSTRACT

BACKGROUND: Diabetes mellitus is a well recognized risk factor for acute stroke, resulting in a greater ischemic to hemorrhagic stroke ratio in the people with diabetes compared with the general population. As there are controversies in different international studies regarding the level of LDL-C in diabetic and non-diabetic stroke patients, so there is an intense need to evaluate the level of LDL-C in diabetic and non-diabetic stroke patients (Control group) in our setup.

OBJECTIVE: The aim of this study was to evaluate the association of Low Density Lipoprotein-Cholesterol (LDL-C) level in the diabetic and non-diabetic stroke patients.

MATERIAL AND METHOD: This was a cross-sectional study, comprised of 100 subjects, 50 were diabetic and 50 were non-diabetic stroke patients of ages between 30 to 90 years. The study duration was 6 months. The subjects underwent a detailed history and examination. Individuals with a history of medications known to affects body composition, patients on anti-coagulants and having a history of blood dyscrasias like leukemia, thalassemia, polycythemia and having clotting disorders, extradural and intradural hemorrhage as a cause of stroke were excluded from the study. Fasting (overnight) as well as random (two hours after meal) blood samples were drawn from the participants for biochemical assays. The serum LDL-C level, blood sugar (random and fasting), blood pressure (systolic and diastolic) of diabetic stroke subjects were compared with Non-diabetic stroke subjects.

RESULTS: The LDL-C level was not significantly high in diabetic as compared to non-diabetic stroke subjects.

CONCLUSION: Low-density lipoprotein cholesterol (LDL-C) is not an independent predictor of macrovascular disease such as stroke.

KEYWORDS: Diabetes mellitus, low-density Lipoprotein-Cholesterol (LDL-C), Blood pressure, Stroke

INTRODUCTION

Low-density lipoprotein (LDL) are spherical particles of 2229 nm in diameter, composed of a core of esterified cholesterol and triglyceride, a surface lipid coat of unesterified cholesterol and phospholipids, an essential structure protein, apo B, and sometimes small apo S, such as apo C-111 and apo E that modulate LDL metabolism. Type-1 diabetic mellitus (DM) may be associated with elevation of VLDL triglyceride and LDL-C, if diabetes control is very poor or if the patient is actually ketotic. In contrast, type-2 DM is usually associated with lipid abnormalities, most common of which are high triglycerides, reduced HDL-C levels, and the presence of smaller, CE-depleted LDL; this pattern is called insulin resistance/diabetic dyslipidemia. Low-density lipoprotein cholesterol (LDL-C) has now largely replaced total cholesterol as the primary lipid measurement for evaluation of risk due to atherogenic lipoproteins. LDL-C is a measure of the total cholesterol content of LDL particles, reflecting both the number of LDL particles and their individual cholesterol content. Most current guidelines include LDL-C as a primary target for initiating and adjusting lipid-lowering interventions. Cerebrovascular disease (CVD) causes significant worldwide morbidity and mortality and contribute to substantial health care spending. The treatment of hypercholesterolemia, and specifically elevated LDL-C, represents an established strategy to diminish incident CV events and mortality. Diabetes mellitus accelerates all the sequence of events, leading to atherosclerosis. Type-2 diabetes mellitus is an independent risk factor for the development of atherosclerosis and atherosclerotic disease, commonly referred to as macrovascular disease, and is responsible for more than 50 % of all mortality in type-2 diabetes mellitus. Every year millions of CVD cases are reported in the hospitals but a large number of people that never reach to hospital and expire as unreported in which hundreds of people may be due to lipid, carbohydrate, and protein related cardiac dysfunctions associated to cerebrovascular disease. Atherosclerosis is a multi-step chronic inflammatory disease, largely characterized by the formation of lipid and immune-cell-containing
plaques in the intima of large and mid-sized arteries, it is often the underlying cause of CVDs and stroke.9

Stroke may be defined as cerebrovascular events with focal neurological deficits lasting for more than 24 hours. Strokes are classified into hemorrhagic, non-hemorrhagic (ischemic) and intermediate based on computerized tomography (CT) or magnetic resonance imaging (MRI) scan reports. If focal neurological signs are present, and provided there is no hemorrhage on CT, then the stroke is considered as non-hemorrhagic (ischemic)10 and about 85% of all strokes are ischemic strokes.11 According to World Health Organization, the prevalence of cardiovascular diseases will double by 2020 and will rank Before the HIV/AIDS infection.12 Cerebrovascular disease causes significant worldwide morbidity and mortality and contributes to substantial healthcare spending. Numerous studies have established the continuous, graded, benefit conferred by LDL-C reduction on cerebrovascular event risk and mortality.13

Research shows that the risk of ischemic stroke is multiplied 2 to 3 times in people with diabetes. However, the risk of having a hemorrhagic stroke (caused by bleeding in and around the brain) is probably similar to that of people who do not have diabetes.14 A new study in Italy has found that glycated LDL levels increased heart attack and stroke risk not just in diabetes but also in persons without diabetes.15 Every year, over 1, 30,000/- people in the United Kingdom suffer a stroke. This equates to one person every 5 minutes. Most people affected are over the age of 65 years, but all ages are at risk of having a stroke, including children and even babies. Stroke is the third most common cause of mortality in the United Kingdom. It is also the single most common cause of severe disability and more than 2, 50000/- people live with disability caused by stroke.16 In the US population, more than 6% of individuals aged 65 to 74 and more than 11% of those aged 75 and older have a history of stroke.17 The available estimated incidence of stroke in Pakistan is 250/1,00000 translating to 350,000 new cases every year.18 Epidemiological and clinical studies have clearly established the link between low-density lipoprotein cholesterol (LDL-C) and atherosclerosis-related cardiovascular consequences.19 In 1988, the National Cholesterol Education Program (NCEP) in the United States identified LDL-C as the primary target of cholesterol-lowering therapy.20 The Framingham 21 and Multiple Risk Factor Intervention Trial (MRFIT), 22 showed the positive relationship between LDL-C and risk of cardiovascular disease (CVD). Moreover observational studies in the general population have not always found that LDL-C is an important independent predictor of stroke.23 Few patients presented elevated LDL cholesterol compared to the literature, making hypercholesterolemia be considered as a less common cardiovascular risk factor compared to hypertension and low HDL cholesterol which were very common.23 Cardiovascular diseases are increasing day by day due to over utilization of fats or due to genetic reasons. It is a leading cause of morbidity and mortality from infancy to old age but the authentic and accurate biomarkers of CVDs are lacking. It not only delayed clinical diagnosis but also increased risk manifold and resulted in accidental death of patients. Therefore, an early identification and treatment of risk factors are much needed to accelerate disease prevention and morbidity improvement.24

Since controversies exist in different studies on the issue, the present study was designed to evaluate LDL-C levels in diabetic and non-diabetic stroke subjects the community hospital Saidu Sharif Swat.

MATERIAL AND METHODS
This was a cross-sectional study carried out by the department of Physiology, Saidu Medical College, Swat in collaboration with the Department of Medicine Saidu Teaching Hospital, Swat. The study comprised of 100 subjects between 30-90 years of age, having study duration of 6 months. They were divided into two groups, 50 subjects with diabetic stroke and 50 with Non-diabetic stroke patients (Control group). Subjects taking medications known to affect lipid profile, on anticoagulants, and having a history with endocrinopathies (e.g. Down syndrome, Cushing syndrome, acromegaly, thyrotoxicosis, etc.) or any other major illness were excluded from the study. Patients having intra-cerebral tumors, CSF obstruction, Extradural and Intradural haemorrhage as cause of stroke were also excluded from the study.

After obtaining informed consent, a detailed history, general physical and systemic examination was performed. Blood pressure was
measured in the right arm in lying position. Blood samples were taken to estimate fasting LDL-C with (LDL-Cholesterol liquicolor reagent kit, Human diagnostics worldwide Manufacturer), random (two hours after meal) and fasting (overnight) blood sugar. CT scan was done in each and every stroke patient to differentiate between Ischemic and Hemorrhagic stroke.

Statistical analysis was done using SPSS version 16. Mean and standard deviation (SD) were determined for quantitative data. Comparative analysis between the two groups was done using two tailed student's t-test. P value <0.05 was considered statistically significant, while p<0.001 was taken as highly significant.

RESULTS
Our study was comprised of 100 subjects. Out of 100 subjects 50 were diabetic and 50 were non-diabetic stroke group. In diabetic group 96% patients had Ischemic stroke while 4% had hemorrhagic stroke. On the other hand in non-diabetic group 76% patients had Ischemic while 24% had hemorrhagic stroke, showing significantly high ischemic to hemorrhagic ratio in diabetic stroke as compared to non-diabetic stroke patients. In our study the Low-density Lipoprotein -Cholesterol (LDL-C) level of diabetic stroke was 129.94 ± 45.63 and that of non-diabetic stroke subjects group was 114.44±42.79, with p-value 0.083, showing that the LDL-C level in diabetic stroke patients was not significantly different compared to the non-diabetic stroke patients group (table-2). The fasting blood sugar level of diabetic stroke was 218.50 ± 74.94 and that of Non-diabetic stroke group was 95.12 ± 14.12. Similarly random blood sugar level of diabetic stroke was 304.66 ± 79.22 and that of control was 140.24 ± 21.21. Blood sugar, both fasting & random was statistically highly significant in diabetic stroke as compared to control group (table-1).

The high prevalence of complications at presentation of type-2 diabetes in middle age suggests that the current organization of health care is sub-optimal, since diabetes is often diagnosed only when it becomes symptomatic and tissue damage has often already occurred. So regular screening of the population in middle age to detect diabetes before its complications ensue may be required, to prevent complications of diabetes.25

The present study (the mean ± SD, LDL-C value is 129.93±45.63, 114.44±42.79 in diabetic and non-diabetic stroke subjects respectively, with p-value 0.083, showing no statistically significant difference between the two groups) is in

Table 1:
Blood Sugar values in diabetic and non-diabetic stroke patients
Variables expressed as mean ± S.D

<table>
<thead>
<tr>
<th>B Sugar Fasting (mg/dl)</th>
<th>Diabetic (n = 50)</th>
<th>Control (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± S.D</td>
<td>Range</td>
</tr>
<tr>
<td>B Sugar Fasting (mg/dl)</td>
<td>218.50 ± 74.94</td>
<td>100-200</td>
</tr>
<tr>
<td>B Sugar Random</td>
<td>304.66 ± 79.22</td>
<td>60-110</td>
</tr>
</tbody>
</table>

** Highly Significant

Table 2:
LDL-C and Blood Pressure in diabetic and non-diabetic stroke patients

<table>
<thead>
<tr>
<th></th>
<th>Diabetic (n = 50)</th>
<th>Control (n = 50)</th>
<th>p -value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>129.94±45.63</td>
<td>30—271</td>
<td>114.44±42.79</td>
</tr>
<tr>
<td>BP Systolic</td>
<td>147±25.49</td>
<td>100—200</td>
<td>146.76±37.35</td>
</tr>
<tr>
<td>BP Diastolic</td>
<td>92.30±12.34</td>
<td>60—110</td>
<td>90.00±16.00</td>
</tr>
</tbody>
</table>

P-value< 0.05 is significant
accordance with the study report, stated that the pattern of dyslipidemia frequently observed in people with diabetes includes raised triglycerides, decreased levels of HDL-cholesterol and slightly raised or normal plasma concentrations of LDL-cholesterol, with LDL-C not being significantly different from that in non-diabetic individuals.  

The present study is also in accordance to the observational studies in the general population stated that the low-density lipoprotein cholesterol (LDL-C) is not an important independent predictor of stroke. As a result some have argued that to reduce risk of future cardiovascular events in people with diabetes it may be more important to modify HDL-cholesterol and triglycerides level than to lower total cholesterol or LDL-cholesterol levels. 

The present study is not in accordance to the Framingham, and Multiple Risk Factor Intervention Trial (MRFIT), showed the positive relationship between LDL-C and risk of cardiovascular disease (CVD).

The present study is also not in accordance to the study conducted in 1988, the National Cholesterol Education Program (NCEP) in the United States identified LDL-C as the primary target of cholesterol-lowering therapy.

The present study is also not in accordance to, a new study in Italy has found that glycated LDL levels increased heart attack and stroke risk not just in diabetes but also in persons without diabetes. So finally we can conclude that in our study the LDL-C level in diabetic and non-diabetic stroke subjects were not significantly different and so the LDL-C level is not an important predictor of stroke in diabetic subjects in our study.

**Conclusion:** Low-density lipoprotein cholesterol (LDL-C) is not an independent predictor of macrovascular disease such as stroke.

**Recommendations:** As Low-density lipoprotein cholesterol (LDL-C) is not an independent predictor of macrovascular disease like stroke, therefore there is intense need to sought for other risk factors of macrovascular disease in diabetic subjects, to prevent cardiovascular and cerebrovascular disease especially stroke in high risk diabetic patients.

**REFERENCES**


20 Brown V W. LDL-CHow low should you go, medscape cardiology. 2007; 2-10.


