INTRODUCTION

Cholesterol, a lipid molecule is biosynthesized by all animal cells. It is an essential structural component of animal cell membranes and helps in maintaining both membrane structural integrity and fluidity. In addition to this cholesterol serves as a precursor for the biosynthesis of steroid hormones, bile acid and vitamin D. Factors that may result in increased cholesterol levels in the body include inactivity, obesity, genetic factors and an unhealthy diet. The high cholesterol levels or hyperlipidemias may contribute to high concentrations of its precursor triglycerides and low density lipoproteins in plasma of the individuals. High triglyceride levels signal insulin resistance. This study was designed to determine an association of hyperlipidemia and diabetes mellitus with depression. Method: This case-control study involved 30 patients diagnosed with type 2 Diabetes Mellitus (DM) and hyperlipidemia (HL), and 30 non-diabetic healthy individuals having normal glucose tolerance test and no other co-morbidity. All subjects were of 30–50 years age. Blood samples from all participants were collected for determination of the HbA1C and lipid profiles. PQ9 score questionnaire for depression was asked from all subjects. Results: Patients suffering with hyperlipidemias and diabetes mellitus had higher incidence of depression compared to healthy subjects (p<0.05). Conclusion: Depression was more prevalent in hyperlipidemic and diabetic patients.

Keywords: Diabetes mellitus, hyperlipidemias, depression, serotonin, tryptophan

MATERIAL AND METHODS

This case-control study was conducted from January to June 2008 in Karachi, Pakistan. Sample size of 124 was calculated on 80% confidence interval for sample size calculation using open epi sample size calculator. However, this was a pilot study which was conducted only for a period of six months so we included all those patients who fit into our inclusion criteria. This involved 30 patients diagnosed with diabetes type 2 and hyperlipidemia (DM+HL) from one private-sector hospital and 30 non-diabetic healthy individuals. Both groups
had 15 men and 15 women subjects of age 35 to 55 years. The study was done in accordance with the ethical recommendations and practices of the hospital.

The non-diabetic healthy subjects were of the same age as the diabetics with normal glucose tolerance test and no other comorbidity. Blood samples from all the participants were collected from the antecubital vein for the determination of the HbA1c and lipid profiles. HbA1c was determined by GlucoMen A1c test kit method and plasma lipid profile through ELISA kit methods. The samples for analysis were stored at -70 °C. A questionnaire PHQ 9 was asked from all the participants to assess for the grade and severity of depression in them.

Data was analyzed by two-way ANOVA followed by Tukey’s Post-hoc test using SPSS-20. Results were presented as Mean±SEM.

RESULTS

The results are presented in Table-1. There was a significant effects of disease ($F$=496.12, $p<0.01$), gender ($F$=32.45, $p<0.01$) and a significant interaction between the two factors ($F$=5.16, $p<0.01$). Cholesterol levels were significantly higher in DM+HL patients as compared to healthy subjects ($p<0.01$) in both male and female groups.

Two-way ANOVA for LDL data showed significant effects of disease ($F$=439.93, $p<0.01$), non-significant of gender ($F$=3.81, $p>0.05$) and interaction of two factors ($F$=3.41, $p>0.05$). Post-hoc analysis by Tukey’s test showed significantly increased LDL levels in DM+HL patients than healthy individuals ($p<0.01$) in both male and female groups.

VLDL was also significantly affected by the disease condition of patient. Two-way ANOVA showed significant effects of disease ($F$=580.58, $p<0.01$), gender ($F$=6.43, $p<0.01$) but non-significant effects of interaction between the two factors ($F$=3.17, $p>0.05$). DM+HL patients showed significantly higher VLDL levels as compared to healthy male and female subjects ($p<0.01$).

The levels of HDL were also significantly different among the healthy and diseased subjects. Two-way ANOVA revealed that there was a significant effect of disease ($F$=95.19, $p<0.01$), gender ($F$=6.57, $p<0.05$) and a non-significant interaction of these two factors ($F$=0.587, $p>0.05$). Tukey’s test showed that HDL levels were significantly higher in DM+HL patients as compared to healthy male and female groups ($p<0.01$).

There was significant effects of disease ($F$=628.26, $p<0.01$) but non-significant effects of gender ($F$=0.695, $p>0.05$) and non-significant interaction of two factors ($F$=0.15, $p>0.05$). Post-hoc analysis by Tukey’s test showed significantly increased TAG levels in patients as compared to that of healthy male and female subjects ($p<0.01$).

Analysis of HbA1c data by two-way ANOVA revealed that there was a significant effects of disease ($F$=268.54, $p<0.01$) but non-significant effects of gender ($F$=0.000, $p>0.05$) and interaction of two factors ($F$=2.796, $p>0.05$). Tukey’s test showed that there was a significantly higher level of HbA1c in DM+HL patients than normal healthy participants ($p<0.01$) confirming the existence of diabetes in these patients.

Two-way ANOVA for PHQ 9 score showed that there was a significant effects of disease ($F$=76.62, $p<0.01$), gender ($F$=4.578, $p<0.05$) and non-significant interaction of two factors ($F$=0.946, $p>0.05$). Post-hoc analysis by Tukey’s test revealed that the depression is higher in DM+HL patients as evident by significantly higher PHQ 9 scores as compared to healthy subjects ($p<0.01$). (Table-1).

Table-1: Lipid profile, HbA1c and PHQ-9 score of healthy participants and DM+HL patients (Mean±SEM)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Healthy Controls</th>
<th>DM+HL Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males (n=15)</td>
<td>Females (n=15)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>135.5±2.8</td>
<td>145.5±4.4</td>
</tr>
<tr>
<td>TAG (mg/dl)</td>
<td>130.2±2.16</td>
<td>131.7±1.7</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>76.7±2.18</td>
<td>79.4±1.78</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>20.4±0.86</td>
<td>21.8±0.92</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>29.6±1.32</td>
<td>26.3±1.07</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.4±0.21</td>
<td>5.0±0.12</td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td>0.2±0.10</td>
<td>0.4±0.13</td>
</tr>
</tbody>
</table>

*p<0.01

DISCUSSION

There is an established link between occurrences of DM with HL. These conditions may touchdown in a paired fashion with amplification of one condition may augment the other condition worsening the state of the patient. However, until now the association of these two conditions with psycho-neurological deficits was not assessed. The present study was done to find a possible positive link of the two conditions DM and HL with depression. For the reason the blood lipid profile and HbA1c were determined in all subjects participating in the study.

The lipid profile of healthy subjects had no significant difference, however, the diabetic subjects has a rise in the total cholesterol levels. Likewise, the LDL
and very low density lipoprotein (VLDL) showed the same tendency. VLDL is known to convert into the body to LDL through digestion through lipase enzymes. It is seen that the good cholesterol (also termed as HDL) that transports the excess harmful levels of cholesterol to liver was decreased in the test subjects than in healthy group. The sugar levels evaluated by HbA1c showed that the normal subjects were within the normal limits while the tests subjects exceeded the limits when compared with the healthy subjects. This showed the positive correlation of the diabetes with the lipid profile, depicting the rise of cholesterol and LDL levels with increasing blood sugar levels and declining in HDL levels. This affirmative connection of the two conditions becomes the hallmark of development of coronary heart disease and psycho-neurological deficits among which depression is the most important concern.

To further affirm this connection, PQ9 score questionnaire was given to all subjects. PQ9 score is a designed questionnaire relating the condition of the patient, and the score at the end may enable the researcher to categorically group the individuals under no depression, mild, moderate, or severe depression. It was found that over all the healthy subjects suffered least depression than that of DM+HL patients. The depression scale was further dissected to the classes of no depression, mild, moderate and severe depression. It was observed that the majority of the healthy males had no depression and only a few demonstrated mild depressions, and practically nil showed moderate and severe depression. Likewise, the healthy females showed the same tendency. However, there was a little additional number of female healthy subjects suffering through mild depression than that of the male healthy subjects.

Upon comparison of both the healthy groups with their corresponding test groups, it was observed that the test subjects showed higher frequency of depression in terms of the severity-based gradation. The male DM+HL patients showed higher number of mild and moderate depression than no and severe depression cases. In the female subjects, moderate depression was highest compared to severe depression. Categorically the severe depression was more than mild depression versus no depression in female patients. Overall it was seen that the test subjects suffering through both DM and HL were more subjected to depression than healthy individuals. This may be linked with the possibility of decreased transportation of tryptophan in the brain subsequent to DM and HL. The diminished levels may reduce serotonin, a known neurotransmitter, leading to depression in affected individuals. This may become essential to check for depression in the subjects suffering from either or both of the states that are DM and HL. The HL itself is considered injurious for the cardiac health and revealed as a primary cause of myocardial infarction. However, the HL may cause increase in the cholesterol levels with a rise in lipoprotein levels in blood.

There are different types of lipoproteins in the body dependent upon their density gradient. These are VLDL, LDL and HDL. VLDL and LDL transport cholesterol particles from the liver to all parts of the body especially to the peripheries and excess may form plaques in the walls of arteries, making them hard and narrow. The HDL picks up excess cholesterol from the peripheries of the body and transports it back to the liver. The rising amounts of these lipoproteins hamper the body normal insulin functioning. This is due to the fact that the VLDL and LDL take excess fatty acids to the adipose tissues making more of the bulk of the adipose tissue causing obesity. Obesity in turns causes the resistance of the action of insulin and leads to type 2 DM. The whole cycle of the decreased transport of essential amino acids to the brain especially that of tryptophan takes place leading to decreased synthesis of the serotonin. Upon the decrease in serotonin, the sleep, mood and behaviour get affected leading to insomnia, depression, anxiety and memory loss.

Our study is limited in the sense that we were not able to acquire the calculated sample size. However, the present study addresses very important psycho-neurological concerns of depression that may affect individuals suffering through DM and HL.

**CONCLUSION**

DM and HL are most of the times linked but their association with depression is seldom studied. The hidden tip of the iceberg in form of depression, once diagnosed with its associated ailments will not only improve the quality of life but also the better compliance towards the DM and HL drugs for the contend living of the affected individuals.

**REFERENCES**


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