Research Article

Relationship Between Lipid Profile And Inflammatory Markers In Type 2 Diabetes Mellitus

Ullal Harshini Devi¹a, Shilpa S Shetty¹, Suchetha Kumari N²

¹Central Research Laboratory, KSHEMA, Nitte (Deemed to be University), Deralakatte, Mangalore, India.
²Department of Biotechnology Engineering, NMAMIT, Nitte, Karkala

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ABSTRACT

Inflammatory response is one of the main causative factors for the aetiology of Type 2 Diabetes mellitus. Diabetes mellitus may play a crucial role in the pathogenesis of the disease and is associated with dyslipidaemia. The study aims to determine the relationship between lipid profile and inflammatory markers in type 2 diabetes mellitus. A total of 140 study subjects were recruited in the study in which 70 were non-diabetic subjects served as control and 70 were known cases of type 2 diabetes mellitus between the age group 30-60 years. FBS, HbA1C, Lipid profile, CRP and Interleukin 6 were estimated. C-reactive protein and Interleukin 6 levels of diabetic group showed a significant correlation with Total Cholesterol, Triglyceride, LDL cholesterol whereas a significant negative correlation was observed with HDL-Cholesterol in type 2 diabetes mellitus patients. The study concludes that there is a relationship between the lipid profile and inflammatory markers in T2DM and suggests a significant role of the inflammatory markers in the pathogenesis of dyslipidaemia in diabetes.
INTRODUCTION:
Type 2 Diabetes mellitus (T2DM), a metabolic syndrome characterized by chronic hyperglycaemia due to an absolute or relative lack of insulin and/or insulin resistance, resulting mainly in dysregulation of carbohydrate, protein, and lipid metabolism, accounting for the symptoms and complications of diabetes [1]. Deregulated lipid metabolism and inflammatory states are suggested risk factors for cardiovascular disease, which is a leading cause of diabetic death [2].

Diabetes is increasingly emerging as a major public health burden across the world. In 2013, the global prevalence of diabetes was estimated to be 8.4%, with 382 million people living with diabetes and over 5 million diabetes-related deaths [3]; it is expected that the number of people living with diabetes will be more than double between 2000 and 2030 [4]. The World Health Organization projects that diabetes will be the seventh leading cause of death in 2030 [5]. Abnormal lipid profile is often seen in patients with diabetes because insulin regulates several steps of lipid metabolism. Dyslipidaemia in diabetics is often characterized by elevated fasting and postprandial levels of serum triglycerides, total cholesterol and LDL cholesterol and a significant decrease in the HDL cholesterol levels [6].

Inflammation plays important role in pathogenesis of the disease and inflammatory markers including interleukin-6 (IL-6) and C- reactive protein (CRP) levels are found to be increased in T2DM patients [7]. CRP is mainly released by the hepatocytes predominantly under the control by the IL-6 [8]. Elevation of CRP was related to an increased risk of developing T2DM [9,10] and was suggested as an independent risk determinant for newly diagnosed T2DM [11,12]. IL-6, a pleiotropic cytokine having a key impact on both immunoregulation and nonimmune events in most cell types and tissues outside the immune system. [13].

The present study was aimed to investigate the relationship between inflammatory markers and lipid profile in Type 2 diabetes patients.

MATERIALS AND METHODS:

Ethical Clearance:
This study was reviewed and approved for human subjects by the Central Ethics Committee of Nitte – (Deemed to be University), Ref NU/CEC/Ph.D-18/2014 dated 16.12.2014.

Study site:
The study was conducted at the Justice K S Hegde Charitable Hospital, Deralakatte, Mangalore.

Study population:
A total number of 140 samples were included in the study and divided into the diabetic group (n=70) and the control group (n=70) between the age group 30-60 years. The diabetic group is comprised of 35 males and 35 female whereas the non-diabetic group includes 35 male and 35 female.

Inclusion Criteria:
- Patients diagnosed with type 2 diabetes mellitus.
- Age group of 30-60 years from both the sexes.
- Subjects consenting to participate in the study.

Exclusion criteria:
- Pregnant women
- Subjects not willing to give consent.

METHODS:
Fasting blood samples were collected from the study participants. Body weight and Height were measured. Body mass index (BMI) was calculated by dividing body weight in kilograms with height in square meters (Kg/m²). Fasting blood sugar was measured by glucose oxidase method (Lypho CHEK™AGAPPE). Glycated haemoglobin (HbA1C) was measured by Ion Exchange Resin method using Spectrophotometer (NyoCard READER). Total cholesterol, Triglyceride and HDL-cholesterol levels were measured using commercially available kits (Lypho CHEK™AGAPPE). LDL-cholesterol was determined indirectly by Friedewald formula as TC - (HDL+VLDL) [14] and VLDL was calculated as Triglyceride/5. C-Reactive Protein was measured using commercially available Human CRP Ultra EIA kit (Xema Co., Ltd., Russia). Interleukin-6 was determined using commercially available Human Interleukin-6 ELISA kit (Biolegend, Inc., San Diego, CA).
Statistical analysis:
Statistical analysis was performed using Statistical Package for the Social Sciences version 16 software. Data were expressed as mean ± SD. The comparison between the groups were performed by student’s t-test. Pearson correlation analysis were used to analyse the correlation among the variables. P-values < 0.05 are considered statistically.

RESULTS
A total of 140 study subjects were recruited and evaluated the level of lipid profile and inflammatory markers. Out of 140 subjects, 70 were diabetic and 70 were non-diabetic subjects. Non-diabetic group consists of 25% male and 25% female and diabetic group consists of 25% male and 25% female. Table 1 represents the mean age, height, weight, body mass index, Fasting blood sugar (FBS), HbA1C (Glycated haemoglobin) of both non-diabetic and diabetic subjects. Plasma FBS (fasting blood Sugar) level of diabetic group was significantly higher (p<0.0001) than that of the non-diabetic group as shown in table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non-diabetic (N=70)</th>
<th>Diabetic (N=70)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>45.57±8.13</td>
<td>51.79 ± 6.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.19±10.12</td>
<td>160.53 ± 10.42</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>57.83±10.51</td>
<td>57.89 ± 7.96</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>22.09±2.20</td>
<td>22.47 ± 2.52</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>94.83±13.68</td>
<td>202.72 ± 78.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>4.37±0.70</td>
<td>6.65 ± 1.62</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(BMI: Body Mass Index, FBS: Fasting Blood Sugar, HbA1C: Glycated Haemoglobin)

Table 1: Physical and clinical characteristics of non-diabetic and diabetic individuals (Data are expressed as Mean ± SD), (P<0.05 were significant).

Total cholesterol, Triglyceride, LDL-cholesterol and VLDL were significantly higher in diabetic group compared to that of non-diabetic group, except for HDL cholesterol which was lower in diabetic group compared to non-diabetic group (Table 2).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non-Diabetic</th>
<th>Diabetic</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC in mg/dl</td>
<td>171.43±34.83</td>
<td>234.08 ± 35.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TG in mg/dl</td>
<td>127.62±44.58</td>
<td>191.6 ± 34.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL in mg/dl</td>
<td>46.42±8.62</td>
<td>32.56 ± 7.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL in mg/dl</td>
<td>99.78±36.42</td>
<td>163.2 ± 36.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VLDL in mg/dl</td>
<td>25.52±8.92</td>
<td>38.32 ± 6.97</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(Abbreviations: TC= Total Cholesterol; TG= Triglycerides; HDL = High Density Lipoprotein; LDL = Low Density Lipoprotein, VLDL= Very Low Density Lipoprotein)

Table 2: Comparison of the mean lipid profile levels of type 2 diabetic and non-diabetic individuals (Data are expressed as Mean ± SD), (P<0.05 were significant).

Inflammatory markers C-Reactive protein and Interleukin 6 were significantly higher in diabetic group when compared to non-diabetic group (Table 3)
Table 3: Comparison of inflammatory markers in diabetic and non-diabetic individuals (Data are expressed as Mean ± SD), (P<0.05 were significant).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non-Diabetic</th>
<th>Diabetic</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP in mg/L</td>
<td>1.14±0.60</td>
<td>3.52 ± 0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-6 in pg/ml</td>
<td>1.34±0.72</td>
<td>8.01 ± 1.49</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(Abbreviations: CRP = C-Reactive Protein, IL-6 = Interleukin 6)

Pearsons correlation between lipid profile and inflammatory markers was studied. C-Reactive Protein and Interleukin 6 levels of diabetic group showed a significant correlation with Total Cholesterol, Triglyceride, LDL cholesterol whereas a significant negative correlation was observed with HDL-Cholesterol (Table 4)

Table 4: Correlation among CRP, IL-6 and lipid profile in type 2 diabetes mellitus subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CRP</th>
<th>IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol in mg/dl</td>
<td>0.34**</td>
<td>0.3028*</td>
</tr>
<tr>
<td>Triglyceride in mg/dl</td>
<td>0.3439**</td>
<td>0.2766*</td>
</tr>
<tr>
<td>HDL-Cholesterol in mg/dl</td>
<td>-0.2675*</td>
<td>-0.2365*</td>
</tr>
<tr>
<td>LDL Cholesterol in mg/dl</td>
<td>0.3253**</td>
<td>0.2945*</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.005 by Pearson correlation coefficient.

DISCUSSION:
Metabolically triggered inflammation, a key step in the pathogenesis of diabetes mellitus which accelerates atherosclerosis and premature death in subjects with diabetes [15]. The increased frequency of traditional risk factors such as obesity, dyslipidaemia, hypertension which might be attributed from atherosclerosis in diabetes [16]. Recent research has shown few novel disease related risk factors which may account for increased frequency of T2DM includes - Pro inflammatory cytokines and C-Reactive Protein, an acute phase reactant [17]. Interaction between the inflammatory response and disrupted lipid homeostasis has been the focus of research aiming at understanding the development of T2DM [18].

In the present study, the relationship between lipid profile and inflammatory markers – C-Reactive Protein and Interleukin 6 in Type 2 Diabetes mellitus was studied. Results from the present study confirmed previously reported associations between lipid levels and inflammatory markers [18, 19, 20]. Interleukin 6 and C Reactive Protein has shown positive correlation with total cholesterol, triglyceride, LDL Cholesterol and negatively correlated with HDL-Cholesterol. This is in accordance to the observations of Namita et.al [21] which showed significant positive correlation of total cholesterol, triglyceride, LDL cholesterol and significant negative correlation of HDL-cholesterol with C-Reactive Protein and Interleukin 6. Few studies have also demonstrated strong independent positive correlation of serum CRP with dyslipidaemia [22,23,24].

Duggirala et al study observed significant positive correlation between C Reactive Protein and Total cholesterol, triglyceride, LDL cholesterol and significant negative correlation with HDL-cholesterol [19]. Consistent with the findings, the present study observed a significant association among lipid levels and inflammatory markers in type 2 diabetes mellitus. Noruyuki et al [25] study mentioned that the association between inflammatory markers and lipids has been shown to be a risk factor not only for the development of atherosclerosis but also for cardiovascular disease in type 2 diabetes mellitus.

CONCLUSION:
The study concludes that there is a strong association between the lipid profile and inflammatory markers in type 2 diabetes mellitus. Since elevated levels of CRP and IL-6 is positively correlated with lipid profile, the changes may be related the degree of severity of the disease and hence may serve as markers of complications in type 2 diabetes.

REFERENCE:
2) Angelo CD, Areeg SF, Hani YZ, Badreldin EA. C-reactive protein is associated with low-density lipoprotein cholesterol and obesity in type 2 diabetic Sudanese. Diabetes, Metab. Syndrome and Obesity: Targets and Therapy, 2015;8:427-435
19) D.Rajarajeswari, J.N.Naidu and B.Sowjanya. Association of dyslipidemia and inflammatory


