The Relationship Between IL-10 and Dislipidemia in Type 2 Diabetics

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The current study was designed to estimate the differences in serum interleukin–10 (IL-10) levels in patients with type II diabetes and control group also to demonstrate whether a relationship was indicated among IL-10 and the changes in the levels of lipid and lipoproteins (dyslipidemia) in the same patients. To achieve this aim, 49 diabetic patients (21 females and 28 males) at ages of 47.23±14.23 y were enrolled. To compare the results, 30 healthy individuals (17 females & 13 males) of ages 39.35± 3.89 y were also included as a control group. Serum IL-10 levels were measured in the patients & the control group by an enzyme linked immunosorbent assay (ELISA).

Fasting blood glucose level (FBGL) was estimated by the glucose-oxidase method. Total cholesterol, triglyceride and HDL were measured by colorimetric method. The results revealed significantly (P<0.001) decreased of serum IL-10 levels in diabetic patients when compared with those of the control group. Total cholesterol, triglycerides, LDL and VLDL values exhibited significantly (P<0.005-0.0001) elevation in the diabetic patients when compared with those of control group. While HDL level significantly (P<0.0001) decreased in diabetic patients in comparison with those of control group. The linear regression analysis revealed a significant negative correlation for cholesterol (r =-0.45, P<0.001), triglycerides (r =-0.37, P<0.05), LDL (r=-0.30, P<0.05) & VLDL(r=-0.37, P<0.05) level and positive correlation HDL (r=0.49, P<0.001) levels with the IL-10 values in the diabetic patients. Such correlation was not observed for the level of cholesterol, HDL and LDL in control group. Serum IL-10, Total cholesterol, triglycerides &HDL levels were shown to be significantly (r=-0.51, P<0.001, r=0.65, P<0.001, r=0.58, P<0.001, r=-0.49, P<0.05), correlated with FBGL in the diabetic patients but not in control group. In conclusion, low level of IL-10 could be involved in pathogenesis of type 2 diabetes and there is association between IL-10 and dyslipidemia in these patients.

INTRODUCTION

Diabetes mellitus (DM), due to its growing incidence, is today a global epidemic. DM is a chronic and evolutive pathological process involved in
metabolic disorders of various nutrients and is characterized by defects of insulin secretion, insulin action or both, with resulting hyperglycemia [1].

It has been suggested that the type 2 diabetes is manifestation of the inflammatory host response. This host response is orchestrated by production of pro and anti-inflammatory cytokine that are under genetic control [2].

IL-10 is a protein product of T helper 2 (Th2) subset cells, macrophage, and hepatocyte. The protein is synthesized as a 178 amino acid precursor and secreted as a 160 amino acid glycoprotein with molecular weight of about 18 kd. IL-10 forms a 35-to 40 –kd homodimer when secreted under physiologic condition. The principal action of IL-10 is to inhibit T cell-dependent immune response [3] that was originally described as a “cytokine synthesis Inhibitory factor” IL-10 inhibits the production of many cytokines implicated in diabetes mellitus including IL-6 and TNF-α [4- 8].

Anti-inflammatory mechanisms might play a protective role against the development of insulin resistance in apparently healthy human[9]. IL-10 at least partly represents the effect of an anti-inflammatory response on the type 2 diabetes and metabolic syndrome [10]. These findings suggest that Th2- type cytokines, particularly IL-10 may have a central role in the control of the disease process . We therefore propose that low IL-10 production capacity is associated with the type 2 diabetes and metabolic syndrome.

In type 2 diabetes mellitus lipid abnormalities are almost the rule. Nowadays frequency of diabetes mellitus is increasing many folds. Research findings show that it is the body composition components, mainly body fate and lipid profiles that are responsible for increase prevalence of this disease [11-13]. In conclusion there is association between low IL-10 level and FBGL in type 2 diabetes and dyslipidemia.

**MATERIALS AND METHODS**

Forty nine patients of type 2 diabetes mellitus were selected randomly, in this study. The patients routinely visited the Specialized Center for Endocrinology and Diabetes – AL-Kindy teaching hospital in Baghdad during January-February 2010. They were 21 females and 28 males. Their mean age was 47.23±14.23y with a range of 23-65 y. The control group consisted of 30 healthy individuals (17 females & 13 males) their mean ages 39.35± 3.89 y with a range 27-50 y. Serum was collected from each blood sample and preserved at -20 C° until analysis. Serum IL-10 level was estimated by an enzyme linked immunosorbent assay (ELISA). Fasting blood glucose level was measured by glucose oxidase method. Total cholesterol, triglyceride and HDL were measured by colorimetric method. Patients with a history of
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myocardial infarction, stroke, and cancer (determined by questionnaire) were excluded.

Statistical analysis

Data analyses were carried out using the statistical package for social sciences (SPSS version 10). The results were expressed as (mean ± SD) and analyzed by the use of independent t-test which was done for the comparison of two groups. The differences were considered significant when P value was <0.05. Pearson's correlation analysis of the data was made by using the statistical program.

RESULTS AND DISCUSSION

The results of determination of IL-10 levels demonstrated significant (P<0.001) decreased in diabetic patients when compared with those of the control group. FBGL, total cholesterol, triglycerides, LDL and VLDL levels exhibited significantly (P<0.005-0.0001) elevation in the diabetic patients when compared with those of control group. While HDL level significantly (P<0.001) decreased in diabetic patients when compare with those of control subjects (Table1). The association between IL-10 level and dyslipidemia were clarified by linear regression analysis. A significant correlation was found for total cholesterol(r =-0.45, P<0.001) triglycerides (r =-0.37, P<0.05), HDL (r=0.49, P<0.001), LDL (r=-0.30, P<0.05), & VLDL(r =-0.37, P<0.05) levels, with the IL-10 values in the diabetic patients such correlation was not observed for the level of cholesterol, HDL and LDL in control group. (Table 2 and fig 1, 2, 3, 4, 5)

Further conformation of the relationship between IL-10, total cholesterol and triglycerides levels with the FBGL values was demonstrated by the linear regression analysis. A significant correlation (r =-0.51, P<0.001), (r =0.65, P<0.001), (r =0.58, P<0.001) & (r =-0.49, P<0.01), for IL-10, total cholesterol, triglycerides & HDL levels were observed with FBGL magnitudes in the diabetic patients, but not in the control group (Table 3 & Fig 6, 7, 8, 9).

The cross sectional nature of the relation between low IL-10 level and lipid and glucose metabolism is one limitation of our study. It is tempting to speculate that the association is between IL-10 and type 2 diabetes. However, on the basis of previous findings on might hypothesize that high level of IL-10 should theoretically cause an up regulation of tyrosine kinase activity of the insulin receptor and decrease lipolysis by counter regulating the effect of TNF-α and IL-6 [14-18]. Therefore, high IL-10 production could confer protection against the type 2 diabetes and metabolic syndrome,
whereas a low IL-10 production capacity would predispose one to the type 2 diabetes and metabolic syndrome.

It might be premature to make solid conclusion regarding the role of cytokines in lipid metabolism, nevertheless, adding the external environmental factors such as food intake and lifestyle, we hypothesize that genotypes of cytokine genes might be one of the internal factors which affects lipid metabolism [19].

In diabetes many factors may affect blood lipid levels this is because carbohydrates and lipid metabolism are interrelated to each other if there is any disorder in carbohydrate metabolism. It also leads disorder in lipid metabolism so there is high concentration of cholesterol and triglycerides and due to this there is reduction in HDL cholesterol level in diabetes. Additionally, Insulin has an effect on lipid metabolism. Insulin deficiency causes excessive metabolism of free fatty acids this may be lead to disorder in lipid metabolism in type 2 diabetes [20, 21].

Our data suggests that anti inflammatory mechanism might play a protective role against the development of insulin resistance in apparently healthy humane.

Table -1: Serum IL-10, Cholesterol, Triglyceride ,HDL,LDL, &VLDL levels in diabetic patients & control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>group</th>
<th>Mean±SD</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBGL (mmol/L)</td>
<td>Control</td>
<td>5.09 ± 0.67</td>
<td>3.70 – 6.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>10.15 ± 2.00</td>
<td>7.30 – 16.00</td>
<td></td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>Control</td>
<td>156.07 ± 37.71</td>
<td>104.98 -234</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>75.97 ± 4.96</td>
<td>66.23 – 92.44</td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>Control</td>
<td>4.05 ± 0.61</td>
<td>2.80 – 5.00</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>6.73 ± 1.23</td>
<td>5.20 – 9.70</td>
<td></td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>Control</td>
<td>1.47 ± 0.40</td>
<td>1.00 – 2.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>2.76±0.96</td>
<td>1.30 – 4.80</td>
<td></td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>Control</td>
<td>1.51±0.20</td>
<td>1.20 – 20</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Patient</td>
<td>1.06±0.097</td>
<td>0.96 – 1.30</td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Patient</th>
<th>Control</th>
<th>Patient</th>
<th>P- value</th>
<th>Control</th>
<th>Patient</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mmol/L)</td>
<td>1.87±0.48</td>
<td>4.381±1.07</td>
<td>0.91 - 2.70</td>
<td>2.25 – 6.56</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL (mmol/L)</td>
<td>0.67±0.2</td>
<td>1.24±0.55</td>
<td>0.45 – 1.23</td>
<td>0.59 – 2.18</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table -2 : The correlation coefficient of serum IL-10, with Cholesterol, Triglyceride, HDL, LDL & VLDL levels of diabetic patients and the control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetic patients</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P- value</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>-0.45</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>-0.37</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>0.49</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>-0.30</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>VLDL (mmol/L)</td>
<td>-0.37</td>
<td>P&lt;0.05</td>
</tr>
</tbody>
</table>

Table -3: The correlation coefficient of FBGL with IL-10, cholesterol, triglyceride levels of diabetic patients and the control group & HDL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetic patients</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P- value</td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>-0.51</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>0.65</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>0.58</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>-0.49</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>
Fig. -1: The correlation of serum Cholesterol level with IL-10 level in A: diabetic patients and B: control group

$r = -0.37$
$p<0.05$

Fig. -2: The correlation of serum Triglyceride level with IL-10 level in A: diabetic patients and B: control group

$r = 0.05$
$p<0.80$

Fig. -3: The correlation of serum HDL level with IL-10 level in A: diabetic patients and B: control group

$r = -0.45$
$p<0.001$
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**Fig. -4:** The correlation of serum LDL level with IL-10 level in A: diabetic patients and B: control group

**Fig 5:** The correlation of serum VLDL level with IL-10 level in A: diabetic patients and B: control group
Fig 6: The correlation of IL-10 level with FBGL in A: diabetic patients and B: control group

Fig 7: The correlation of cholesterol level with FBGL in A: diabetic patients and B: control group
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Fig 8: The correlation of triglycerides level with FBGL in A: diabetic patients and B: control group

Fig 9: The correlation of HDL level with FBGL in A: diabetic patients and B: control group

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