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Serum Interleukin 17 in Type 2 Diabetes Mellitus

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Background: The type 2 diabetes mellitus (T2DM) may alter the function of immune cells and produce inflammation, which is chronic, low grade and associated with insulin resistance

Objectives: The aim of this study was to compare interleukin 17 (IL-17) level in T2DM and healthy control, and evaluate the relationship between IL-17 and anthropometric and laboratory characteristics of diabetic patients.

Patients and Methods: A case-control study was carried out on 32 patients with T2DM (16 males and 16 females, aged 52.1 ± 8.0 years) who were hospitalized in Imam Reza hospital of AJA University of Medical Sciences for diabetes side effects, and 29 healthy control individuals (15 males and 14 females, aged 48.0 ± 8.6 years). Fasting blood sugar (FBS) was assessed colorimetrically by the GOD-POD method, and serum insulin and IL-17 levels were measured by ELISA method. Statistical analysis of the Student's t-test and Pearson correlation coefficient were used.

Results: The serum concentration of IL-17 was significantly higher in the patients with T2DM than in the controls (P = 0.002). It was also significantly higher in both male (P = 0.048) and female (P = 0.003) patients with T2DM than in their related controls. It was also significantly higher in the female than the male T2DM patients (P = 0.001). IL-17 level significantly correlated with age (r = 0.495, P = 0.001), body max index (BMI) (r = 0.347, P = 0.014), fasting blood sugar (r = 0.335, P = 0.043), insulin resistance (r = 0.338, P = 0.043), waist circumference (r = 0.329, P = 0.029) and insulin (r = 0.36, P = 0.025).

Conclusions: It seems that patients with T2DM - especially females - have significantly higher IL-17 level and it correlates with age, insulin resistance, FBS, BMI and waist circumference.

Keywords: Interleukin 17; Diabetes Mellitus; Insulin Resistance

1. Background

Type 2 diabetes mellitus (T2DM) is estimated to affect millions of people around the world. The etiology of T2DM is not yet completely understood. However, it has been shown that a relation exists between incidence of diabetes mellitus and stress. Stress hormones such as glucagon, catecholamines, cortisol and Growth Hormone secretion increase during the stress and emotional stimuli. Some of these hormones are diabetogenic and might be involved in the development of diabetes during the stress.

Military personnel are exposed to a variety of stressors. T2DM may alter the function of immune cells and produce inflammation, which is chronic, low grade and associated with insulin resistance (1-5). Monocytes constitutively and inducibly secrets elevated levels of interleukin (IL)-6, IL- 8, tumor necrosis factor (TNF)-α and IL-1β in T2DM patients (1, 6, 7). Furthermore, B-cells secret elevated levels of IL-8 and decreased levels of the anti-inflammatory cytokine such as IL-10 in T2DM patients (7). Recent studies have been demonstrated that T- helper cells 17, as a subset of CD4+ T-cells, has an important role in the development of autoimmunity in animal and human models of diabetes mellitus (8, 9). T-helper cells 17 produce IL-17. The IL-17 family of cytokines has been implicated in the pathogenesis of inflammatory conditions, including rheumatoid arthritis, psoriasis and systemic sclerosis (10-12). This cytokine promotes inflammation through a widely expressed family of IL-17 receptors (7, 13). In addition, it has been shown that proinflammatory and inflammatory cytokines, such as IL-6, IL-1β and TNF-α, can exacerbate insulin resistance (14).

2. Objectives

As yet, there are a few studies about relationship of pro-inflammatory cytokine IL-17 with anthropometric such as body max index (BMI) and waist circumference, and with laboratory characteristics of diabetes mellitus (insulin, insulin resistance, and fasting blood sugar) in T2DM. Given these observations, we hypothesized that the level of IL-17 is high in these patients and correlates with anthropometric and laboratory characteristics of diabetes mellitus.

3. Patients and Methods

3.1. Subjects

The protocol was approved by the ethics committee of AJA University of Medical Sciences, Iran, and all subjects gave informed consent before participation in the study. This study was designed as a case-control survey in Imam Reza Hospital of AJA University of Medical Sciences to investigate the serum IL-17 level in patients with diabetes mellitus and apparently healthy people. In this study, blood sample were obtained from 32 patients with diabetes mellitus and 29 individuals without diabetes. Patients who were hospitalized for the side effects of diabetes mellitus and fasting blood sugar (FBS) over 134 mg/dL were considered as the case group. Age- and sex-matched healthy control subjects were selected from hospital staff or individuals who accompany with patients referred to the hospital. All subjects met the following criteria: no history of liver, respiratory, thyroid diseases or other illness and any current infectious condition. They were not on any drug therapy except drugs for controlling of diabetes.

3.2. Sample Collection

Fasting blood collection was carried out on the morning. Blood specimens were obtained by venipuncture, collected in 10-mL glass vacuum tubes without additive, and allowed to clot. Upon completing sample collection, blood was centrifuged at 2000 g for 10 minutes, and then the serum was isolated and stored at -70° C for later analysis of glucose, IL-17 and insulin.

3.3. Determination of Anthropometric Data

Anthropometric measurements (body height and weight and waist circumference) were performed by trained personnel, with the participants wearing only light underwear and without shoes. BMI was calculated as body weight (in kilograms) divided by body height (in meters) squared. Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest with the subject standing at the end of normal expiration.

3.4. Analysis of serum

Serum glucose concentration was assessed colorimetrically by the GOD-POD method using affiliated kits (Pars azmoon, Karaj, Iran). Serum insulin concentration was analyzed by ELISA technology using commercially available kits (Monobind, Inc. Lake Forest, CA, USA). IL-17 level was measured by commercial ELISA kit (eBioscience, San Diego, CA). Insulin resistance value were calculated using the homeostasis model assessment, HOMA- IR, as fasting insulin (IU/L) × fasting glucose (mmol/L) /22.5 as previously reported by Matthows (15).

3.5. Statistical Analysis

The data are presented as a Mean ± SD (standard deviation of mean). The two-tailed student's unpaired t-test and Pearson correlation were used as statistical analysis. A p-value of < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 18 for windows.

4. Results

A total of 32 diabetic patients (16 males and 16 females, aged 52.1 ± 8.0) and 29 healthy individuals (15 males and 14 females, aged 48.0 ± 8.6) participated in the study. There were no significant differences between groups regarding sex (P = 0.592) and age (P = 0.128). Anthropometric and laboratory characteristics of diabetic and non-diabetic individuals are summarized in Table 1. As expected, the mean concentration of fasting blood sugar (FBS) was significantly higher in the patients with T2DM compared with controls (P = 0.001). FBS was significantly higher in the both male (P = 0.008) and female (P = 0.001) patients with T2DM than in their related controls. The serum concentration of insulin proved to be significantly higher in the patients with T2DM than in the controls (P = 0.005). It was also significantly higher in the both male (P = 0.041) and female (P = 0.036) patients with T2DM than in their related controls. The insulin resistance was also significantly lower in the controls than in the patients with T2DM (P = 0.002). It was also significantly higher in the both male (P = 0.01) and female (P = 0.008) patients with T2DM than in their related controls. The waist circumference and BMI were significantly higher in the patients with T2DM than in the controls (P = 0.001). They were also significantly higher in the both male and female patients with T2DM than in their related controls. In addition, BMI was significantly higher in the female diabetic patients than the male diabetic patients (P = 0.01; Table 1). The serum concentration of IL-17 proved to be significantly higher in the patients with T2DM than in the controls (P = 0.002). It was also significantly higher in the both male (P = 0.048) and female (P = 0.003) patients with T2DM than in their related controls. It was also significantly higher in the female (6.8 ± 4.2) than the male (3.1 ± 2.5) T2DM patients (P = 0.001; Table 1). IL-17 level significantly correlates with age (r = 0.495, P = 0.001), BMI (r = 0.347, p = 0.014), fasting blood sugar (r = 0.335, p = 0.043), insulin resistance (r = 0.338, P = 0.043), waist circumference (r = 0.329, P = 0.029 and insulin (r = 0.36, P = 0.025) (Table 2).

5. Discussion

In this study, the relationship of serum IL-17 level with anthropometric and laboratory characteristics of diabetes mellitus in human T2DM were investigated. The present study showed that IL-17, insulin, insulin resistance, fasting blood sugar, waist circumference and BMI

Table 1. Anthropometric and Laboratory Data of Diabetic Patients and Control Healthy Participants [a,b]

Variable	Healthy Control	Type 2 Diabetes	P Value
Fasting blood sugar, mg/dL	95.1 ± 5.9	166.1 ± 60.5	0.001
Male	96.9 ± 5	149.3 ± 67.7	0.008
Female	93.16.3 ± 6.3	182.5 ± 48.8	0.001
Insulin, μIU/mL	91 ± 7.9	27.7 ± 24.3	0.005
Male	10.9 5.3	30.4 ± 24.6	0.041
Female	9.2 ± 8.8	24.1 ± 20.5	0.036
Insulin resistance	2.09 ± 1.95	11.1 ± 10.8	0.002
Male	2.13 ± 1.2	14.2 ± 12.6	0.010
Female	2.07 ± 2.36	6.8 ± 6.4	0.008
IL-17, pg/mL	1.95 ± 2.13	5.01 ± 3.92	0.002
Male	1.52 ± 1.2	3.1 ± 2.5	0.048
Female	2.35 ± 2.7	6.8 ± 4.2	0.003
Waist circumference, cm	83.2 ± 5.2	88.2 ± 5.1	0.001
Male	84.5.3 ± 3.5	88.3 ± 5.9	0.048
Female	81.4 ± 5.5	88.1 ± 4.2	0.001
BMI, kg/m^2	25.6 ± 2.8	28.1 ± 3.1	0.001
Male	25.22.4 ± 2.4	26.1 ± 2.3	0.001
Female	25.9 ± 3.1	30.1 ± 2.3	0.001

[a] Abbreviations: BMI: body max index; IL-17, Interleukin 17.
[b] Data are presented as Mean ± SD.

Table 2. Correlation of Serum IL-17 With Serum Insulin and FSB and With Insulin Resistance, BMI, Waist Circumference and Age in Type 2 Diabetes Mellitus [a]

Insulin	Insulin Resistance	FSB	BMI	Waist Circumference	Age
IL-17					
r = 0.36	R = 0.338	r = 0.335	r = 0.347	r = 0.329	r = 0.495
P = 0.025	P = 0.043	P = 0.043	P = 0.014	P = 0.029	P = 0.001

[a] Abbreviations: FBS: Fasting blood sugar; BMI: body max index; IL-17, Interleukin 17.

were significantly higher in the diabetic patients than in the controls. IL-17 and BMI was also significantly higher in female than male. Moreover, IL-17 significantly correlates with insulin, insulin resistance, fasting blood sugar, waist circumference, BMI and age. However, these correlations were moderate. Serum FBS and insulin concentrations and also insulin resistance were higher in patients with diabetes mellitus than in the individuals without diabetes which are in agreement with other studies (16, 17). The National Institutes of Health reported that 45.7% of diabetics were obese, and 78.5% were overweight (18). In addition, it has been shown that waist circumference and BMI - as the obesity markers - are the major risk factor of developing diabetes (19, 20). These are supported by our study, which we showed that the waist circumference and BMI were significantly higher in the diabetic patients than in the control individuals. It has been shown that the blood level of IL-17 increases in obesity (21) and it is higher in diabetic patients (22). In addition, it has been indicated that IL-17 positively correlates with waist circumference and BMI (23). These are in agreement with our results that IL-17 significantly correlated with BMI and waist circumference and it was significantly higher in the diabetic patients than in the controls. Moreover, serum IL-17 was significantly higher in the female diabetic patients than in the related controls. This is supported by Kandeel et al. reports (23). Also, the results of our study corroborate the rise in serum IL-17 level in the male diabetic patients as compared to the non-diabetic males. IL-17 was also significantly higher in the diabetic females than in the diabetic males. As BMI was also significantly higher in the diabetic females than the diabetic males, it seems that the higher level of IL-17 in females may be due to the high level of BMI in the diabetic females. In consistence with the previous studies (7, 22) results of this study showed a significant positive correlation between Il-17 level and age. A number of studies have reported a positive correlation between serum IL-17 and

glucose levels (23, 24). Similar to these report, in our study IL-17 correlated with FBS. Our results also showed that there was a significant positive correlation between IL-17 and insulin resistance and also insulin level. It has been shown that IL-17 inhibits glucose uptake in vitro and impairs glucose and insulin metabolism in metabolic syndrome and diabetes in young mice (25). IL-17 induces expression of IL-6. IL-6 is known to induce insulin resistance in vitro and in vivo (26). It seems that patients with type 2 diabetes mellitus, especially females, have significantly higher IL-17 level and IL-17 correlates with age, insulin resistance, FBS, BMI and waist circumference.

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Authors' Contributions

All authors contributed in the analysis and interpretation of the data, drafting the article and revising it, and gave final approval of the version to be published.

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