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ORIGINAL ARTICLE

Tumor Necrosis Factor Alpha is not affect by Type II diabetes in Obese Individuals

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ABSTRACT
Recent evidence has demonstrated chronic systemic inflammation in both obesity and type II diabetes, although the molecular mechanisms for this are less understood. In present study, we aimed to compare serum Tumor necrosis factor alpha (TNF-α) between adult obese men with and without type 2 diabetes (T2D). A total forty four sedentary adult obese men with T2D (n=24) and without T2D (n=24) matched for age (43 ± 4 year of old) and body mass index (31 ± 2 kg/m2) were participated in this study. Fasting blood samples were collected for measuring glucose, insulin and serum TNF-α in two groups. All anthropometrical markers were also measured. All subjects were asked to avoid any serious physical activity 48 before blood samples. Comparisons between the means of each group were done using the independent t-test. There were no statistically significant differences between the non-diabetic and diabetic rats with regard to the anthropometrical parameters (P > 0.05). We also observed that serum TNF-α was not difference between diabetes and non-diabetes subjects (p ≥ 0.005). Based on these data, we can say that serum TNF-α does not affect by T2D in obese individuals.

Keywords*: Obesity, Type II diabetes, Glucose, Tumor necrosis factor alpha*

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INTRODUCTION

Undoubtedly, impaired insulin secretion and insulin resistance are the main causes of diabetes disease; however, other internal and environmental factors are involved in incidence of this disease. Meanwhile, obesity, nutritional behaviors and reduced physical activity are considered as the main environmental factors involved in prevalence of this disease. However, it should not be ignored that the peptides secreted from adipose tissue and inflammatory cytokines secreted from adipose tissue and other tissues are also involved in prevalence of diabetes, especially in obese patients and those with high lipid levels [1]. These factors alongside sedentary lifestyle in obese individuals play an important role in increasing severity of the disease and other obesity-related diseases [2].

Among inflammatory cytokines, tumor necrosis factor alpha plays an important role in development of metabolic disorders such as obesity and insulin resistance [3]. Tumor necrosis factor alpha (TNF-α) is synthesized and secreted mainly by adipose tissue. Furthermore, macrophages are involved in production of this cytokine. It is observed that there is a significant association between systemic levels of TNF-α and cardiovascular risk factors such as blood triglyceride levels [4]. This inflammatory cytokine has multiple functions such as cardiac hypertrophy and impaired contractile function [5]. It is reported that TNF-α levels are 7.5 times more in obese subjects compared to the subjects with normal body weight [6]. Researchers also confirmed increased production of VLDL by TNF-α, which justifies the relationship between this cytokine and TG [7]. It is known that muscle protein synthesis is inhibited by higher levels of this inflammatory cytokine [8, 9, 10].

On the other hand, several studies reported increased levels of this inflammatory cytokine in both diabetic obese [11] and non-diabetic obese subjects [12]. Since type 2 diabetes results from obesity and most diabetic patients are obese, it is wondered whether diabetes independently affect TNF-α levels apart from the obesity or obesity increases levels of TNF-α in obese compared to normal weight subjects. In this

context, few studies have compared baseline levels of this inflammatory cytokine in obese diabetic and non-diabetic subjects. Hence, the present study aimed to compare serum levels of TNF-α in obese diabetic and non-diabetic obese subjects.

MATERIAL AND METHODS

Human Subjects and study inclusion: In this semi-experimental study, a total forty four sedentary adult obese with (n=24) and without (n=24) T2D matched for age (43 ± 4 year of old), height (174 ± 3 cm) and BMI (31 ± 2 kg/m2) were recruited in study through an accessible sampling. All variables were non-smokers, non-athletes and non-alcoholic. After the nature of the study was explained in detail, informed consent was obtained from all participants. All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months. Those with other chronic disease such as asthma, kidney, cancer and heart disease were excluded. Those patients unable to avoid taking hypoglycemic drugs or other therapeutic drugs within 12 hours before blood sampling were excluded.

Anthropometrics: All anthropometric measurements were made by the same trained general physician and under the supervision of the same pediatrician following standard protocols. Each subject's body mass and height were measured. Weight was measured to the nearest 100 g using digital scales. Standing height was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer. Abdominal obesity was determined as waist circumference measured in a standing position. Hip circumference was measured at the maximum circumference between the iliac crest and the crotch while the participant was standing and was recorded to the nearest 0.1 cm. Obesity was measured by body mass index (BMI). BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m2). Resting blood pressure (BP) levels were measured in the right arm with a cuff sphygmomanometer after a participant had been resting for 10 min.

Blood sampling and analyses: Subjects attended human lab on one morning at 08.00 a.m and fasting venous blood was collected from subjects. All participants refrained from any severe physical activity 48 h before measurements. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Blood samples were dispensed into EDTA-coated tubes and centrifuged for 10 minutes in order to separate serum. Serum insulin was determined by ELISA method (Demeditec, Germany). The homoeostasis model assessment (HOMA) for estimating insulin resistance and insulin sensitivity was calculated of fasting glucose and insulin [13]. Serum TNF-α was determined by ELIZA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human TNF-α). The sensitivity of the TNF-α assay was 5.0 Pg/mL.

Data analysis: Data were analyzed by computer using the Statistical Package for Social Sciences (SPSS) for Windows, version 15.0. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. Comparisons between the means of each group were done using the independent t-test. The differences between the groups were considered to be significant at a p-value of ≤ 0.05.

RESULTS

As mentioned above, in this study we compared serum TNF-a between adult males with type II diabetes with those with no-diabetes symptom. All variables represented by mean and standard deviation.

Table 1 shows the descriptive anthropometric of the study groups. Based on these data, we observed no significant difference between all anthropometrical markers between two groups (p ≥ 0.05). These data showed that all of subjects in two groups are obese.

Table 1: Mean and standard deviation of anthropometric characteristics of studied group.

Variables	Non-asthmatic	Asthmatic
Age (year)	42.8 ± 4.1	41.4 ± 3.03
Height (cm)	173 ± 3.5	175 ± 3.4
Weight (kg)	94.1 ± 5.4	95.8 ± 5.2
Systolic Pressure (mmHg)	135 - 12	165 ± 17
Diastolic Pressure (mmHg)	87 ± 8	91 ± 9
Waist circumference (cm)	106 ± 6	104 ± 4
Hip circumference (cm)	104 ± 4	102 ± 4
WHO	1.02 ± 0.02	1.02 ± 0.02
Body mass index (kg/m^2)	31.3 ± 1.62	31.2 ± 0.62
Body Fat (%)	31.1 ± 1.14	31.7 ± 1.16

Table 2 presents the circulating, fasting concentrations for glucose, insulin and serum TNF-a as well as insulin resistance and insulin sensitivity in studied group. Based on data of independent T test, no significant difference was sowed in serum TNF-a between two groups (p = 0.374).

Table 1: Mean and standard deviation of clinical characteristics of studied groups.

Variables	Diabetes subjects	Healthy subjects
Insulin (μIU/ml)	8.31 ± 1.17	8.55 ± 1.83
Fasting glucose (mg/dl)	221 ± 43	100 ± 6
Insulin resistance (HOMA-IR)	4.48 ± 0.87	2.11 ± 0.46
Insulin sensitivity (HOMA-IS)	0.50 ± 0.02	0.60 ± 0.04
Beta cell Function (HOMA-BF)	20.4 ± 6.25	85.1 ± 25
Tumor necrosis factor-alpha (pg/ml)	38.3 ± 5.35	36.8 ± 6.19

DISCUSSION

Clinical studies consistently addressed that inflammatory markers are associated with insulin resistance and type 2 diabetes [14, 15]. However, it is recently addressed that type 2 diabetes is a disease associated with inflammation [16] because inflammatory markers are introduced as proper predictors of cardiovascular diseases [17, 18]. TNF-α is one important and effective cytokine among inflammatory or proinflammatory cytokines. This cytokine is mainly secreted by activated macrophages. In addition, several tissue macrophages are involved in secretion of systematic levels of this cytokine [19]. Most studies addressed increased levels of this inflammatory cytokine in presence of obesity [20]. In other words, researchers emphasized that obesity or increased body fat percentage determines serum or plasma levels of this cytokine [21]. Based on this evidence, it is concluded that obese individuals have higher levels of TNF-α as an inflammatory cytokine compared to those with normal weight.

Several studies reported increased levels of TNF-α in obesity-related disease such as cardiovascular diseases, type 2 diabetes and metabolic syndrome compared with healthy subjects or subjects with normal body weight [22]. Scientific studies addressed TNF-α as an important determinant of inflammation in diabetes [23]. Obesity ultimately leads to Type 2 Diabetes. In other words, most obese individuals are diabetic. In addition, it is reported that levels of TNF-α in both obese and diabetic subjects are higher than those with normal weight. However, it is not known that whether higher levels of this cytokine lead to obesity in these patients or presence of type 2 diabetes changes levels of this cytokine compared to healthy subjects. So far, most studies compared levels of this cytokine or other inflammatory cytokine among normal weight and obese subjects or between diabetics and non-diabetics subjects. Few studies compared levels of this cytokine or other inflammatory cytokine among obese diabetic and non-diabetic obese subjects. In this context, the findings obtained from this study showed that although higher levels of blood glucose and insulin resistance are observed in obese diabetics subjects compared to non-diabetics obese subjects, no significant difference was observed in levels of TNF-α between them. On the other hand, serum levels of TNF-α in both diabetic and non-diabetic obese subjects were the same as with each other.

Based on above materials, diabetic patients have higher levels of TNF-α compared to healthy subject [24]. However, scientific sources addressed that obese individuals, whether diabetic [11] or non-diabetic [12], have higher levels of TNF-α than those with normal weight. It is possible that TNF-α did not differ significantly between obese diabetic and non-diabetic subjects due to small sample size, which is one main limitations of the present study. Based on this evidence, it can be concluded that obesity in type 2 diabetes determines different levels of TNF-α in healthy subjects, not presence of type 2 diabetes in these patients. However, it is essential to conduct cellular and molecular studies to prove this theory further in the future.

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