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Serum TNF-α in sedentary obese and normal weight individuals

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ABSTRACT: Obesity is an established risk factor for type 2 diabetes, metabolic syndrome and cardiovascular diseases. This study aimed to compare serum TNF-α between obese and normal weight men. For this purpose, thirteen adult obese men aged 35 to 45 years and the same number normal weight adult men matched for age that were recruited to participate in this study. Serum TNF-α was measured after an overnight fast in subjects of two groups. All participants refrained from any severe physical activity 48 h before measurements. Differences between groups were calculated using the independent samples t-test. The level of significance was taken as $p<0.05$. TNF alpha serum levels were higher in obese than in normal weight individuals ($p=0.004$). This observation supports of obesity or overweight have a pivotal role in systemic inflammation and chronic diseases such as type II diabetes, metabolic syndrome or others.

Keywords: Inflammation. Obesity, Body mass index

INTRODUCTION

Nowadays, obesity is of prime significance for health science researcher as the most prominent non-contagious metabolic dysfunctions. The increasing growth of obesity and its hazardous consequences concomitant to societies' industrialization and changes in people's life style highlight the prevention and treatment of obesity as the main challenge for health system. Obesity is accompanied by many diseases such as cardiovascular diseases, diabetes type-2, and metabolic syndrome [1]. Aside from genetic factors, nutrition pattern and hormonal dysfunctions are also the main factors inducing chronic diseases in the presence of obesity [2, 3].

Scientific studies have frequently reported the increase of inflammatory cytokine's serum levels in fat individuals and respective diseases as compared to healthy individuals with normal weight (4, 5, 6]. Scientific references have always emphasized higher levels of inflammatory cytokines such as IL-6, CRP, TNF-α, leptin, and resistin yet lower levels of anti-inflammatory cytokines such as adiponectin and IL-10 in obesity-induced diseases including diabetes type 2 and cardiovascular diseases [7, 8, 9].

Among the mediators secreted by adipose tissue, although TNF-α – as a pre-inflammatory cytokine is firstly secreted by adipose tissue, it can also be produced by macrophages and other cells. For the first time, the relationship between obesity and the pre-inflammatory cytokine TNF-α and also its role in the relationship between obesity and inflammation were examined by Hotamisligil *et al* [10]. This cytokine plays a critical role in inflammation process. Its concentration increases can accelerate the synthesis of some interleukins such as IL-8 with special importance in the outbreak of arthrosclerosis process [11]. TNF-α acts as a gene expression regulator in adipose cells [12]. Since adipose tissue is one of the key sources of TNF-α production, the expression of cytokine in human's adipose tissue and muscle increases obesity outbreak [13, 14]. Based on scientific resources, TNF-α expression severely increases in the adipose cells of fat individuals and patients resistant to insulin [10]. TNF-α serum level and expression increase in fat individuals' adipose cells. Its serum level decrease is observed following weight loss [15]. Despite the abovementioned, there are also studies contributing to cytokines' indifference among fat individuals as compared to individuals with normal weight [16]. Their indifference in fat and normal individuals can be also observed in some other studies [17, 18]. Due to this conflict, the present study compares TNF-α serum levels in adult fat men versus men with normal weight. All of them have passive and still life style.

METHOD AND SUBJECTS

Participants included thirteen adult obese men aged 39 to 3 years and the same number normal weight adult men matched for age that were recruited through an advertisement in a local newspaper.

None of the subjects used drugs or therapies for obesity, and none had a past history of disease or injury that would prevent daily exercise. Participants were non-athletes, non-smokers and non-alcoholics. Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began.

Anthropometry and biochemistry: To measure serum TNF-α, subjects attended human lab on one morning at 08.00 h for documentation of their full history and a physical examination. Blood samples were collected, via the cannulated antecubital vein, between 8:00–9:00 a.m. after an overnight fasting for all subjects. All participants refrained from any severe physical activity 48 h before measurements. Blood centrifuged for 10 minutes in order to separate serum. Serum used to measure TNF-α by ELIZA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human TNF-α, Austria). Anthropometric measurements of height, weight, percent body fat, and circumference measurements were taken study. Weight and height were measured in the morning, in fasting condition, standing, wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m). Abdominal obesity and hip circumference were determined in a standing position at the end of normal expiration and ratio between them (AHO) was calculated for each subjects.

Statistical analysis: The data were reported as mean and standard deviation, and analyzed using the SPSSW statistical package, version 16.0)SPSS Inc., Chicago, IL, USA) for Windows W. All data were tested for normal distribution by the Kolmogorov-Smirnov test. Comparisons of parameters between the two groups were made by Fishes exact test or unpaired Student t test. A p value of less than 0.05 was considered as statistically signigcant.

RESULTS

The participants of present study were in to category based on anthropometrical markers included obese and normal weight groups and main objective was to compare serum TNF-α two groups. Anthropometric and metabolic characteristics of the study participants are described in Table 1. Based on statistical data, we observe that serum TNF-α in obese subjects was significantly higher that normal weight individuals (p = 0.004, Fig. 1).

Table 1: Mean and standard deviation of anthropometric and biochemical variables of studied groups.

Variables	Obese group	Normal weight group	P value
Age (year)	**39.2** *(2.83)*	**38.8** *(2.82)*	*0.682*
Weight (kg)	**94.4** *(7.7)*	**68.1** *(2.74)*	*0.250*
Height (cm)	**173** *(4.5)*	**172** *(2.5)*	*0.000*
Body Fat (%)	**31.9** *(1.3)*	**21.9** *(1.1)*	*0.000*
Body mass index (kg/m^2)	**31.4** *(1.8)*	**23** *(0.4)*	*0.000*
Abdominal circumference (cm)	**105** *(4.7)*	**87** *(2.5)*	*0.000*
Hip (cm)	**107** *(4.7)*	**95** *(3.3)*	*0.000*
Cholesterol (mg/dl)	**201** *(32)*	**183** *(52)*	*0.130*
Triglyceride(mg/dl)	**192** *(51)*	**143** *(54)*	*0.025*
Low density lipoprotein (mg/dl)	**134** *(27)*	**96** *(13)*	*0.000*
high density lipoprotein (mg/dl)	**46.7** *(3.8)*	**48** *(3.5)*	*0.347*
TNF-α (pg/ml)	**38.5** *(10.7)*	**28.1** *(5.1)*	*0.004*

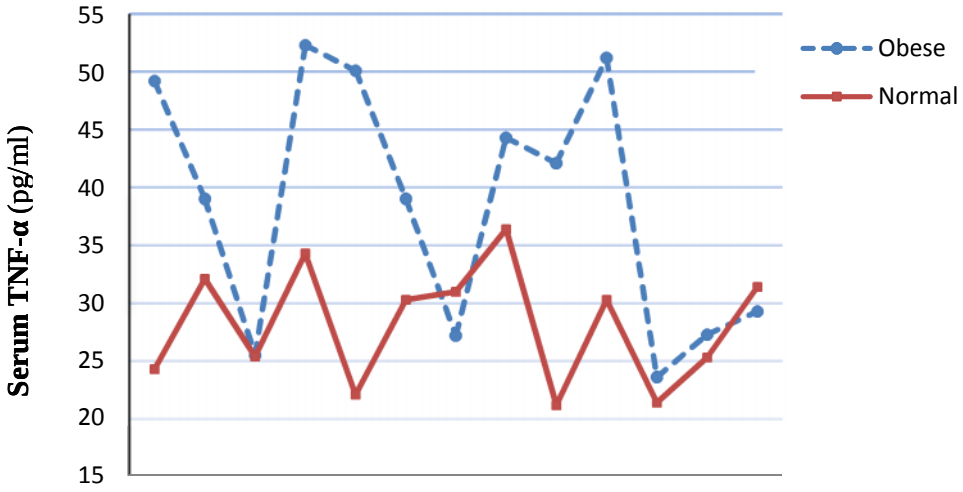

Fig. 1. Serum TNF-α in obese and normal weight subjects. This Fig shows that this pro-inflammatory cytokine is higher in obese than normal weight subjects.

DISCUSSION

Several studies have been studied concerning the basic levels of inflammatory or anti-inflammatory cytokines in fat individuals as compared to individuals with normal weight or healthy versus fat individuals. Most resources have implied higher levels of inflammatory cytokines in the presence of obesity [13]. In this regard, results of the present study also showed that fat men have higher levels of TNF-α as an inflammatory cytokine as compared to individuals with normal weight. They have emphasized the existence of systemic inflammation in fat individuals. Namely, results showed an increase of about %30 in fat men as compared to men with normal weight.

This %30 increase of inflammatory cytokines in fat diabetic individuals (versus fat non-diabetic individuals) is also reported before [19]. Based on studies regarding immunity function in the presence of obesity, the increase of adipose tissue levels is accompanied by immunity response dysfunction. Destructive effects of obesity on immunity system function are accompanied by the increase of systemic pre-inflammatory markers derived from adipose tissue [20]. Hence, concerning the key role of adipose tissue in inflammatory processes (especially, in obese individuals), extensive studies have always been administered aiming to determine the relationship between obesity mechanisms and systemic inflammation. Most present studies emphasize that obesity is related to many diseases such as diabetes type 2, cardiovascular diseases, and some cancers[1]. The effect of obesity on obesity-induced disease is complicated due to the interaction between genetic and metabolic factors [2, 3].

TNF-α is among proteins increased in the presence of obesity [21]. Accordingly, determining or measuring its gene expression can be one of the alternative genes for studying obesity, cardiovascular diseases, and other related diseases. Close relationship between the serum concentration of this inflammatory cytokine and systolic blood pressure increase is observed in a wide spectrum of Canadian fat citizens [22].

TNF-α accelerates lipolysis in adipose tissue. Its increase has destructive effect on both adipogenesis and lipogenesis. TNF-α decreases appetite in hypothalamus. It stimulates the secretion of catabolic corticotropin-releasing hormone. TNF-α increase the expression of genes involved in free fatty acids synthesis. Yet, it decreases the genes involved in fatty acids oxidation. TNF-α also increases hepatic insulin resistance by promoting insulin receptors' serine-phosphorylation followed by insulin signaling path. It also stimulates TNF-α secretion by liver. Finally, TNF-α increase is accompanied by immunity cells damage. It increases the inflammatory responses of macrophage and macrophage's phagocytosis [23]. TNF-α also plays a key role in obesity pathogenesis and insulin resistance (24]. This pre-inflammatory cytokine induces insulin resistance by means of destructing the signs of insulin receptors' mediators [25]. The negative regulation of genes required for insulin function, the negative regulation of genes directly affecting insulin function, and increasing free fatty acids by stimulating lipolysis are among other mechanisms introduced for TNF-α [26].

Weight loss in fat patients is accompanied by the reduction of this inflammatory mediator's production and insulin resistance decrease [15]. Human studies and also studies animal species have shown that TNF-α secretion increase by adipose tissue reduces insulin sensitivity [27, 28]. Changes in TNF-α expression in adipose tissue are directly related to obesity degree and hyperinsulinemia levels [13].

Recent studies have always emphasized the pathological role of TNF-α in arthrosclerosis. They have also implied that TNF-α serum levels can be taken as one of the biomarkers of identifying and determining the functional levels and cardiovascular diseases [29]. However, the extent to which inflammatory and anthropometric mediators can regulate TNF-α level in blood circulation is not completely identified, yet. TNF-α not only leads to the cellular death (apoptosis) of endothelial cells, but also induces vascular inflammation in arthrosclerosis [30]. Accordingly, clinical observations have implied that TNF-α level in blood circulation can be one of the biomarkers of cardiovascular diseases and also among the molecular objectives of preventing from the expansion of these abnormalities.

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