ORIGINAL ARTICLES

Interleukins 17 and 23 and Resistin Levels among Obese Diabetic Egyptian Female Patients

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ABSTRACT

Objectives: To assess serum Interleukin 17 and 23 and resistin levels and to evaluate their relationship with BMI, waist circumference in obese diabetic female patients. Subject and methods: Thirty five female diabetic patients were included in the cross sectional study. Controls included 20 age-matched healthy females of the same socioeconomic status. Serum glucose, total cholesterol triglyceride, high density lipoprotein cholesterol (HDL-C), The serum IL-17, IL-23 and resistin concentrations were determined, low density lipoprotein cholesterol (LDL-C) was calculated. Body weight, body height and waist circumference (WC) were measured. Body mass index was calculated. Results: Body mass index and waist circumference were significantly higher in diabetic females. Moreover triglycerides, low density lipoproteins, interleukin 17, interleukin 23 levels and resistin were significantly higher in diabetic females. A significant positive correlation was obtained between the biochemical parameters and anthropometric measurements. Also, blood glucose level was significantly correlated with proinflammatory cytokines as well as resistin. Conclusion: Understanding the inflammatory characterization of Proinflammatory cytokines (interleukin 17, interleukin 23 levels) and resistin might be of fundamental importance for the prevention and treatment of obesity and diabetes.

Key words: proinflammatory cytokine, interleukin 17, interleukin 23, resistin, obesity, diabetes, Egypt.

Introduction

Obesity and overweight have become major medical and social problems, so it is necessary to fully understand the mechanisms and comorbidities involved. Obesity is defined as having a body mass index (BMI) more than 30 kg/m2, while overweight is indicated by a 25- to 30-kg/m2. BMI levels are increasing worldwide with obesity and overweight together accounting for two-thirds of the population in developed countries (Gislette, and Chen, 2010). In Egypt, it is a growing problem as two-thirds of women aged 15-59, and more than half of all men in the same age group, are overweight or obese (El-Zanaty, and Way, 2009). Obesity has been associated with many comorbidities, including hypertension, diabetes, hypercholesterolemia, and heart disease.

Abdominal adiposity is a risk factor for obesity-related complications, and there is increasing evidence that abdominal adiposity may be a contributing factor to complications (Hu et al., 2011; Recio et al., 2012). Waist circumference and waist-to-hip ratio are commonly used measures for estimating abdominal adiposity (Chen et al., 2007; Coutinho et al., 2011). Inflammatory mediators have a surprising impact in obesity (Zúñiga et al., 2010). The increase in proinflammatory cytokine production has been recognized as an important marker of obesity and accompanying metabolic changes (Gislette, and Chen, 2010). Fain, 2006 cited that human adipose tissue is a potent source of inflammatory interleukins plus other cytokines and that the majority of this release is due to the nonfat cells in the adipose tissue except for leptin and adiponectin that are primarily secreted by adipocytes.

Moreover, Resistin is a protein hormone secreted by adipocytes, which leads to insulin resistance (IR) in vivo and in vitro, and is considered to be an important link between obesity and diabetes. It has been involved in the pathogenesis of obesity-mediated IR and type-2 diabetes mellitus (T2DM) (Habib, 2012).

This study aimed to assess serum interleukins 17 and 23 and resistin levels and evaluate their relation with BMI, waist circumference, hip circumference and waist / hip ratio in obese diabetic patients.

Subjects and Methods:

Thirty five female diabetic patients were included in the study. Controls included 20 age-matched healthy females of the same socioeconomic status.
Morning venous blood sample was withdrawn after 12 h over night fasting into plane tube and left to colt. The serum was separated by centrifugation for 10 minutes at 5000 rpm, and stored at −20 until assays.

**Ethics:**

The study and the informed consent procedures were approved by the Ethics Review Committee of the National Research Centre.

**Biochemical Analysis:**

Serum glucose was measured by the glucose oxidase method (Barham and Trinder, 1972) total cholesterol (Allain et al., 1974), triglyceride (Wahlefeld, 1974) and high density lipoprotein cholesterol (HDL-C) (Warnick et al., 1982) were determined by autoanalyzer Olympus 400, low density lipoprotein cholesterol (LDL-C) was calculated according to the equation developed by (Friedewald et al., 1972) as follows:

\[
\text{LDL-C} = \text{Total cholesterol} - \text{Triglyceride/5} + \text{HDL-C}.
\]

The serum IL-17, IL-23 concentrations were measured using commercial human-specific enzyme-linked immunosorbent assay (ELISA) kits from WKEA MED (USA). Resistin was measured using commercial (ELISA) kit from BioVendor Systems.

**Anthropometric parameters:**

Anthropometric parameters including height, weight, waist circumferences, and hip circumferences were measured by practitioners.

Body weight was measured in light clothing with electronic scales to 0.1 kg precision (Seca, Hamburg, Germany). Height was measured in a standing position with fixed stadiometers (Seca). Waist circumference (WC) was measured at the midpoint between the lower rib margin and the iliac crest with the subject standing at the end of normal expiration. Hip circumference (HC) was measured at the level of the greater trochanters with the subject wearing minimum clothing. Non stretchable tap was used for both circumferences. The mean of two readings was taken in for calculating the waist hip ratio (WHR). Body mass index (BMI) was calculated by dividing weight (kg) by the squared value of height in meters. The reference interval of BMI is defined as 18–24.9 kg/m² (controls) and obesity as a BMI of more than 30 kg/m² (study group).

**Results:**

Clinical characteristics and biochemical parameters of study subjects are presented in Table 1. No statistically significant difference in age between both groups. Body mass index and waist circumference were significantly higher in diabetic patients than in the controls (P < 0.0001).

Serum fasting blood sugar, postprandial blood sugar, triglycerides, low density lipoprotein, interleukin 17, interleukin 23 levels were significantly higher in diabetic patients than in the controls. High density lipoprotein was significantly lower in diabetic patients than in the controls (P < 0.01)

Figure 1 reveals the Percentage control of the estimated parameters. Correlation analyses confined to the diabetic patients were performed in an attempt to correlate between the various parameters in this study.

<table>
<thead>
<tr>
<th>Table 1: Mean ± S.D the measured parameters for diabetic patients controls, and significant levels between both groups.</th>
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<tbody>
<tr>
<td><strong>Control (n = 21)</strong></td>
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<tr>
<td><strong>Age (Year)</strong></td>
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<tr>
<td><strong>BMI (kg/m²)</strong></td>
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<tr>
<td><strong>WC (cm)</strong></td>
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<tr>
<td><strong>F.B.S. (mg/dl)</strong></td>
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<td><strong>P.P.B.S (mg/dl)</strong></td>
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<td><strong>Cholesterol (mg/dl)</strong></td>
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<td><strong>T.G. (mg/dl)</strong></td>
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<td><strong>L.D.L. (mg/dl)</strong></td>
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<td><strong>Resistin (ng/ml)</strong></td>
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<td><strong>IL 17 (ng/l)</strong></td>
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<td><strong>IL 23 (ng/l)</strong></td>
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A significant positive correlation was obtained between body mass index and waist circumference (Fig 2) and between the biochemical parameters IL 23, IL 17 and Resistin (Fig 3, 4, 5). There was also a significant positive correlation between the biochemical parameters and anthropometric measurements (Fig 6, 7, 8, 9, 10, 11). Moreover, there was a significant positive correlation between blood glucose and IL 17 and IL 23 (Fig 12, 13).

**Fig. 1:** Percentage control of the estimated parameters.

**Fig. 2:** Correlation between BMI and WC.

**Fig. 3:** Correlation between IL 23 and IL 17.
**Fig. 4:** Correlation between IL 23 and Resistin.

**Fig. 5:** Correlation between IL 23 and BMI.

**Fig. 6:** Correlation between IL 23 and WC.
Fig. 7: Correlation between IL 17 and Resistin.

Fig. 8: Correlation between IL 17 and BMI.

Fig. 9: Correlation between IL 17 and WC.
**Fig. 10:** Correlation between Resistin and BMI.

**Fig. 11:** Correlation between Resistin and WC.

**Fig. 12:** Correlation between Blood Glucose and IL 17.
Discussion:

The present work showed that Body mass index (BMI) and waist circumference were significantly higher in diabetic patients than in the controls (P < 0.0001). Also, triglycerides, low density lipoprotein, levels were significantly higher in diabetic patients than in the controls. Moreover, high density lipoprotein, was significantly lower in diabetic patients than in the controls (P < 0.01). This may be explained by obesity which is the major risk factor for developing diabetes (Sjostrom, et al., 2004; Nguyen et al., 2008). Many studies revealed that obesity is a strong predictor of diabetes in both genders and extends to all ethnic groups (Colditz et al., 1995). An estimate from the National Center for Health Statistics (NHANES III) reported that 78.5% of diabetics were overweight, and 45.7% were obese. A meta-analysis of ten publications reveals an odds ratio of 2.14 for obese subjects developing type II diabetes (Freemantle et al., 2008).

A number of studies have reported a strong relationship between obesity/overweight and the onset of type 2 diabetes (Wannamethee et al., 2004; Sanada et al., 2012). However, there are many coexisting conditions, such as hypertension, dyslipidemia, or insulin resistance, that may affect this relationship (Gress et al., 2000; Meigs et al., 2006). Guidelines published by the USA National Institutes of Health, considered that overweight and obesity are the second leading cause of preventable death in the USA, behind smoking (NHLBI, 1998).

Regarding the proinflammatory cytokines interleukin 17, interleukin 23 levels, our study showed that they were significantly higher in diabetic patients than in the controls. Also, they were significantly correlated with BMI and WC. Increased blood levels of IL-17 and IL-23 in obesity among both humans and mice have been reported by several studies (Sumarac-Dumanovic et al., 2009; Winer et al., 2009).

Sumarac-Dumanovic et al., 2009 compared the serum cytokines from 26 obese women with those from 20 lean women and found that IL-17 and IL-23 were increased in the obese group. In mice, it was shown that T cells from obese mice induced by a high-fat diet had a greater Th17 T-cell subpopulation and produced more IL-17 (Winer et al., 2009).

Moreover, elevated plasma free fatty acids, inflammatory markers, and altered adipokine concentrations have been observed in obese diabetic patients (McTernan et al., 2002; Gharibeh et al., 2010). Several factors may be responsible for this enhanced production of IL-17 in obesity. First, the secretion of IL-6 by adipocytes and tissue-derived macrophages is increased in obesity (Winer et al., 2009).

The results of the present study showed that Resistin was significantly higher in diabetic patients than in the controls and it was significantly positively correlated with biochemical parameters (IL-17 and IL-23) and anthropometric measurements (BMI and WC).

Initial studies showed that resistin was up-regulated in rodent model of obesity and IR, and down-regulated by an insulin-sensitizer, rosiglitazone. Moreover, immune neutralization of resistin reduced hyperglycemia and improved insulin sensitivity. These observations lead to the consideration of resistin as a potential etiological link between obesity and diabetes. (Steppan et al., 2001).

A study by McTernan et al., 2002 reported the presence of resistin in adipose tissue, thus linking resistin as a possible pathogenic factor increased in central adiposity. Also a positive correlation of plasma resistin was observed with age, insulin, BMI, waist circumference, body fat content and homoeostasis model assessment (HOMA) (Gharibeh et al., 2010).

Similarly, another investigation suggested that plasma resistin had a role in linking central obesity and insulin resistance to type 2 DM, and resistin levels correlated significantly with BMI, waist circumference,
WHR, fasting blood sugar (FBS), and HOMA score (Chanchay et al., 2006; Li et al., 2009). They reported that resistin levels were increased with central obesity, but not with simple adiposity. They also observed a weak correlation of resistin with insulin resistance and revealed that central obesity was significantly related to plasma resistin levels. Waist circumference, fat mass percentage, WHR, and BMI were positively correlated with resistin in both genders. In another study, resistin levels were reported to be positively correlated with changes in BMI and visceral fat areas assessed by hydro densitometry or dual-energy X-ray absorptiometry (Yannakoulia et al., 2003; Vozarova et al., 2004).

They observed a positive correlation between resistin concentrations and body fat mass assessed by bioimpedance in healthy subjects. Some investigations of human resistin in relation to obesity have shown higher serum resistin levels in obese subjects compared with lean subjects (Vozarova et al., 2004). Studies in human subjects have highlighted increased resistin expression in adipose tissue particularly abdominal depots (McTernan et al., 2002; Zhang et al., 2002).

Recently, Habib. 2012 found that diabetic patients in Saudi Arabia have significantly higher resistin levels that were positively correlated with body fat mass. He cited that this was supporting the evidence that resistin plays an important role in the pathogenesis of obesity and insulin resistance.

In contrast, other human studies showed no correlation between serum or plasma levels of resistin with any markers of adiposity (Silha et al., 2003). Also, according to a report by (Heilbronn et al., 2004) there was no relationship between resistin serum levels and percentage body fat, visceral adiposity, and BMI. This lack of significant correlation between serum resistin and increased adiposity was partly due to the confounding effects of age, because non-obese subjects were significantly younger than obese subjects in their study.

A significant positive correlation was obtained in this study between body mass index and waist circumference. BMI does not distinguish between muscle and fat accumulation (Bray et al., 2012), and there is evidence that whereas higher fat mass is associated with greater risk of premature death, higher muscle mass reduces risk (Bigaard et al., 2004). As well, BMI does not distinguish between fat locations, where central or abdominal fat deposition is thought to be particularly perilous (Ruhl and Everhart, 2010; Lumeng and Saltiel, 2011). Waist circumference (WC) has emerged as a leading complement to BMI for indicating obesity risk. A number of studies have found that WC predicted mortality risk better than BMI (Pischon et al., 2008; Petursson et al., 2011). A recent WHO report summarized evidence for WC as an indicator of disease risk, and suggests that WC could be used as an alternative to BMI (WHO, 2011).

A key limitation, mentioned in the WHO report, of using WC as a proxy for abdominal fat distribution is that it is sensitive to body size (height and weight) as well as to fat percentage and distribution. In fact, WC is highly correlated with BMI, to the extent that differentiating the two as epidemiological risk factors can be difficult (Moore, 2009).

**Conclusion:**

Obese diabetic patients have significantly higher IL-17 and 23 and resistin levels that are positively correlated with BMI and central fat. Understanding the inflammatory characterization of proinflammatory cytokines (interleukin 17, interleukin 23 levels) and resistin might be of fundamental importance for the prevention and treatment of obesity and diabetes.

**References**


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