Sex Differences in Serum Leptin and Adiponectin levels in Apparently Healthy Iranian Adults

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ABSTRACT: Leptin and adiponectin are two important adipose tissue derived cytokines. Serum adiponectin levels decrease in obesity and chronic disease, whereas leptin shows a positive correlation with inflammation. Given that serum leptin and adiponectin levels vary among different ethnic groups, the aim of this study was to determine the serum levels of leptin and adiponectin in a random sample of apparently healthy adults, with regard of sex difference. A cross sectional study was designed on 150 apparently healthy men and women, age 25-50 years living in Tabriz, Iran. Anthropometric parameters were measured including weight, height, body mass index (BMI) and waist circumference (WC). Serum leptin and adiponectin levels were determined using fasting blood samples. There was no statistically significant difference in BMI and age between genders. However, weight, height and WC were significantly higher in men. Median (25-75 percentile) of serum leptin levels were 6.80 (3.86 - 13.56) and 13.42 (4.93 - 25.44) ng/ml and mean (SD) of adiponectin levels were 31.13 (7.94) and 30.13 (8.59) ng/ml in men and women respectively. Leptin levels were significantly higher in females (P=0.006), while it was not observed any statistically significant difference in serum adiponectin levels in two sexes (P=0.459). In conclusion, we found that leptin levels are remarkably higher in women whereas that of adiponectin don’t differ significantly in two sexes.

Keywords: Sex difference, Leptin, Adiponectin, Adults

INTRODUCTION

White adipose tissue, a main place for storage of fat, consists of adipocytes, intracellular fluid, vascular tissues and other type of cells which secrete wide range of adipocytokines such as leptin, visfatin, resistin and adiponectin (Wozniak et al., 2009).

Adiponectin is an important adipocytokine in circulation. Unlike other adipocytokines which increase in obesity and chronic diseases (Zhuo et al., 2009), adiponectin levels decrease with excess body fat (Nayak et al., 2010), type 2 diabetes (Hotta et al., 2000) and cardiovascular disease (Kumada et al., 2003).

Leptin is another important adipocytokine identified in 1994 (Zhuo et al., 2009) and shows a positive correlation with adiposity (Ganji et al., 2009), including body mass index (BMI), adipose tissue mass, percentage of body fat, and sum of skin-fold thicknesses (Miller et al., 2001). Also this adipocytokine plays a crucial role in food intake and energy expenditure regulation (Monti et al., 2006).

Men and women are different in terms of body composition and fat distribution. Women have more body fat than men, while men have more muscle tissue. Considering the fat distribution, men have more visceral fat and women have more subcutaneous fat (Kuk et al., 2005). On the other hand, as leptin and adiponectin are mainly released from adipose tissue, adipocytokines levels seem to be different in two sexes.

Given that serum leptin and adiponectin levels vary among different ethnic groups (Mente et al., 2010, Moore et al., 2003), moreover decreased adiponectin and increased leptin serum levels are associated with pathogenesis of obesity, type 2 diabetes and cardiovascular disease (Zhuo et al., 2009), the aim of this study was to determine the serum levels of these two adipocytokines in a random sample of apparently healthy adults who live in Tabriz, Iran, with regard of sex differences.
MATERIALS AND METHODS

Subjects
This cross-sectional study was carried out on 150 apparently healthy individuals living in Tabriz, Iran. Inclusion criteria were filling out the informed consent form and age 25-50 years. Exclusion criteria were high physical activity level, pregnancy and lactation, taking any anti-inflammatory medications or having any evidence of chronic disease.

Anthropometric Measurements
Anthropometric measurements were done with light clothing and no shoes. Weight was determined to the nearest 0.1 kg using a standardized analogue scale (Seca, Germany), and height was measured to the nearest 0.1 cm using a portable stadiometer (Seca, Germany). BMI (weight in kilograms divided by height in meters squared, kg/m²) was calculated. WC was measured at the narrowest point between the lowest rib and the uppermost lateral border of the right iliac crest to the nearest 0.1 cm using a non-stretchable tape measure.

Biochemical analyses
Blood samples were drawn after overnight fasting and centrifuged at 3500 rpm for 10-12 minute. Serums were separated and stored at -70 °C. Leptin and adiponectin levels were measured using ELISA kits from (Boster Biological Technology, LTD)

Statistical analyses
Continuous data were summarized as mean (SD) and median (25-75 percentile) in non-normal cases, while frequency numbers and percentage was used for qualitative data. The Kolmogorov–Smirnov test was used to determine the normality of the distribution. Continuous variables were compared between men and women using independent samples t-test and man whitney U test was used for non-normal data. P-value < 0.05 considered significant. Data analysis was performed using SPSS, ver.13 (SPSS Inc. IL, Chicago, USA).

RESULTS
The half of subjects was male and majority of subjects were married (72%), non smoker (82.7%) and not using alcohol (96.7%). Anthropometric indices including weight, height, BMI and WC are presented in Table 1. The mean (SD) of the age was 36.76 (8.87). Subjects were in random range of weight, BMI and WC. There was no statistically significant difference in BMI (P=0.053) and age (P=0.667) between genders. However, weight, height and WC were significantly different in two sexes and they were greater in males. Biochemical variables including leptin and adiponectin are represented as mean (SD) and median (25-75 percentile) in Table 2. Serum leptin levels were significantly different among men and women (P=0.006) but it was not observed any statistically significant difference in serum adiponectin levels in two sexes (P=0.459).

Table 1. Demographic characteristics of the study population divided by gender

<table>
<thead>
<tr>
<th></th>
<th>Total (n= 150)</th>
<th>Male (n= 75)</th>
<th>Female (n= 75)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36.76 (8.87)</td>
<td>37.09 (9.02)</td>
<td>36.43 (8.76)</td>
<td>0.667</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.54 (13.07)</td>
<td>75.58 (12.12)</td>
<td>67.49 (12.80)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>166.48 (9.54)</td>
<td>173.62 (6.51)</td>
<td>159.35 (6.13)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.92 (4.83)</td>
<td>25.16 (4.21)</td>
<td>26.68 (5.31)</td>
<td>0.053</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>87.86 (11.44)</td>
<td>91.27 (11.36)</td>
<td>84.5 (10.56)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

a- BMI= body mass index: calculated as kg/m2
b- WC= waist circumference
†- Independent Samples T-Test
Table 2. Comparison of serum adiponectin and leptin levels in two sexes

<table>
<thead>
<tr>
<th></th>
<th>Total (n= 150)</th>
<th>Male (n= 75)</th>
<th>Female (n= 75)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin* (ng/ml)</td>
<td>30.63 (8.26)</td>
<td>31.13 (7.94)</td>
<td>30.13 (8.59)</td>
<td>0.459†</td>
</tr>
<tr>
<td>Leptin† (ng/ml)</td>
<td>8.43 (4.25 - 20.05)</td>
<td>6.80 (3.86 - 13.56)</td>
<td>13.42 (4.93 - 25.44)</td>
<td>0.006‡</td>
</tr>
</tbody>
</table>

a- Values are expressed by Mean (SD)
b- Values are expressed by Median (25 -75 percentile)
†- Independent Samples T-Test
‡ - Mann-Whitney U Test

DISCUSSION

In this cross-sectional study on random sample of apparently healthy adults, we found a difference in serum leptin concentration between genders. It was significantly higher in women. This study is in accordance with previous studies which evaluated serum leptin levels in two sexes (Carraro and Ruiz-Torres, 2006, Ganji et al., 2009, Aref hosseini et al., 2011, Monti et al., 2006). It seems this variation might be as a result of metabolic and physiologic differences between men and women.

Several studies have shown that serum leptin concentration is dependent to adipose mass size (Maffei et al., 1995, Dagogo-Jack et al., 1996). According to the higher fat body mass of women, they may have higher leptin concentration than men.

Sexual hormones may contribute to gender difference in serum leptin concentration. Carraro et al. showed a negative correlation of testosterone with serum leptin in males, not in females. Of course a physiologic decline in testosterone with aging in males has shown the same negative relationship with serum leptin (Carraro and Ruiz-Torres, 2006). Estrogens stimulate expression of ob gene and release of leptin which can be another cause of high concentration of this hormone in women (Piemaria et al., 2003).

In our study, there was no significant difference in serum adiponectin concentration between men and women. This finding is consistent with Westerbacka et al. study who declared that there was no evidence of a sex difference in adiponectin levels when the amount of intra-abdominal and hepatic fat was similar in both sexes (Westerbacka et al., 2004). On the other hand, Ahonen et al. found a sex-specific difference in adiponectin levels. These authors reported that women have higher adiponectin concentration than men (Ahonen et al., 2008). Physiologically, men have more visceral fat and women have more subcutaneous fat (Kuk et al., 2005). Also adiponectin is synthesized mainly in subcutaneous fat cells of which women have relatively more than men and it is secreted mostly by adipocytes (Ahonen et al., 2008).

Contrary to this finding, Halleux C.M showed that secretion of adiponectin and regulation of adiponectin gene expression occurs in visceral adipose tissue (Halleux et al., 2001). So, examination of the main site of adiponectin secretion will help researchers to clarify the sex differences in serum levels of this adipocytokine. However we didn't examine amount of fat and its distribution among participants.

Numerous studies have shown that adiponectin levels are also reduced in obese rodents (Kadowaki et al., 2006) and humans (Diz and Iglesias, 2003). So, BMI is negatively correlated with adiponectin levels (Kistorp et al., 2005). In present study, BMI of participants was in a normal range and didn't show any extent variety. This normal distribution of BMI might influence our results in representing the gender difference in serum adiponectin concentration.

It should be mentioned that several other factors not investigated here might affect serum adiponectin levels and contribute to the observed no significant difference in serum adiponectin concentration in both sexes. Liver carries out a role in adiponectin elimination (Gatselis et al., 2013). Therefore, it can be speculated that patient with liver cirrhosis have elevated plasma adiponectin levels (Adamczak et al., 2005). Furthermore, Doumatey et al demonstrated that adiponectin is associated with renal function in non diabetic West Africans (Doumatey et al., 2012). We couldn't exclude individuals with minor liver or renal dysfunction. However, it is unlikely because in our study only healthy individuals took part.

Limitations of the study are lack of determination of sex hormones and of accurate measurement of fat distribution. Also we didn't examine physical activity levels in study population which might contribute to differences in serum leptin and adiponectin concentration among subjects (Reseland et al., 2001, Oberbach et al., 2006).

In conclusion, we found a sex difference in serum leptin concentration whereas no significant difference was observed in serum adiponectin levels among male and female.
ACKNOWLEDGMENT

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