Research Article

Adiponectin Gene Variants and Abdominal Obesity in an Iranian Population

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Introduction. Waist-to-height ratio (WHtR) can be effective for the diagnosis of abdominal obesity and the risk of type 2 diabetes. The role of genetic factors in the development of obesity has been broadly recognized. Adiponectin’s level is inversely correlated with body fat percentage and is reduced in obesity and type 2 diabetes. The aim of this study was to examine the association between WHtR and adiponectin gene polymorphisms in Iranian population. Methods. This study was conducted on 610 subjects from two Iranian populations. Anthropometric characteristics were measured by routine methods. Blood samples were collected in tubes (3–5 mL) containing EDTA and were stored at 20°C. After DNA extraction, genotyping was performed using PCR-RFLP technique. Results. There were statistically significant differences in genotype frequencies of −11391G/A in centrally obese (WHtR > 0.5) and noncentrally obese (WHtR ≤ 0.5) subjects (P value < 0.044). In centrally obese subjects, the frequencies of GG and GA+AA genotypes were 89.4% and 10.6%, respectively, while the frequencies of GG and GA+AA genotypes were 95.9% and 4.1%, respectively, in noncentrally obese subjects. Conclusions. The frequency of GG genotype was significantly increased in subjects with WHtR > 0.5 compared with the other group. After adjustment for diabetes, abdominal obesity was significantly associated with the −11391 G/A polymorphism.

1. Introduction

Extensive epidemiological studies have shown that obesity is a significant risk factor for several important diseases, including coronary heart disease, stroke, type 2 diabetes, hypertension, some forms of tumors, and musculoskeletal disorders [1]. The prevalence of obesity and overweight in developing countries, including Iran, is increasing [2, 3].

Studies have shown that obesity is more associated with body fat distribution (central obesity) than with general obesity measured by body mass index (BMI) and plays a more effective role in determining one's health [4]. It has been proposed that waist-to-height ratio (WHtR) can be effective for the diagnosis of abdominal obesity and the risk of type 2 diabetes [5]; its use and associated risk factors were first suggested in the mid-1990s [6, 7]. According to a study, BMI and WHtR in males and BMI, WHtR, and waist circumference (WC) in females were the best predictors of diabetes incident [8]. Other studies have also shown that the waist-to-hip ratio (WHR) and WHtR are better anthropometric indices than BMI and waist circumference (WC) [9–11]. In comparison with BMI, WC is more responsive to diet and exercise in that any increase in muscle mass can lead to more noticeable changes in WC and WHtR than in BMI [12]. In
fact, the use of WC as the only indicator of abdominal obesity may lead to overestimation of associated risks in tall people and underestimation of the risks in short people [13].

The effectiveness of anthropometric indicators for predicting health risk factors such as cardiovascular disease is related to genetic factors and might vary in different populations. The role of genetic factors in the development of obesity and diabetes has been broadly recognized [14–16].

Adiponectin is an abundant adipose-derived protein whose levels are inversely correlated with body fat percentage [17] and are reduced in obesity [18], type 2 diabetes [19], dyslipidemia [20], and coronary heart disease [21]. Adiponectin plays an important role in different metabolic processes including glucose regulation and fatty acid metabolism [22]. Individuals with visceral adipose tissue have been found to have lower levels of adiponectin [23]. Single nucleotide polymorphisms have been identified in adiponectin gene, including polymorphism at positions −11391 G/A, −11377 G/C, +45 T/G, and +276 G/T [24]. Recent molecular epidemiological studies have evaluated the association between polymorphisms of adipokine genes and the risk of obesity [25]. In addition several studies have shown that +45 T/G polymorphism is significantly associated with obesity and type 2 diabetes [26].

Established upon the best anthropometric index, this study is the first to evaluate the association between abdominal obesity, type 2 diabetes, and adiponectin. The aim of this study was to examine the association between WHtR and adiponectin gene polymorphisms in an Iranian population.

2. Method

This cross-sectional study was conducted on 610 subjects who were selected from Kerman (n = 310) and Tehran populations (n = 300) [27]. The selection of the patients was carried out based on a hospital based clinics approach including diabetes clinic.

After obtaining informed consent, personal and demographic information was completed, through questionnaires, for each participant. Waist circumference was measured with a tape measure resting on the distance between the smallest area below the rib cage and the iliac crest with the patient's lung at the end of expiration [24]. Height was measured using a SECA height meter with an accuracy of 0.1 cm. WHtR was calculated by dividing waist circumference (in cm) by height (in cm) [11]. The diagnosis of diabetes was based on the American Diabetes Association Criteria [28]. Fasting blood glucose was taken from the participants and blood samples were collected in tubes (3–5 mL) containing EDTA and were stored in 20°C. This study was approved by the Ethics Committee of Tehran University of Medical Sciences.

DNA samples in tubes containing EDTA were extracted using salting-out method. Molecular analysis of adiponectin gene +45 T/G polymorphism was examined based on method described by Schäffler and his colleagues [29]. Molecular analysis of the −11391 G/A polymorphism was performed by PCR-RFLP [30]. Statistically analysis was performed by chi-square, t-test, and regression tests using SPSS software version 16. In the univariate model, the association between abdominal obesity and adiponectin gene polymorphisms was investigated. In adjusted models, this association was examined with regard to diabetes.

3. Result

This study was conducted on 610 subjects of two Iranian populations, 66% of whom were female and 34% were male. Table 1 summarizes mean and standard deviation of age and anthropometric indices of subjects and their association with adiponectin gene polymorphisms. When patients were stratified, there were statistically significant differences between genotype frequencies of −11391 G/A in centrally obese (WHtR > 0.5) and noncentrally obese (WHtR ≤ 0.5) subjects (P value < 0.05), but there were no statistically significant differences between genotype frequencies of +45 T/G in centrally obese (WHtR > 0.5) and noncentrally obese (WHtR ≤ 0.5) subjects (P value = 0.162).

In Table 2, there were no statistically significant differences between genotype frequencies of −11391 G/A in diabetic subjects and nondiabetic subjects (P value = 0.117); also, there were no statistically significant differences between genotype frequencies of +45 T/G in diabetic subjects and nondiabetic subjects (P value = 0.337).

Table 3 shows the association between abdominal obesity and adiponectin gene polymorphisms in logistic regression. As it can be observed in the univariate model, none of these polymorphisms were associated with abdominal obesity, but after adjustment for diabetes, −11391 G/A polymorphism was significant.

4. Discussion

The aim of this study was to evaluate the effect of two common polymorphisms of the adiponectin gene and WHtR, as an indicator of abdominal obesity. The results of this study were based on study by Esmaillzadeh and his colleagues where the cutoff point of waist-to-height ratio is considered to be 0.5 cm [31]. We found significant associations between −11391 G/A polymorphism and WHtR in the subjects and, after adjustment for diabetes, abdominal obesity was still significantly associated with the −11391 G/A polymorphism.

WHtR had the highest risk-adjusted incidence of diabetes than other anthropometric indicators in all quartiles including BMI, when compared with other central obesity indicators, having significantly lower area under the curve than WHtR [32]. According to a study on a group of men, a strong correlation was found between WHtR and the risk of type 2 diabetes. This study determined WHtR as the best predictor of obesity and diabetes in adult males because the predictive power of anthropometric indicators in each population varies from race to race, suggesting that WHtR should be used as a screening indicator [32–34].

Other studies have shown that WHtR is strongly related to visceral adipose tissue while adiponectin is inversely associated with visceral adipose tissue [35, 36]. Previous studies have also reported that WHtR is a stronger predictor of visceral adipose tissue than BMI and WC [6, 37]. Thus, WHtR
Table 1: Mean and standard deviation (SD) of anthropometric characteristics and age.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Weight</th>
<th>Height</th>
<th>BMI</th>
<th>Waist</th>
<th>WHtR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>± SD</td>
<td>Mean</td>
<td>± SD</td>
<td>Mean</td>
<td>± SD</td>
</tr>
<tr>
<td>+45</td>
<td>47.75</td>
<td>1.26</td>
<td>69.13</td>
<td>1.29</td>
<td>160.76</td>
<td>10.4</td>
</tr>
<tr>
<td>TG, GG</td>
<td>49.41</td>
<td>1.21</td>
<td>69.06</td>
<td>1.18</td>
<td>160.39</td>
<td>9.64</td>
</tr>
<tr>
<td>Total</td>
<td>48.25</td>
<td>1.25</td>
<td>69.11</td>
<td>1.25</td>
<td>160.65</td>
<td>10.17</td>
</tr>
<tr>
<td>−11391</td>
<td>48.19</td>
<td>1.24</td>
<td>69.05</td>
<td>1.25</td>
<td>161.07</td>
<td>10.18</td>
</tr>
<tr>
<td>GA, AA</td>
<td>46.69</td>
<td>1.19</td>
<td>68.5</td>
<td>1.28</td>
<td>159.42</td>
<td>12.843</td>
</tr>
<tr>
<td>Total</td>
<td>48.04</td>
<td>1.24</td>
<td>68.99</td>
<td>1.25</td>
<td>160.91</td>
<td>10.46</td>
</tr>
</tbody>
</table>

All variables were nonsignificant.

Table 2: Genotype frequencies of adiponectin in diabetic and nondiabetic subjects.

<table>
<thead>
<tr>
<th></th>
<th>Diabetic</th>
<th>Nondiabetic</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+45</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>228 (71.0%)</td>
<td>180 (69.1%)</td>
<td>408 (70.2%)</td>
<td>0.337</td>
</tr>
<tr>
<td>TG + GG</td>
<td>93 (29.0%)</td>
<td>81 (30.9%)</td>
<td>174 (29.8%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>321 (100%)</td>
<td>261 (100%)</td>
<td>583 (100%)</td>
<td></td>
</tr>
<tr>
<td>−11391</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG</td>
<td>296 (91.5%)</td>
<td>235 (88.7%)</td>
<td>531 (90.5%)</td>
<td>0.117</td>
</tr>
<tr>
<td>GA + AA</td>
<td>26 (11.3%)</td>
<td>30 (8.1%)</td>
<td>56 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>322 (100%)</td>
<td>265 (100%)</td>
<td>587 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Genotype frequencies of adiponectin in central obesity (WHtR > 0.5) and noncentral obesity (WHtR ≤ 0.5) subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Abdominal obesity</th>
<th>Total</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (WHtR &gt; 0.5)</td>
<td>No (WHtR ≤ 0.5)</td>
<td>Crude model</td>
</tr>
<tr>
<td>+45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>346 (71.0%)</td>
<td>62 (63.9%)</td>
<td>408 (69.9%)</td>
</tr>
<tr>
<td>TG + GG</td>
<td>141 (29.0%)</td>
<td>35 (36.1%)</td>
<td>176 (30.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>487 (100%)</td>
<td>97 (100%)</td>
<td>584 (100%)</td>
</tr>
<tr>
<td>−11391</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG</td>
<td>437 (89.4%)</td>
<td>94 (95.9%)</td>
<td>531 (90.5%)</td>
</tr>
<tr>
<td>GA + AA</td>
<td>52 (10.6%)</td>
<td>4 (4.1%)</td>
<td>56 (9.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>489 (100%)</td>
<td>98 (100%)</td>
<td>587 (100%)</td>
</tr>
</tbody>
</table>

is a strong anthropometric index for predicting adiponectin levels [38].

As reported by Dolley et al., there is a significant association between −11391 G>A polymorphism and WHR changes evaluated during a 7-year follow-up period. However, this study did not include BMI changes over the time period [39]. Conversely, Fumeron et al. found no association between the −11391 G>A and WHR at baseline during a 3-year follow-up period [40]. Furthermore, −11391 G/A polymorphism was associated with higher adiponectin levels in obese children [41]. This is supported by a study in Denmark which found relationships between −11391 G/A polymorphism and obesity [42].

Stumvoll et al. showed that, in individuals without familial predisposition to type 2 diabetes, adiponectin polymorphism may moderately increase the risk of obesity and secondarily cause insulin resistance. Furthermore, they suggested that the G allele was significantly associated with obesity [26]. Also in the present study, the genotype frequency of GG was higher in centrally obese subjects and this finding could be a fact to consider G allele as a risk factor for abdominal obesity.

In 2010, the findings of a study showed that the frequencies of allele A −11391 G/A polymorphism in women and allele G +45 T/G polymorphism in both men and women have a supporting role in weight gain [30].

In a non-diabetic Korean population association between +45 T/G polymorphism and serum levels of adiponectin and obesity and insulin resistance was found [43]. These results are in contrast to the findings of our study. Moreover, a study conducted in Italy demonstrated significant associations between +276 and +45 T/G polymorphisms and insulin resistance and other parameters such as weight gain [44].

In a study of Indian population, Ranjith and his colleagues found no association between G allele of SNP +45 and obesity, while +45 T/G genotype was only associated with low WC. This study found that the +45 T allele has a lower frequency compared with the +45 G allele [45]. Nevertheless, in Arnaiz-Villena’s study, the +45 T allele had more frequency [46].

In this study we concluded that there is significant association between the −11391 G/A polymorphism and abdominal obesity.
It is recommended that future studies be replicated in other populations and also other polymorphisms of adiponectin be considered.

**Abbreviations**

WHR: Waist-to-height ratio  
WC: Waist circumference  
BMI: Body mass index.

**Conflict of Interests**

The authors declare that they have no competing interests.

**Acknowledgment**

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**References**


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