

Adiponectin gene variants and abdominal obesity in an Iranian population

Moloud Payab¹ · Mahsa M. Amoli² · Mostafa Qorbani^{3,4} · Shirin Hasani-Ranjbar^{1,5}

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Abstract

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 is to investigate 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 –11391 G/A in centrally obese (WHtR >0.5) and noncentrally obese (WHtR ≤0.5)

subjects (P value <0.044). In the former, 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 to the other group. After adjustment for diabetes, abdominal obesity was significantly associated with the –11391 G/A polymorphism.

Keywords Obesity · Adiponectin · Diabetes · Abdominal obesity · Polymorphism · Waist-to-height ratio · Metabolic syndrome

Abbreviations

WHtR Waist-to-height ratio
WC Waist circumference
BMI Body mass index

S. Hasani-Ranjbar and M. M. Amoli equally contributed as corresponding authors.

✉ Mahsa M. Amoli
amolimm@sina.tums.ac.ir

✉ Shirin Hasani-Ranjbar
Sh_ha-sani@sina.tums.ac.ir; shirinhasanir@yahoo.com

Moloud Payab
Moloudpayab@gmail.com

Mostafa Qorbani
mqorbani1379@gmail.com

¹ Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Shariati Hospital, 5th Floor, North Kargar Ave, 1411413137 Tehran, Iran

² Metabolic Disorders Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

³ Department of Community Medicine, Alborz University of Medical Sciences, Karaj, Iran

⁴ Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

⁵ Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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). These studies have also suggested a more effective role of obesity 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]. The use and associated risk factors of WHtR 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 are the best predictors of diabetes incidence in a population [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 the overestimation of associated risks in tall people and the underestimation of the risks in short ones [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]. Like so, a reduction in adiponectin level may enhance the probability of 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.

Materials and methods

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 resting on a hospital-based clinic approach covering a diabetes clinic.

After obtaining informed consent, personal and demographic information for each participant was collected by questionnaires. 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 made 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 is approved by the Ethics Committee of Tehran University of Medical Sciences.

DNA samples in EDTA containing tubes were extracted using salting-out method. The molecular analysis of adiponectin gene +45 T/G polymorphism was examined based on a method described by Schaffler and his colleagues [29]. The molecular analysis of the –11391 G/A polymorphism was performed by PCR–RFLP [30]. Statistical 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.

Result

This study was conducted on 610 subjects from two Iranian populations. 66 % of participants were female and 34 % were male. Table 1 summarizes the mean and standard deviations 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

Table 1 Mean and standard deviation (SD) of anthropometric characteristics and age

	Mean \pm SD					
	Age	Weight	Height	BMI	Waist	WHtR
+45						
TT	47.75 \pm 1.26	69.13 \pm 1.29	160.76 \pm 10.4	26.78 \pm 4.73	91.4 \pm 11.04	0.56 \pm 0.072
TG, GG	49.41 \pm 1.21	69.06 \pm 1.18	160.39 \pm 9.64	26.76 \pm 4.72	91.26 \pm 11.51	0.55 \pm 0.069
Total	48.25 \pm 1.25	69.11 \pm 1.25	160.65 \pm 10.17	26.77 \pm 4.72	91.36 \pm 11.18	0.56 \pm 0.071
–11391						
GG	48.19 \pm 1.24	69.05 \pm 1.25	161.07 \pm 10.18	26.80 \pm 4.65	91.25 \pm 11.20	0.56 \pm 0.071
GA, AA	46.69 \pm 1.19	68.5 \pm 1.28	159.42 \pm 12.843	25.91 \pm 4.59	90.23 \pm 11.11	0.56 \pm 0.073
Total	48.04 \pm 1.24	68.99 \pm 1.25	160.91 \pm 10.46	26.71 \pm 4.65	91.15 \pm 11.19	0.56 \pm 0.072

* All variables were non significant

Table 2 Genotype frequencies of adiponectin in diabetes and non-diabetes subjects

	Diabetes	Non-diabetes	Total	<i>P</i> value
+45				
TT	228 (71.0 %)	180 (69.1 %)	408 (70.2 %)	0.337
TG + GG	93 (29.0 %)	81 (30.9 %)	174 (29.8 %)	
Total	321 (100 %)	261 (100 %)	583 (100 %)	
–11391				
GG	296 (91.5 %)	235 (88.7 %)	531 (90.5 %)	0.117
GA + AA	26 (11.3 %)	30 (8.1 %)	56 (9.5 %)	
Total	322 (100 %)	265 (100 %)	587 (100 %)	

of –11391 G/A in centrally obese (WHtR >0.5) and noncentrally obese (WHtR \leq 0.5) subjects (*P* value <0.05). However, there were no statistically significant differences between genotype frequencies of +45 T/G in centrally obese (WHtR >0.5) and noncentrally obese (WHtR \leq 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 non-diabetic subjects (*P* value = 0.117). In addition, there were no statistically significant differences between genotype frequencies of +45 T/G in diabetic subjects and non-diabetic ones (*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. However, after adjustment for diabetes, –11391 G/A polymorphism was significant.

Discussion

The aim of this study was to evaluate the effect of two common polymorphisms of the adiponectin gene and WHtR as indicators of abdominal obesity. The results of

this study were based on a study by Esmailzadeh et al. 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 established between WHtR and the risk of type 2 diabetes. This study determined WHtR as the best predictor of obesity and diabetes in adult males. This is mainly because the predictive power of anthropometric indicators in each population varies from race to race, which is 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 compared to BMI and WC [6, 37]. Thus, WHtR 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 WHtR changes, which was evaluated during a 7-year follow-up period. However, this study did not include BMI changes over this time period [39]. Conversely, Fumeron et al. found no association between the –11391 G>A and WHtR at the 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].

Table 3 Genotype frequencies of adiponectin in central obesity (WHtR >0.5) and non-central obesity (WHtR ≤0.5) subjects

Variable	Abdominal obesity		Total	OR (95 % CI) Crude model	Adjusted for diabetes
	Yes (WHtR >0.5)	No (WHtR ≤0.5)			
+45					
TT	346 (71.0 %)	62 (63.9 %)	408 (69.9 %)	0.72 (0.45–1.14)	0.72 (0.45–1.14)
TG +GG	141 (29.0 %)	35 (36.1 %)	176 (30.1 %)		
Total	487 (100 %)	97 (100 %)	584 (100 %)		
–11391					
GG	437 (89.4 %)	94 (95.9 %)	531 (90.5 %)	2.79 (0.98–7.92)	3.07 (1.1–8.77)
GA + AA	52 (10.6 %)	4 (4.1 %)	56 (9.5 %)		
Total	489 (100 %)	98 (100 %)	587 (100 %)		

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]. In addition, in the present study, the genotype frequency of GG was higher in centrally obese subjects and this finding could be a facet 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, an association was found between +45 T/G polymorphism and serum levels of adiponectin, as well as obesity and insulin resistance [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 et al. 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 to the +45 G allele [45]. Nevertheless, in Arnaiz-Villena's study, the +45 T allele was reported to have a higher 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 need to be considered.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical standard The study has been approved by ethical committee of Tehran University of Medical Sciences.

Informed consent Informed consents have been obtained from all patients participating in the study.

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