Original Article

Association of Adiponectin 45T/G (rs2241766) and Visfatin 4689G/T (rs2110385) Gene Polymorphisms with Susceptibility to Obesity

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Abstract

Background: This study aimed to see whether the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms in an Iranian population are linked to obesity and/or obesity-related traits in normal and obese individuals. **Methods:** 230 obese individuals and 169 healthy controls had their genomic DNA taken. The alleles and genotypes of the rs2241766 and rs2110385 polymorphisms were determined using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. **Results:** Obese individuals had considerably greater frequencies of the G allele and GG genotypes of the rs2241766 polymorphism than healthy controls (35% vs 21%, Probability *(P)* <0.0001, odds ratios (OR): 1.99, 95% confidence intervals (CI): 1.45–2.75 and 21% vs 7%, $P = 0.002$, OR: 3.52, 95% CI: 1.81–6.85, respectively). In comparison to healthy controls, obesity patients had substantially lower frequencies of the T allele and TT genotype of the rs2241766 polymorphism (65% vs 79%, $P < 0.0001$, OR: 0.50, 95% CI: 0.36–0.69 and 51% vs 65%, $P = 0.008$, OR: 0.58, 95% CI: 0.39–0.87, respectively). Obese individuals had substantially higher frequencies of the G allele and GG genotype in the rs2110385 polymorphism than healthy controls (77% vs 69%, $P = 0.01$, OR: 1.47, 95% CI: 1.07–2.0 and 61% versus 51%, $P = 0.047$, OR: 1.5, 95% CI: 1.0–2.2, respectively). When compared to healthy controls, the frequency of the T allele in the rs2110385 polymorphism was considerably lower in obese individuals (23% vs 31%, $P = 0.01$, OR: 0.68, 95% CI: 0.5–0.93). Furthermore, these single nucleotide polymorphisms (SNPs) were shown to have a strong link to clinical data in obese individuals. In the case of adiponectin, 45T/G (rs2241766) genotypes, serum low-density lipoprotein, waist circumference, and diastolic blood pressure were substantially different among the rs2241766 genotypes ($P = 0.007$, $P = 0.000$, and $P = 0.011$, respectively). In the instance of the visfatin 4689G/T (rs2110385) gene polymorphism, serum triglycerides was substantially different among the rs2110385 genotypes ($P = 0.039$). **Conclusions:** In the Iranian population, our findings revealed a strong link between adiponectin and visfatin gene polymorphisms and obesity and several obesity-related clinical characteristics. These SNPs might be used to identify those who are at risk of becoming obese.

Keywords: *Adiponectin, obesity, polymorphism, visfatin*

Introduction

Obesity has become a major and expensive public health problem across the globe, affecting individuals of all ethnicities.[1] Accumulation of adipose tissue, as a main characteristic of obesity, could regulate the secretion of numerous soluble substances called adipokines, which play important roles in the development of obesity and its associated complications.[2] Rapid developments in human genome research have provided scientists with a number of new candidate genes whose expression in adipose tissue is proposed to be implicated in predisposition to human obesity such as peroxisome proliferator-activated receptor gamma, adrenoreceptors beta, hormone-sensitive lipase, uncoupling protein 2, tumor necrosis factor-alpha, the hormone leptin as well as adiponectin and visfatin.[3]

Adiponectin, which is a protein secreted by adipose tissue is encoded by the adiponectin ADIPOQ, also known as APM1 gene.[4] It is located on chromosome 3q27 and has been suggested that this region may include an obesity susceptibility locus.[5] Based on mutation screening in French and Japanese populations, thirteen single nucleotide polymorphisms (SNPs) for the adiponectin gene have been found.[6] Four

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SNPs in the promoter region, rs266729 and rs17300539 in the intron, and rs1501299 in the exon were shown to be associated with insulin resistance and obesity.[7] Moreover, variation in rs2241766 polymorphism was significantly associated with obesity in studies conducted in Belgium[8] and China.[9] However, conflicting results were published for the Swedish[10] and Chinese populations.[4]

Another gene, which is mostly expressed in visceral fat and adipose tissue, is visfatin (PBEF1).[11] It is located on chromosome 7q22.[12] This chromosomal region has previously been reported to have a linkage with the insulin response to aerobic exercise training in Caucasians,[13] insulin resistance syndrome phenotypes in Mexican-Americans,[14] and bio mass index (BMI) in the National Heart, Lung, and Blood Institute's Family Blood Pressure Program.[15] Thus, based on its chromosomal location, the visfatin gene may be a candidate for glucose and obesity-related phenotypes.

Since, there is no report regarding polymorphisms of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) in obese Iranian individuals, the aim of this study was to assess polymorphism of the two SNPs described in obese and healthy Iranian population. In addition, the possible association of each polymorphism has been evaluated with regard to obesity and/or related features (metabolic and anthropometric factors).

Methods

The study subjects

The obese patients were age-, gender-, and ethnicity-matched with the healthy control group. As part of the Cohort research in Amol, the case and control populations were recruited from clinics in Amol, Iran. Obese patients were entered in our survey according to the World Health Organization standard using the BMI ≥30 kg/m^2 (weight/height^2).[16] The minimum required sample volume estimated for this study was 150 persons for each case and control based on the probability of error Type I = 1.96 and probability of error Type II = 0.86.[10] Excluded criteria were included as follows: (I) cholesterol >300 mg/100 ml, (II) triglycerides (TG) >400 mg/100 ml, (III) blood pressure >140/90 mmHg, (IV) fasting blood sugar (FBS) >126 mg/100 ml. Written informed consent was obtained from all participants. All participants were requested to complete a self-questionnaire about the name, age, gender, smoking, general health, alcohol consumption, and medication usage. The Human Research Ethics Committee of Iran University of Medical Sciences (IR.IUMS.REC. FMD.1389.12247) approved this study.

Anthropometric measurement and arterial blood pressure

Anthropometric measurements such as weight, height, waist circumference, and BMI were measured in all study subjects before breakfast through a standard technique. Indeed, height was measured without shoes to the nearest 0.5 cm by a stadiometer. Weight was measured by wearing light clothes without shoes to the nearest 0.1 kg by a mechanical beam balance. Waist circumference was evaluated at the umbilical region between the lowest rib margin and the iliac crest. BMI was calculated according to the standard formula; weight (kilograms) divided by height squared (square meters). Moreover, arterial blood pressure as systolic and diastolic blood pressure were measured twice for each individual.[17]

Blood collection

All individuals had a blood sample (10 ml) drawn following an overnight fast between 7:00 PM and 9:00 AM. For biochemical analysis, the serum from a 5 ml venous blood sample was isolated and refrigerated at -80°C. Another 5 ml venous blood sample was collected in 1 mg/ml ethylene diamine tetra acetic acid (EDTA)-treated tubes, sealed with aluminum foil, transported to the laboratory room on ice (within 1–3 hours), the buffy coat detached, and the sample was kept at -80°C for DNA extraction and molecular analysis.

Biochemical analyses

The glucose-oxidase peroxidase (GOD-PAP) technique was used to assess FBS using commercially available kits (Biorex Fars Co. Shiraz, Iran). The glycerine phosphate oxidase peroxidase (GPO-PAP) technique was used to analyze TG using commercially available kits (Biorex Fars Co. Shiraz, Iran). The cholesterol oxidase peroxidase (CHOD-PAP) technique was used to quantify total cholesterol using commercially available kits (Biorex Fars Co. Shiraz, Iran). Through a direct enzymatic approach, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were tested using commercially available kits (Biorex Fars Co. Shiraz, Iran). Hitachi 911 Automatic Analyzer performed all of the above analyzes (Roche Diagnostics).

DNA extraction and genotyping

DNP TM Kit High yield DNA extraction and purification kit (CinnaGen Co, Tehran, Iran) was used to extract genomic DNA from a buffy coat of 5 ml peripheral blood and kept at -80°C. Primer sequences were verified by nucleotide blast software and the polymerase chain reaction-restriction fragment length polymorphism technique was used to investigate the genotype distributions of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) polymorphisms.

Polymerase chain reaction-restriction fragment length polymorphism for adiponectin was performed in 25 μL and

included 30 ng DNA, PCR buffer (10 mM), Magnesium chloride (MgCl2, 1.5 mM), Deoxynucleoside triphosphates (dNTP, 0.2mM) (0.2 mM), forward and reverse primer (0.4 µM each), and 1 U Taq polymerase. Amplification was performed in a thermal cycler with the following cycles; 3 minutes at 96°C, followed by 40 cycles; 30 seconds at 94°C, 30 seconds at 60°C, and an extension of 30 seconds at 72°C. Then, 10 µL of PCR product of each sample was digested with the 8 units of SmaI restriction enzyme for 16 hours at 30°C. Then, the limited fragments were loaded into a 3% agarose gel, electrophoresed, and analyzed for the correlative pattern of bands. Forward and reverse primers for adiponectin for PCR amplification of the fragment which included SNP + 45T > G were as follows; 5′-GCAGCTCCTAGAAGTAGACTCTGCTG-3′ and 5′-CCCCAAATCACTTCAGGTTGCTTATGG-3′, respectively.[18]

Polymerase chain reaction-restriction fragment length polymorphism for visfatin was done in 25 µL and consisted of: 10 ng DNA, PCR buffer (10 mM), dNTP (0.2 mM), MgCl2 (1.5 mM), forward and reverse primer (20 µmol/l each), and 1 U Taq polymerase. Amplification was handled in a thermal cycler with the following cycles; 5 minutes at 94°C, followed by 35 cycles; 45 seconds at 94°C, 60 seconds at 60°C and an extension of 60 seconds at 72°C. Then, 15 µL of PCR product of every sample was digested with the 5 units of AluI restriction enzyme for 16 hours at 37°C. Afterward, the limited fragments were loaded into a 3.5% agarose gel, electrophoresed, and analyzed for the correlative pattern of bands. Forward and reverse primers for adiponectin for PCR amplification of the fragment which included SNP -4689G/T as follows; 5′-GGTGGGCACTCAGACTGGT-3′ and 5′-CAAGAAGTTTCCTCAGACCTGC-3′, respectively.[19]

Statistical analysis

The statistical analysis was done using the SPSS program for Windows (version 22, SPSS, Inc., Chicago, IL). The normality of our data was determined using the normality test, and the results were expressed as mean standard deviation (SD) or median (percentile 5 and 95). We generated odds ratios (OR) and 95 percent confidence intervals (CI). To determine the correlations of the SNPs (45T/G and 4689G/T) with clinical data such as hypertension and hypertriglyceridemia, logistic regression was used. The frequencies of alleles and genotypes were determined. The exact test (www.coggenomics.org/software/stats) was used to determine Hardy Weinberg equilibrium (HWE). The Mann–Whitney U test or the student's *t*-test was used to compare the two groups. The one-way analysis of variance (ANOVA) or Kruskal–Wallis test was used when there were more than two groups. The Chi-squared test was used to compare the frequencies of alleles and genotypes in the case and control groups. *P* values less than 0.05 were deemed statistically significant in all statistical analyzes.

Results

There were 230 obese patients (128 males and 102 females) and 169 healthy controls in the research (88 males and 81 females). The obese patients' and healthy controls' mean age SDs were 39 ± 14.3 and 42.1 ± 12.1, respectively. Table 1 shows the demographic and clinical characteristics of healthy controls and obese people. Because case and control individuals were matched for age, gender, and ethnicity, there were no significant differences in age and gender between healthy subjects and obese patients ($P = 0.64$ and $P = 0.47$, respectively). Cigarette smoking was one of the variables that did not exhibit significant differences between case and control patients ($P = 0.7$). BMI (kg/m2), serum TG (mg/dl), serum total cholesterol, serum LDL (mg/dl), diastolic blood pressure (mm Hg), systolic blood pressure (mm Hg), hip

Table 1: Demographic and clinical data of healthy controls and obese subjects

	Control subjects (*n*=169)	Obese subjects (*n*=230)	*P*
Age (years)	39 (31-50)	42 (36-50)	0.64
Gender, N (women/men)	81/88	102/128	0.47
BMI[1] (kg/m^2)	22.9 (22.5-22.4)	32 (31-33)	<0.001
Serum TG[2] (mg/dl)	91 (64.5-138)	145 (98-215)	<0.001
Serum total cholesterol	171 (149-199)	193 (171-222)	<0.001
Serum HDL[3] (mg/dl)	47 (37-57)	42 (34-50)	<0.001
Serum LDL[4] (mg/dl)	98 (80-121)	113 (95-132)	<0.001
Fasting blood sugar (mg/dl)	91 (84-105)	93 (87-103)	0.098
Diastolic blood pressure (mm Hg)	70 (62-80)	80 (72-88)	<0.001
Systolic blood pressure (mm Hg)	105 (100-115)	120 (110-125)	<0.001
Waist circumference (cm)	80 (76.5-83)	101 (94-105)	<0.001
Hip circumference (cm)	96 (93-98)	110 (106-112)	<0.001
Waist/Hip ratio	0.84 (0.79-0.87)	0.93 (0.86-0.96)	<0.001
Cigarette smoking, *n* (%)	11 (6.5)	13 (5.7)	0.7

[1]Body Mass Index. [2]TriGlyceride. [3]High-Density Lipoprotein. [4]Low-Density Lipoprotein

Table 2: Allele and genotype distribution of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms in obese patients and healthy controls

	Control (*n*=169) *n* (%)	Obese (*n*=230) *n* (%)	*P*	OR (95% CI[1])
Adiponectin (rs2241766)				
T	266 (79)	299 (65)	<0.0001	0.50 (0.36-0.69)
G	72 (21)	161 (35)	<0.0001	1.99 (1.45-2.75)
TT	109 (65)	118 (51)	0.008	0.58 (0.39-0.87)
TG	48 (28)	63 (28)	0.82	0.95 (0.62-1.48)
GG	12 (7)	49 (21)	0.002	3.52 (1.81-6.85)
HWE		0.73		
Visfatin (rs2110385)				
G	234 (69)	353 (77)	0.01	1.47 (1.07-2.0)
T	104 (31)	107 (23)	0.01	0.68 (0.5-0.93)
GG	86 (51)	140 (61)	0.047	1.5 (1.0-2.2)
GT	62 (37)	73 (32)	0.3	0.80 (0.53-1.2)
TT	21 (12)	17 (7)	0.09	0.56 (0.28-1.07)
[2]HWE		0.59		

[1]Confidnce Interval. [2]Hardy Weinberg equilibrium

circumference (cm), waist circumference (cm), and waist/hip ratio were all significantly higher in obese patients than healthy subjects ($P < 0.0001$, Table 1). Healthy controls had considerably greater serum HDL (mg/dl) than obese individuals ($P < 0.0001$, Table 1).

Allele and genotype frequencies of the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms

Table 2 shows the allele and genotype frequencies of the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms in obese patients and healthy controls. The rs2241766 and rs2110385 genes exhibit substantial relationships with illness risk in the Iranian population, according to data analysis. Furthermore, no significant divergence from HWE was seen in the control group for the rs2241766 and rs2110385 polymorphisms ($P = 0.73$ and $P = 0.59$, respectively).

In the rs2241766 polymorphism, the T allele frequency was significantly lower in obese patients compared to healthy controls (65 percent vs 79 percent, $P < 0.0001$, OR: 0.50, 95 percent CI: 0.36–0.69), whereas the G allele frequency was significantly higher in obese patients compared to healthy controls (35 percent vs 21 percent, $P < 0.0001$, OR: 1.99, 95 percent CI: 1.45–2.75). Furthermore, the frequency of the TT genotype was significantly lower in obese patients than in healthy controls (51 percent vs 65 percent, $P = 0.008$, OR: 0.58, 95 percent CI: 0.39–0.87), whereas the frequency of the GG genotype was significantly higher in obese patients than in healthy controls (21 percent vs 7 percent, $P = 0.002$, OR: 3.52, 95 percent CI: 1.81–6.85).

In the rs2110385 polymorphism, the frequency of the G allele was significantly higher in obese patients compared to healthy controls (77 percent vs 69 percent, $P = 0.01$, OR = 1.47, 95 percent CI: 1.07–2.0), while the frequency of the T allele was significantly lower in obese patients (23 percent vs 31 percent, $P = 0.01$, OR = 0.68, 95 percent CI: 0.5–0.93). Furthermore, the GG genotype was shown to be substantially more common in obese individuals than in healthy controls (61 percent versus 51 percent, $P = 0.047$, OR: 1.5, 95 percent CI: 1.0–2.2).

Allele and genotype frequencies of the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms based on gender

In obese patients and healthy controls, the genotype distribution of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms was classified based on gender [Table 3]. The TT genotype of the adiponectin 45T/G (rs2241766) gene polymorphism was considerably reduced in male obese individuals compared to healthy ones ($P = 0.004$). In male and female obese participants, the frequency of the GG genotype of the rs2241766 gene was significantly higher than in healthy controls ($P = 0.001$ and $P = 0.04$, respectively). Only the GG genotype in female obese participants exhibited a significant increase compared to healthy controls ($P = 0.04$) in the visfatin 4689G/T (rs2110385) gene polymorphism.

Association of the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) genotypes with clinical data

Next, we looked into whether the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms are linked to clinical manifestations like serum TG, total cholesterol, HDL, and LDL, FBS, systolic and diastolic blood pressure, waist circumference, and hip circumference [Table 4].

Table 3: Genotype distribution of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms based on gender in the obese patients and healthy controls

[1]SNP	Gender	Genotypes	Control *n* (%)	Obese *n* (%)	*P*	OR (95% CI[2])
Adiponectin (rs2241766)	Male	TT	58 (66)	59 (46)	0.004	0.44 (0.25-0.75)
		TG	24 (27)	38 (30)	0.62	1.16 (0.63-2.11)
		GG	6 (7)	31 (24)	0.001	4.36 (1.73-10.98)
	Female	TT	51 (63)	59 (58)	0.48	0.81 (0.44-1.47)
		TG	24 (30)	25 (24)	0.44	0.77 (0.39-1.49)
		GG	6 (7)	18 (18)	0.04	2.68 (1.01-7.10)
Visfatin (rs2110385)	Male	GG	48 (54)	77 (60)	0.33	1.31 (0.75-2.27)
		GT	28 (32)	42 (33)	0.87	1.04 (0.58-1.87)
		TT	12 (14)	9 (7)	0.11	0.48 (0.19-1.19)
	Female	GG	38 (47)	63 (62)	0.04	1.83 (1.01-3.30)
		GT	34 (42)	31 (30)	0.10	0.60 (0.32-1.11)
		TT	9 (11)	8 (8)	0.45	0.68 (0.25-1.85)

[1]SNP: single nucleotide polymorphism. [2]Confidnce Interval

After an ANOVA test, serum LDL, waist circumference, and diastolic blood pressure were substantially different among the rs2241766 genotypes (P = 0.007, P = 0.000, and P = 0.011, respectively) in the case of adiponectin 45T/G (rs2241766) genotypes. After post-hoc analysis, it was shown that in obese individuals with the rs2241766 GG genotype, serum LDL was considerably higher than in those with the rs2241766 TT genotype (P = 0.003). It was also shown that in obese individuals with the rs2241766 GG genotype, the waist circumference was considerably higher than in those with the rs2241766 TT and TG genotypes (P = 0.001 and P = 0.002, respectively). Furthermore, we found that in obese individuals with the rs2241766 GG genotype, diastolic blood pressure was considerably higher than in those with the rs2241766 TG genotype (P = 0.009). Only the serum TG was substantially different among the rs2110385 genotypes (P = 0.039) following an ANOVA test in the instance of the visfatin 4689G/T (rs2110385) gene polymorphism. After post-hoc analysis, it was shown that in obese individuals with the rs2110385 GG genotype, blood TG was considerably higher than in those with the rs2110385 TT genotype (P = 0.002).

Furthermore, after adjusting for age and gender, logistic regressions for OR and 95 percent confidence intervals (CI) were used to assess the associations of hypertriglyceridemia (serum TG >150 (mg/dl) and hypertension (systolic/diastolic blood pressure >130/85 (mmHg) with adiponectin (TG + GG, TT as reference) genotypes in obese and control groups [Table 5]. The visfatin GT + TT genotype was shown to be substantially associated with hypertriglyceridemia in obese patients (P = 0.02, OR = 0.55, 95 percent CI: 0.32–0.94). Indeed, in obese individuals, the GT + TT genotype exhibited lower hypertriglyceridemia than the GG genotypes of the rs2110385 gene when compared to healthy participants.

Discussion

In an Iranian sample of 230 obese patients and 169 healthy controls, we looked at the pathogenic involvement of the adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms in obesity susceptibility. The rs2241766 and rs2110385 polymorphisms are strongly connected with obesity in our case control research, and might be considered a genetic susceptibility risk factor for obesity development in the Iranian population.

The T allele and TT genotype of the rs2241766 gene were shown to be less common in obese patients than in healthy controls (P<0.0001 and P=0.008, respectively, Table 2). Indeed, our findings suggest that the T allele and TT genotype of the rs2241766 gene may operate as a preventive risk factor, lowering the probability of obesity development. The G allele and GG genotype of the rs2241766 gene, on the other hand, were more frequent in obese individuals than in healthy control group (P<0.0001 and P=0.002, respectively, Table 2). According to our findings, the G allele and GG genotype of the rs2241766 gene are regarded to be a sensitive risk factor and may enhance the possibility of obesity progress. Furthermore, we found that the rs2241766 polymorphism is linked to obesity and several clinical characteristics, which is in line with previous research.[4,20-22]

The T allele was less frequent in the obese individuals than in the healthy controls for rs2110385 (P=0.01, Table 2). Furthermore, our results revealed that the T allele of the rs2110385 gene may function as a protective factor, lowering the likelihood of obesity progress. The G allele and GG genotype of the rs2110385 gene, on the contrary, were more common in obese patients than in healthy group (P=0.01 and P=0.047, respectively, Table 2). In line with our findings, the G allele and GG genotype of the rs2110385

Table 4: Association of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) genotypes with various clinical features of the obese patients

Variables	rs2241766 TT	rs2241766 TG	rs2241766 GG	*P*	Post-Hoc	Corrected *P*
Serum TG[1] (mg/dl)	139±112	159±99	157±89	0.208	TT vs TG	0.12
					TT vs GG	0.25
					TG vs GG	0.92
Serum total cholesterol	184±37	190±45	191±47	0.328	TT vs TG	0.22
					TT vs GG	0.31
					TG vs GG	0.94
Serum HDL[2] (mg/dl)	46±15	43±12	44±12	0.307	TT vs TG	0.11
					TT vs GG	0.31
					TG vs GG	0.63
Serum LDL[3] (mg/dl)	102±32	110±34	117±31	0.007	TT vs TG	0.06
					TT vs GG	0.003
					TG vs GG	0.21
Fasting Blood Sugar (mg/dl)	97±28	100±36	95±16	0.650	TT vs TG	0.58
					TT vs GG	0.46
					TG vs GG	0.39
Waist circumference (cm)	90±11	91±12	97±16	0.000	TT vs TG	0.62
					TT vs GG	0.001
					TG vs GG	0.002
Diastolic blood pressure (mm Hg)	77±12	73±12	79±13	0.011	TT vs TG	0.01
					TT vs GG	0.29
					TG vs GG	0.009
Systolic blood pressure (mm Hg)	113±14	112±15	116±14	0.171	TT vs TG	0.32
					TT vs GG	0.19
					TG vs GG	0.06
Variables	**rs2110385 TT**	**rs2110385 TG**	**rs2110385 GG**	***P***	**Post-Hoc**	**Corrected *P***
Serum TG[1] (mg/dl)	128±72	146±180	158±104	0.039	TT vs TG	0.56
					TT vs GG	0.002
					TG vs GG	0.69
Serum total cholesterol	180±41	183±32	190±42	0.079	TT vs TG	0.65
					TT vs GG	0.03
					TG vs GG	0.33
Serum HDL[2] (mg/dl)	45±12	48±21	44±14	0.176	TT vs TG	0.36
					TT vs GG	0.39
					TG vs GG	0.20
Serum LDL[3] (mg/dl)	104±35	100±39	109±31	0.216	TT vs TG	0.61
					TT vs GG	0.19
					TG vs GG	0.14
Fasting Blood Sugar (mg/dl)	95±20	102±48	98±29	0.388	TT vs TG	039
					TT vs GG	0.35
					TG vs GG	0.44
Waist circumference (cm)	90±12	88±10	93±13	0.064	TT vs TG	043
					TT vs GG	0.08
					TG vs GG	0.06
Diastolic blood pressure (mm Hg)	77±12	76±10	76±12	0.948	TT vs TG	0.79
					TT vs GG	0.77
					TG vs GG	0.95

Contd...

Table 4: Contd...

Variables	rs2110385 TT	rs2110385 TG	rs2110385 GG	*P*	Post-Hoc	Corrected *P*
Systolic blood pressure (mm Hg)	113±14	112±12	113±14	0.350	TT vs TG	0.65
					TT vs GG	0.25
					TG vs GG	0.26

**P* value correction by Bonferroni method. Data represented as mean±SD. [1]TriGlyceride. [2]High-Density Lipoprotein. [3]Low-Density Lipoprotein

Table 5: Associations between hypertriglyceridemia (Serum TG >150 (mg/dl)) and hypertension (systolic/diastolic blood pressure >130/85 (mmHg)) with adiponectin (TG + GG, TT as reference) and visfatin (GT + TT, GG as reference) genotypes in obese and control groups

Genotypes (*n*)	Hypertension		Hypertriglyceridemia	
	Control subjects	Obese subjects	Control subjects	Obese subjects
	P, OR (95% CI)		*P*, OR (95% CI)	
Adiponectin 45T/G (rs2241766)				
TT	1 (REF)		1 (REF)	
TG + GG	0.41, 0.51 (0.10-2.53)	0.91, 0.96 (0.5-1.9)	0.12, 1.8 (0.86-3.9)	0.1, 1.5 (0.92-2.61)
Visfatin 4689G/T (rs2110385)				
GG	1 (REF)		1 (REF)	
GT + TT	0.95, 1.05 (0.25-4.4)	0.4, 0.7 (0.36-1.46)	0.23, 0.62 (0.29-1.34)	0.02, 0.55 (0.32-0.94)

gene are considered to be a susceptible risk factor and may increase the probability of obesity development. Moreover, we observed that the rs2110385 polymorphism is associated to obesity and several clinical characteristics, which is in accordance with earlier studies.[19,23]

In obese patients and healthy controls, we looked at the genotype distribution of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) gene polymorphisms based on gender [Table 3]. In the instance of rs2241766, the TT genotype was shown to have a substantial protective impact against obesity in males, but the GG genotype was found to be a sensitive risk factor for obesity in both men and women. Only the GG genotype was shown to be a sensitive risk factor for obesity development in women in the instance of rs2110385.

Finally, we looked at the relationship between the genotypes of adiponectin 45T/G (rs2241766) and visfatin 4689G/T (rs2110385) and several clinical characteristics in obese individuals [Table 4]. In obese individuals, the GG genotype in rs2241766 was shown to be a risk factor for elevated serum LDL, waist circumference, and diastolic blood pressure. Furthermore, in obese individuals, the GG genotype in rs2110385 was a sensitive risk factor for elevated serum TG. GT + TT genotypes in rs2110385 were also shown to be a protective risk factor for hypertriglyceridemia in obese persons [Table 5].

Conclusions

In summary, our data revealed that polymorphisms in the adiponectin and visfatin genes are linked to obesity and several obesity-related clinical characteristics in the Iranian population. These findings provide some insight into the involvement of adiponectin and visfatin genes in obesity etiology. However, further analysis with more advanced tools in large cohorts of various ethnicities is certainly needed to assess the exact interaction between obesity and the two SNPs described, as well as their relationship with obesity-related clinical data. Integrating these data would be a promising strategy to provide implications for the prevention of obesity.

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Conflicts of interest

There are no conflicts of interest.

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