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ORIGINAL ARTICLE

Obesity is associated with IL-6 gene polymorphisms rs1800795 and rs1800796 but not SOCS3 rs4969170

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Abstract

Background An imbalance of inflammatory factors can stimulate obesity by inducing chronic inflammation in adipose tissue. Interleukin-6 (IL-6) is a cytokine with both inflammatory and anti-inflammatory functions. Suppressor of cytokine signaling 3 (SOCS3) acts as an inhibitor for a number of cytokine signals. The IL-6 and SOCS3 genes are known to be involved in lipid and energy metabolism, although it is unclear how these genes relate to obesity. The aim of this study is to determine whether the obesity risk is associated with the IL-6 (rs1800795, rs1800796) and SOCS3 (rs4969170) gene polymorphisms.

Methods and results Based on their body mass index (BMI) scores, 185 people were determined, of whom 90 were from the control group and 95 were obese. Anthropometric measurements and biochemical parameters of the study subjects were documented during the examination. Genomic DNA isolation was performed from the blood samples of all participants. IL-6 (rs1800795, rs1800796) and SOCS3 (rs4969170) polymorphisms were detected by real-time quantitative polymerase chain reaction (qRT-PCR) from genomic DNA samples. The IL-6 rs1800795 and rs1800796 variants showed a significant difference between the control and obese groups ($p=0.027$; $p=0.013$). The SOCS3 rs4969170 variation did not substantially differ between the control and obese groups ($p=0.825$).

Conclusion In our study, IL-6 rs1800795(G/C) and rs1800796(G/C) polymorphisms appeared to be a risk factor for obesity. The C allele was associated with the obesity phenotypes. However, the SOCS3 rs4969170 (A/G) polymorphism was not linked to an increased risk of obesity. IL-6 polymorphisms may be new targets for obesity treatment.

Keywords IL-6 · SOCS3 · Obesity · Polymorphism

Introduction

Obesity is a worldwide health problem that shortens the life expectancy and causes a number of diseases such as heart disease, diabetes, hypertension and atherosclerosis [1]. Obesity is a complex disease caused by genetic, metabolic, social and environmental factors, characterized by increased production and secretion of various inflammatory molecules in recent years. The imbalance of inflammatory factors contributes to the pathogenesis of obesity and related diseases by causing chronic inflammation in adipose tissue [2].

IL-6 is a cytokine with both inflammatory and anti-inflammatory effects [3] and plays a role in the regulation of body weight and lipid metabolism [4]. The primary source of circulating IL-6 is adipose tissue, and increased IL-6 release seems to be strongly correlated with obesity [5]. Genetic variants, particularly functional polymorphisms in the promoter region of genes, can alter the function and expression of genes associated with energy intake and energy

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expenditure [6, 7]. Single nucleotide polymorphisms (SNPs) of IL-6 have been investigated in many populations for their association with various chronic diseases. The rs1800795 (-174 G/C) and rs1800796 (-572 G/C) SNPs located in the promoter region of IL6 have been associated with obesity and metabolic diseases in different ethnic groups [8]. Several genetic studies have examined the IL-6 rs1800795 polymorphism's affect on IL-6 transcription and its relationship to the risk of obesity [9, 10]. While some studies have suggested that IL-6 rs1800795 variant increases the risk of obesity [11–13], others have found no association [7]. One study found a significant relationship between the IL-6 rs1800796 variant and elevated waist circumference, insulin resistance, low IL-6, and high hs-CRP levels [14]. The association of IL-6 rs1800795 and rs1800796 polymorphisms with obesity risk is not yet clear.

SOCS3 acts as an inhibitor for a number of cytokine signaling and blocks the access of transcription activators to cytokine receptor binding sites, as well as inhibits the function of leptin and a number of pathways in the insulin signaling to regulate energy balance [15]. SOCS3 gene expression is increased in obesity and plays a role in the inhibition of leptin and insulin signaling, two important hormones involved in the control of energy metabolism. Therefore, increased SOCS3 expression is linked to a variety of metabolic processes in obese people, such as decreased energy expenditure, adiposity, insulin and leptin resistance [16]. Studies investigating the relationship between SOCS3 gene polymorphisms and obesity are very limited. In a study evaluating 30 candidate genes and 355 genetic variants, the SOCS3 gene rs4969170 variant was found to be associated with body mass index (BMI), and it was stated that it may be effective in energy metabolism [17]. The aim of this study is to determine whether the obesity risk is associated with the IL-6 (rs1800795, rs1800796) and SOCS3 (rs4969170) gene polymorphisms.

Materials and methods

Study groups

A total of 185 individuals (90 controls and 95 obese), 144 (77.8%) women, and 41 (22.2%) males who applied to Marmara University Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, participated in the study. Individuals' BMI values were assessed using the World Health Organization classification (WHO) [18]. This classification identified individuals with a BMI between 18.5 and 24.9 kg/m^2 as normal (control), and individuals with a BMI between >30 kg/m^2 as obese (patient). The mean age of the healthy control group was 30 (20–50) and the mean age of the obese group was 33 (20–54). The study participants' anthropometric measurements, including height, weight, BMI, basal metabolic rate (BMR) (kcal/day), BMR %, BMR ratio, waist circumference (WC), waist-hip ratio (WHR), waist-height ratio (WHtR), fat mass (FM) %, and free fat mass (FFM) were taken in accordance with conventional procedures. Systolic and diastolic blood pressure measurements and some biochemical parameters [glucose, triglyceride, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL)] were recorded during the examination. The study protocol complied with the ethical guideline for the 2013 Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Istanbul Aydin University (Ethic No: B.30.2.AYD.0.00.00-050.06.04/398).

Linkage disequilibrium analysis

Linkage disequilibrium at the IL-6 locus was assessed based on SNPs genotyped in the Ensemble Genome Browser.

Caucasian CEU samples (https://www.ensembl.org). Pairwise $|D'|$ and r-values were computed for the 2 SNPs (rs1800795 and rs1800796) ($D=0.999985$, $r^2=0.050594$) 2 SNPs were identified to be polymorphic (minor allele frequency (MAF ≥ 0.05). For these, pairwise $|D'| \geq 0.8$ -values were high, and, therefore, they were considered to be in a single haplotype block and strong linkage disequilibrium.

Genotyping

Genomic DNA was isolated from whole blood with the QIAamp DNA Blood Mini kit (Qiagen, GmBH, Hilden, Germany). DNA concentration measurements were performed with the NanoDrop device (Thermo Scientific, Foster City, CA, USA), and the samples with a measurement ratio of DNA A260/A280 $\cong 1.8$ were accepted as pure.

Using 7500 Fast Real-Time PCR System (Applied Biosystems, Foster City, CA, USA) from the obtained DNAs, rs1800795 and rs1800796 polymorphisms in the IL-6 gene and rs4969170 polymorphisms in the SOCS3 gene were determined using "assays" specially designed for each variant (Thermo Scientific, Foster City, CA, USA). qRT-PCR detection of PCR products is made possible by including in the reaction a fluorescent molecule that reports an increase in fluorescent signal. In this study, 2×96-well format were used for 185 samples. For each sample in qRT-PCR analysis, 2.75 µL of dH_2O, 5 µL of master mix kit, 0.25 µL of genotyping assay, and 2 µL of DNA (10 ng/uL) were used in a total reaction volume of 10 µL. qRT-PCR conditions were set for a total of 40 cycles of 15 min at 95 °C and 1 min at 60 °C, after an initial denaturation step of 10 min at 95 °C. Results were analyzed according to VIC/FAM fluorescence reactions. Primers are shown in (Table 1).

Table 1 IL-6 SNP rs1800795, rs1800796 and SOCS3 SNP rs4969170 primers

IL-6 rs1800795
Assay ID: C_1839697_20
Context Sequence [VIC/FAM]:
ACTTTTCCCCCTAGTTGTGTCTTGC**[C/G]**ATGCTAAAGGACGTCACATTGCACA
IL-6 rs1800796
Assay ID: C_11326893_10
Context Sequence [VIC/FAM]:
ATGGCCAGGCAGTTCTACAACAGCC**[C/G]**CTCACAGGGAGAGCCAGAACACAGA
SOCS3 rs4969170
Assay ID: C_29949384_10
Context Sequence [VIC/FAM]:
CTTTCCATTGTTTTTAGAGACCACA**[A/G]**CCTGCTTTCTTCTAGAGTACTTTTT

Statistical analyses

Descriptive statistics for categorical variables are presented as frequency and percentage. The conformity of the numerical variables to the normal distribution was checked with the "Kolmogorov Test". For data with a normal distribution, the descriptive statistics of numerical variables were reported as mean (X) standard deviation (SD), and for data without a normal distribution, as median (min-max) values. The "Independent Sample T Test" was used for the comparison of two independent groups with normal distribution, and the "Mann-Whitney U Test" was used for the comparison of two independent groups without normal distribution. Genotype and allele distributions were calculated by chi-square test and logistic regression. Hardy-Weinberg equilibrium (HWE) was tested in groups using the chi-squared test, and $p < 0.05$ was considered a significant departure from HWE. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of the associations between IL-6, SOCS3 genes polymorphisms and obesity risk. The relationship between the variants was examined with the "Spearman Correlation Coefficient". For the significance level of the tests, $p < 0.05$ and $p < 0.01$, $p < 0.001$ were accepted. Statistical analysis of the data was performed with SPSS v26 (IBM Inc., Chicago, IL, USA) statistical package program.

Results

A total of 185 people, 95 of whom were obese and 90 were control, participated in the study. The distribution of anthropometric data and biochemical parameters in healthy control and obese groups are shown in Table 2. In our study, there is a statistically significant difference between the obese and control groups for height (cm), weight (kg), BMI, BMR, WC (cm), waist-hip ratio, waist-height ratio, fat mass %, free fat mass, systolic and diastolic blood pressure, glucose, triglyceride, LDL and HDL. The fact that the anthropometric and biochemical characteristics significantly differed between the two groups indicates that the experimental group was picked appropriately.

The genotype distribution and allele frequencies of the IL-6 gene variants rs1800795 and rs1800796 as well as the SOCS3 gene variation rs4969170 were investigated between the obese and control groups. (Table 3). The IL-6 gene rs1800795 G/G (Wild Type), G/C (Heterozygous mutant), rs1800796 G/G (Wild Type), G/C (Heterozygous mutant), and the SOCS3 gene rs4969170 A/A (Wild Type), A/G (Heterozygous mutant) genotypes were detected in all obese and control groups, but no homozygous mutant genotype was detected.

The IL-6 rs1800795 variant showed a significant difference between the control and obese groups ($p = 0.027$). The G/C heterozygous mutant genotype was found to possibly enhance the risk of obesity. Additionally, the obese and control groups differed significantly in terms of the IL-6 rs1800796 variation ($p = 0.013$). It was discovered that the G/C heterozygous mutant genotype may be linked to obesity. The C allele in the IL-6 rs1800795 and rs1800796 variations was found to possibly increase the risk of obesity.

The SOCS3 rs4969170 variation was unrelated to obesity risk and did not substantially differ between the control and obese groups ($p = 0.825$). Correlation analysis was performed between variants IL-6 rs1800795, IL-6 rs1800796 and SOCS3 rs4969170. No statistically significant relationship was found between the variants.

The association between the study group's anthropometric and demographic data and the variations (risk factors) was investigated (Table 4). There is a significant difference between IL-6 rs1800795 G/G and G/C genotypes in terms of weight, BMI, BMR (kcal/day), waist circumference, waist-height ratio, glucose, triglyceride and HDL cholesterol. Those with the IL-6 rs1800795 G/C genotype have higher weight, BMIs, BMRs (kcal/day), waist circumference, waist-height ratio, glucose and triglyceride level, and lower HDL cholesterol.

The waist circumference, waist-height ratio, weight, and waist-hip ratio, BMI characteristics were significantly different between the IL-6 rs1800796 G/G and G/C genotypes. In

Table 2 Distribution of anthropometric and biochemical parameters in healthy control and obese groups

	Control (n = 90)	Obese (n = 95)	p-value
Age	30 (20–50)	33 (20–54)	**0.004***
Sex (n,%)			
Female/Male	66 (%73.3) / 24 (%26.7)	78 (%82.1) / 17 (%17.9)	0.151
Height (cm)	166 (142–191)	161.5 (146–186)	**0.001***
Weight (kg)	60.20 (44.8–84.2)	110.60 (73.3-178.3)	**< 0.001****
BMI	24.00 (17.30–65.80)	36.90 (18.70–56.10)	**<0.001****
BMR (kcal/gün)	1461 (734–2749)	1582 (982–2486)	**<0.001****
BMR %	91 (39–131)	92 (49–129)	0.309
BMR rate	1 (0–2)	1 (0–2)	0.735
WC	71.5444 ± 6.97211	109.7263 ± 13.8198	**<0.001****
WHR	0.780 (0.630–0.980)	0.800 (0.631–1.040)	**<0.001****
WHtR	0.470 (0.360–0.890)	0.620 (0.360–0.860)	**<0.001****
FM %	29.20 (4.90–57.40)	40.50 (8.50–55.50)	**<0.001****
FFM	50.10 (9.30–99.90)	55.400 (36.50–99.90)	**<0.001****
Systolic blood pressure	110 (61–173)	110 (84–152)	**<0.001****
Diastolic blood pressure	72 (53–116)	75 (39–109)	**<0.001****
Glucose	83 (86–149)	88 (68–179)	**<0.001****
Triglyceride	71 (30–365)	86 (37–257)	**<0.001****
Cholesterol	176 (98–289)	176 (121–247)	0.240
LDL	105 (30-191.4)	109 (51–168)	**<0.001****
HDL	60.5444 ± 16.37082	45.8316 ± 8.84579	**<0.001****

BMI body mass index, *BMR* basal metabolic rate, *WC* waist circumference, *WHR* waist-hip ratio, *WHtR* waist-height ratio, *FM* fat mass, *FFM* free fat mass, *LDL* low density lipoprotein, *HDL* high density lipoprotein, *cm* centimeter, *kg* kilogram

The Bold values denote statistical significance of *p < 0.01, **p < 0.001

heterozygous people with the IL-6 rs1800796 G/C genotype, the values for weight, BMI, waist circumference, waist-to-height ratio, and waist-to-hip ratio were higher.

Only the height data show a statistically significant difference between the SOCS3 rs4969170 A/A and A/G genotypes, and this finding is not important for our investigation. The rs4969170 SOCS3 gene variation is not linked to any additional risk factors.

Discussion

Unbalanced production of inflammatory factors may contribute to the pathogenesis of obesity and obesity-related diseases [19]. The SOCS3 gene is known to be induced by a variety of cytokines, including IL-6 [20]. SNPs in the IL-6 gene's promoter region have been implicated in a few of recent studies as potential risk factors for the emergence of obesity, but this subject is still controversial. On the other hand, studies on SOCS3 promoter region polymorphism in obesity are quite insufficient. In animal models, the SOCS3 gene has been demonstrated to have a significant role in the development of obesity; however, there is a limited amount of data from human studies [21].

The IL-6 and SOCS3 genes are known to be involved in BMI, lipid and energy metabolism, although it is unclear how these genes relate to obesity. Studies examining the associations between the IL-6 rs1800795, rs1800796 and SOCS3 rs4969170 gene polymorphisms and risk of obesity remain controversial. These variations have been associated with obesity in some studies, but not in others. Our aim was to evaluate the accurately determine role of these there polymorphisms in obesity risk.

This study found an association between the risk of obesity and the IL-6 rs1800795 G/C and IL-6 rs1800796 G/C heterozygous genotypes. The C allele increases the likelihood of obesity risk in both forms. The SOCS3 rs4969170 variation did not vary between the control and obese groups significantly and was not linked to an increased risk of obesity.

In a meta-analysis study, it was concluded that the IL6 rs1800795 polymorphism minor (C) allele increased the risk of obesity, while the rs1800796 polymorphism was not associated with obesity [22]. Similarly, the rs1800795 polymorphism was demonstrated to be strongly related with a higher risk of obesity in another meta-analysis study involving 7210 cases [23]. Consistent with the meta-analysis research, it was determined that the IL-6 rs1800795 polymorphism also

Table 3 Allele frequencies and genotype distribution of IL-6 gene rs1800795, rs1800796 and SOCS3 gene rs4969170 variants

Genotype	Control (n/%)	Obese	OR (%95 Cl)	p-value
Gene/IL-6/ rs1800795				
GG (Wild Type)	59 (%65.6)	47 (%49.5)	0.682 (0.482–0.965)	**0.027***
GC (Heterozygous mutant)	31 (%34.4)	48 (%50.5)	1.325 (1.029–1.706)	
CC (Homozygous mutant)	–	–	–	
Allele Frequency				
G	0.8277	0.7473		
C	0.1723	0.2527		
Gene/IL-6/ rs1800796				
GG (Wild Type)	88 (%97.8)	84 (%88.4)	0.192 (0.044–0.842)	**0.013***
GC (Heterozygous mutant)	2 (%2.2)	11 (%11.6)	1.106 (1.022–1.197)	
CC (Homozygous mutant)	–	–	–	
Allele Frequency				
G	0.9888	0.9420		
C	0.0122	0.0580		
Gene/SOCS3/ rs4969170				
AA (Wild Type)	15 (%16.7)	17 (%17.9)	0.931 (0.495–1.752)	0.825
AG (Heterozygous mutant)	75 (%83.3)	78 (%82.1)	1.015 (0.890–1.158)	
GG (Homozygous mutant)	–	–	–	
Allele Frequency				
A	0.1648	0.1696		
G	0.8358	0.8304		

CI confidence interval, *OR* odds ratio

The Bold values denote statistical significance of *p < 0.05

increased the risk of obesity in our study. However, unlike the meta-analysis studies, it was observed that the rs1800796 variant enhanced the risk of obesity.

Kubaszek et al. discovered that individuals with the IL-6 1,800,795 C/C genotype had higher serum glucose levels and were more resistant to insulin. The subjects with the C/C genotype were also shown to have greater BMI and less energy expenditure when compared to the ones having the G allele [24]. In a study involving 149 children and adolescents aged 9.5–18 years, it was shown that carriers of the C allele for the IL-6 1,800,795 polymorphism have higher BMI. The polymorphism was found to potentially have an impact on adipose tissue [25]. The rs1800796 variant was strongly linked in a study of the Mexican-American population to increased waist circumference, insulin resistance, low IL6 levels, and high hs-CRP levels [14].

In our study, in which genotypes and risk factors including anthropometric measurements and biochemical parameters were compared, weight, BMI, BMR (kcal/day), waist circumference, waist-height ratio, glucose and triglyceride values were higher in IL-6 rs1800795 G/C genotype compared to G/G genotype, whereas HDL cholesterol was lower. We hypothesize that the C allele may affect appetite, energy metabolism, weight gain, and the risk of obesity in people. IL-6 is one of the basic elements of the immune response and also plays a role in the regulation of energy homeostasis. Studies revealed that patients on IL-6 antagonists have reduced appetite, delayed gastric emptying, had lower postprandial glycemia, and had better control of their weight. [26]. In mouse models of type 2 diabetes or obesity, treatment of IL-6 led to lower body mass and appetite suppression via the production of glucagon-like peptides [27, 28]. Although further research is needed to determine the precise mechanisms involved, it is supposed that IL-6 may be effective in processes related to appetite, energy metabolism, and obesity. SNPs can affect the bioactivity of IL-6. rs1800795, which results in a G-to-C mutation in the transcriptional promoter of the IL-6 gene, can cause changes in IL-6 expression [29]. Carriers of this mutation may show an increased risk for obesity.

IL-6 rs1800796 G/C genotype subjects had higher weight, BMI, waist circumference, waist-to-height ratio, and waist-to-hip ratio values than did wild type individuals. Similar to this, we assume that the C allele may be related to the risk of obesity and a high BMI.

Genome-wide association studies have discovered numerous links between obesity and genetic variants (GWAS). In a study investigating possible genes in pathways linked to BMI and food intake, SOCS3 rs4969170 was shown to be highly associated with BMI [17]. Another study in the chronic

Table 4 The relationship between the anthropometric and demographic data of the study group and the risk factors

Risk factors and genotypes	IL-6 rs1800795		p-value	IL-6 rs1800796		p-value	SOCS3 rs4969170		p-value
	GG (n = 106)	GC (n = 79)		GG (n = 172)	GC (n = 13)		AA (n = 32)	AG (n = 153)	
Height (cm)	164 (142–191)	165 (146–189)	0.715	164 (146–191)	165 (142–181)	0.733	167 (154–191)	163 (154–191)	**0.048***
Weight (kg)	71.00 (44.8–178.3)	91.70 (50.9–168.7)	**0.046***	77.70 (45.9–178.3)	114.80 (44.80–149.90)	**0.019***	83.40 (55.80–166.90)	79.80 (44.80–178.30)	0.239
BMI	24.00 (17.30–65.80)	36.90 (18.70–56.10)	**0.012***	25.00 (17.30–65.80)	37.90 (22.20–52.50)	**0.029***	30.50 (18.90–56.40)	31.80 (17.30–65.80)	0.535
BMR (kcal/day)	1461.00 (734–2749)	1582.00 (982–2486)	**0.047***	1545.01 ± 405.56	1665.9231 ± 543.9967	0.314	1679.2188 ± 457.86304	1527.2222 ± 403.47705	0.089
BMR %	90.9811 ± 17.2940	90.3291 ± 15.7086	0.792	91.0116 ± .15.77473	86.6154 ± .25.63376	0.553	93.3438 ± 14.44815	90.1503 ± 17.00030	0.276
BMR ratio	1.00 (0–2)	1.00 (0–2)	0.711	1.00 (0–2)	1.00 (0–2)	0.831	1.00 (0–2)	1.00 (0–2)	0.483
WC	81 (60–139)	99 (60–146)	**0.020***	84 (60–140)	111 (68–146)	**0.004****	90.00 (63.0–134.0)	89.0 (60.0–146.0)	0.459
WHR	0.7791 ± .07889	0.8014 ± .0.0889	0.073	0.7825 ± 0.08045	0.8692 ± 0.08921	**< 0.001****	0.7972 ± .0.06779	0.7868 ± .0.08690	0.458
WHtR	0.470 (0.360–0.890)	0.620 (0.360–0.860)	**0.009****	0.490 (0.360–0.890)	0.660 (0.470–0.860)	**0.004****	0.0560 (0.380–0.800)	0.540(0.360–0.890)	0.606
FM %	29.20 (4.90–57.40)	40.50 (8.50–55.50)	0.137	31.50 (4.90–57.40)	41.30 (22.40–52.70)	0.100	36.60 (8.50–54.40)	32.70 (4.90–47.40)	0.892
FFM	50.10 (9.30–99.90)	55.40 (36.50–99.90)	0.076	53.30 (9.30–99.90)	59.90 (34.80–88.00)	0.075	58.40 (41.60 –92.80)	52.70 (9.30–99.90)	0.057
Systolic blood pressure	110 (83–173)	110 (84–152)	0.574	110 (83–173)	120 (97–152)	0.259	110 (84–143)	110 (83–173)	0.525
Diastolic blood pressure	72 (53–116)	75 (59–109)	0.384	72 (39–116)	76 (60–107)	0.184	75 (60–92)	72 (39–116)	0.474
Glucose	83.00 (56.0–149.0)	88.0 (68.0–179.0)	**0.003****	85.0 (56–179)	91.0 (70–105)	0.252	84 (56–131)	86 (63–179)	0.696
Triglyceride	71.0 (30.0–365.0)	86.0 (37.0–257.0)	**0.018***	77.0 (30.0–365.0)	86.0 (55.0–262.2)	0.355	69 (30–218)	80 (34–365)	0.119
Cholesterol	176.0 (98.0–289.0)	176.0 (121.0–247.0)	0.702	176.0 (100.0–289.0)	189.0 (98.0–254.0)	0.569	169 (98–289)	177 (100–279)	0.254
LDL	109.1284 ± .35.7010	110.6861 ± 24.6307	0.726	105.0 (37.0–191.40)	125.0 (30.0–171.0)	0.198	106.950 ± 38.26627	110.3883 ± 29.86303	0.635
HDL	52.0 (31.0–117.0)	47.0 (26.0–83.0)	**0.006****	51.0 (26.0–117.0)	47.0 (32.0–77.0)	0.169	51 (34–83)	50 (26–117)	0.296

BMI body mass index, *BMR* basal metabolic rate, *WC* waist circumference, *WHR* waist-hip ratio, *WHtR* waist-height ratio *FM* fat mass, *FFM* free fat mass, *LDL* low density lipoprotein, *HDL* high density lipoprotein, *cm* centimeter, *kg* kilogram

The Bold values denote statistical significance of *p < 0.05, **p < 0.01, ***p < 0.001

hepatitis patient population found that the rs4969170 AA genotype was considerably more prevalent in the insulin-resistant group compared to those without insulin resistance [30]. The SOCS3 rs4969170 variant, however, was not linked to obesity or any other obesity-related factors in our study. These findings suggest that the variation of SOCS3 rs4969168 may have different consequences depending on ethnicity. The effect of the SOCS3 rs4969170 variation on obesity has not been examined elsewhere. Large-scale investigations in many populations are required in this regard.

Conclusion

We found that IL-6 rs1800795 (G/C) and rs1800796 (G/C) polymorphisms appeared to be a risk factor for obesity. Especially, the C allele and the GC genotype in IL-6 were associated with the obesity phenotypes. These findings suggest that the IL-6 polymorphisms may predict the increased risk of obesity and help to identify a new therapeutic approach for this disorder. However, we discovered that the SOCS3 rs4969170 (A/G) polymorphism was not linked to an increased risk of obesity. We recommend future studies with larger samples to analyze the relationship between anthropometric-biochemical parameters and single nucleotide polymorphisms involved in obesity.

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Declarations

Conflict of interest The authors declare that they have no confct of interest.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the local ethics committee (Istanbul Aydin University Ethical Committee (Ethic No: B.3 0.2.AYD.0.00.00-050.06.04/398). All subjects agreed to participate in this study and signed the informed consent form prior to the study.

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