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The importance of *CYP1B1* polymorphism in obesity

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Abstract

Obesity is a multifactorial disease, commonly observed both worldwide and in our country, triggered by environmental and genetic factors, adversely affecting all physiological functions of the body, and leading to an increase in body fat mass. Although various variants associated with susceptibility to obesity have been identified in genomic studies, these variants explain only a small portion of the genetic basis of obesity. This case-control study investigates, for the first time in the Turkish population, the relationship between *CYP1B1* gene rs1056827 and *rs1056836* polymorphisms in obesity patients undergoing surgical intervention (bariatric surgery). Genotyping of the polymorphisms was performed using Real-Time PCR in 63 female and 29 male obesity patients who underwent bariatric surgery and 40 female and 51 male nonobese individuals. In our study, genotype distributions for the *CYP1B1* gene rs1056836 polymorphism were found to be 51.1% CC, 40.2% CG, and 8.7% GG in the case group and 46.2% CC, 47.3% CG, and 6.6% GG in the control group. The frequency of the C allele was 71.2%, and the G allele was 28.8% in the case group, while the frequency of the C allele was 70.3%, and the G allele was 29.7% in the control group. For the rs1056827 polymorphism, the genotype distributions were 10.8% GG, 35.9% GT, and 53.3% TT in the case group and 7.7% GG, 49.4% GT, and 42.9% TT in the control group. The frequency of the G allele was 28.8%, and the T allele was 71.2% in the case group, whereas the frequency of the G allele was 32.4%, and the T allele was 67.6% in the control group. No significant difference was found between the case and control groups in terms of anthropometric measurements and biochemical parameter values for the rs1056836 and rs1056827 polymorphisms of the *CYP1B1* gene. Our study is valuable as it is the first to investigate the association of *CYP1B1*2* (rs1056827) and *CYP1B1*3* (rs1056836) polymorphisms with obesity, and it was determined that there was no difference in the investigated polymorphisms between the control group and the obesity group.

Abbreviations: BMI = body mass index, CRP = C-reactive protein, CYP = cytochrome, CYP1B1 = cytochrome P450 1B1, F = female, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein, M = male, PCR = polymerase chain reaction, SNP = single nucleotide polymorphism, TC = total cholesterol, TG = triglycerides.

Keywords: *CYP1B1*, obesity, polymorphism, rs1056827, rs1056836

1. Introduction

Obesity is recognized as a global health problem due to its association with complex chronic diseases such as cardiovascular diseases, type 2 diabetes, and cancer.[1] Regardless of the treatment method, the response of obesity patients to therapy varies, and it is suggested that environmental factors, as well as genetic variations, play a role in the success of weight loss treatments.[2] The role of genetic factors in obesity is complex and often exhibits familial transmission. It has been noted that individuals with a family history of obesity carry an increased risk of obesity, even if they do not live with other family members.[3] Among the surgical treatment options for obesity, bariatric surgery stands out as the most effective treatment, particularly in patients diagnosed with morbid obesity.[4] Bariatric surgery is indicated for patients with a BMI > 35 kg/m² in cases where traditional clinical treatment demonstrates low efficacy and where there is a high mortality risk due to comorbidities associated with obesity.[2]

Genome-wide association studies in different populations have identified approximately 200 genetic variants associated with obesity, of which only 3% are thought to be related to BMI heritability.[5] Moreover, some single nucleotide polymorphisms (SNPs) are reported to play a significant role in obese populations.[6] Although various variants associated with susceptibility to obesity have been identified in genomic studies,

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these variants explain only a small portion of the genetic basis of obesity.

Cytochrome P450 1B1 (*CYP1B1*), a member of the cytochrome (CYP) superfamily, is a gene expressed in the liver and involved in the metabolism of numerous xenobiotics, including polycyclic aromatic hydrocarbons.[7] The *CYP1B1* gene is located in the 2p22-p21 region and encodes a protein containing 543 amino acids. Studies have shown that *CYP1B1* modulation may reduce adipogenesis and tumor formation, potentially preventing obesity, hypertension, atherosclerosis, and cancer. Therefore, *CYP1B1* might be considered a therapeutic target for the treatment of metabolic diseases.[7] The majority of cytochrome enzyme polymorphisms consist of SNPs. Following polymorphism in genes encoding CYP enzymes, a decrease, increase, or absence in protein expression may occur. The *CYP1B1* gene has 26 polymorphic alleles.[8] Major alleles and polymorphisms of the *CYP1B1* gene include *CYP1B1*2* (Ala119Ser, G/T), *CYP1B1*3* (Leu4326Ser, C/G), and *CYP1B1*4* (Asn453Ser). Although not definitively proven, it is thought that variant alleles are more prone to altering enzyme activities.[9,10]

Understanding the enzymes exhibiting genetic polymorphism in humans and elucidating genetic factors may be important in delaying the progression of and treating many diseases, including obesity. In this study, for the first time in the Turkish population, we aimed to determine the *CYP1B1*2* (rs1056827) and *CYP1B1*3* (rs1056836) alleles of *CYP1B1*2* (rs1056827), a member of the CYP superfamily, which have been previously studied in tissue but not in blood, in obesity patients who underwent bariatric surgery in blood samples by Real-Time PCR technique.

2. Materials and methods

2.1. Selection of case and control groups

The study group consisted of 92 patients diagnosed with obesity who were followed up in the General Surgery Clinic of Afyonkarahisar Health Sciences University between 2022 and 2024, and a control group of 91 nonobese individuals. The patients included in the study group were selected from individuals aged over 18 years with a BMI above 35 kg/m² who underwent bariatric surgery and had no pregnancy or mental disabilities. The control group was composed of volunteer individuals aged over 18 years with a BMI below 30 kg/m², who were not pregnant and had no mental disabilities. Approval for the study was obtained from the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee (2022/501).

2.2. Anthropometric measurements and biochemical analyses

For anthropometric measurements, age, sex, body weight, height, and BMI were determined in 92 patients who underwent bariatric surgery and 91 nonobese individuals in the control group. For biochemical analyses, blood samples collected from the patients and control group participants were used to measure total cholesterol (TC), HDL-C, LDL-C, triglycerides (TG), uric acid, vitamin B12, folic acid, C-reactive protein (CRP), and hemoglobin levels.

2.3. DNA isolation and genotyping

Peripheral blood samples (2 mL) were collected in EDTA tubes from the patients and control group participants for DNA isolation. Genomic DNA isolation was performed using a commercial kit (Roche High Pure PCR Template Preparation Kit) from the collected blood samples. For the DNA samples from the case and control groups, genotyping of the *CYP1B1* gene rs1056836 and rs1056827 polymorphisms was performed using LightCycler® FastStart DNA Master HybProbe (Roche Diagnostics, Germany) and LightSNIP *CYP1B1* rs1056836 and rs1056827 Reagent Mix kits (Tib Molbiol, Germany). The reaction mixture was prepared with a final volume of 20 µL, containing 10 µL of probe master mix, 1 µL of LightSNIP mix for each gene region, 4 µL of ddH_2O, and 5 µL of DNA from each sample. The plate containing the reaction mixtures for each sample was placed into a Real-Time PCR device (LightCycler® 96, Germany). Melting temperature (Tm) data were collected for the rs1056836 and rs1056827 regions, and genotyping was performed to classify DNA samples from case and control groups as homozygous normal (wild type), heterozygous, or homozygous mutant.

2.4. Statistical analyses

Statistical analyses were performed using the SPSS v. 22.0 software (Chicago), and all results were presented as mean ± standard deviation (mean ± SD). To determine statistical differences, genotype and allele frequencies of the *CYP1B1* gene rs1056836 and rs1056827 polymorphisms were analyzed using the chi-square (χ^2) test for 92 patients who underwent bariatric surgery and 91 control group participants admitted to the General Surgery outpatient clinic for non-obesity-related reasons. Comparisons of genetic polymorphisms with anthropometric measurements and biochemical parameter values were conducted using 1-Way ANOVA. *P*-value < .05 was considered statistically significant.

3. Results

3.1. Anthropometric measurements and biochemical parameters of case and control groups

The anthropometric measurements, including age, sex, body weight, height, and BMI, as well as the biochemical parameters, such as TC, HDL-C, LDL-C, TG, uric acid, vitamin B12, folic acid, CRP, and hemoglobin, were analyzed for individuals in the case and control groups.

In terms of anthropometric measurements, the mean age was 37.73 ± 12.49 years in the case group and 50.77 ± 17.72 years in the control group, with a statistically significant difference between the groups (.001, $P < .05$) (Table 1). When sex distribution was analyzed, 69.6% of the case group were female, and 30.4% were male, while 43.9% of the control group were female, and 53.1% were male. The difference in sex distribution between the groups was statistically significant (.001, $P < .05$). In terms of body weight, the mean body weight was 113.23 ± 19.58 kg in the case group and 69.00 ± 8.85 kg in the control group, with a statistically significant difference observed between the groups (.001, $P < .05$) (Table 1). BMI comparisons also revealed a statistically significant difference between the case and control groups (.001, $P < .05$) (Table 1). For height, no statistically significant difference was found between the case and control groups (.432, $P > .05$) (Table 1).

In terms of biochemical parameters, uric acid, CRP, and hemoglobin levels showed statistically significant differences between the groups, while TC, HDL-C, LDL-C, triglycerides, vitamin B12, and folic acid levels did not exhibit statistically significant differences (Table 1).

3.2. Genotype and allele frequencies of CYP1B1 gene rs1056827 polymorphism

The rs1056827 (A119S) polymorphism of the *CYP1B1* gene has 3 distinct genotypes: GG (homozygous normal), GT (heterozygous), and TT (homozygous mutant). The rs1056827 polymorphism in the *CYP1B1* gene occurs due to a G/T substitution at the 119th base.

Within the scope of this study, the genotype ratios for *CYP1B1* gene rs1056827 polymorphism were determined as 10 (10.8%) individuals with GG homozygous normal genotype, 33 (35.9%) individuals with GT heterozygous genotype and 49 (53.3%) individuals with TT homozygous mutant genotype in the case group intervened with bariatric surgery. In the control group, the genotype frequencies were as follows: 7 individuals (7.7%) with the GG homozygous normal genotype, 45 individuals (49.4%) with the GT heterozygous genotype, and 39 individuals (42.9%) with the TT homozygous mutant genotype. When the genotype frequencies were statistically compared between the groups, no significant difference was observed (Table 2).

In the rs1056827 polymorphism of the *CYP1B1* gene, the wild-type allele is G, while the risk (mutant) allele is T. The frequency of the wild-type G allele was found to be 53 (28.8%) in the case group and 59 (30.6%) in the control group. The frequency of the risk allele T was 131 (71.2%) in the case group and 123 (69.4%) in the control group. When allele frequencies were statistically compared between the groups, no significant difference was observed (Table 2).

3.3. Genotype and allele frequencies of CYP1B1 gene rs1056836 polymorphism

Genotype and allele ratios of rs1056836 (V4326L, C/G) and rs1056827 (A119S, G/T) polymorphisms of *CYP1B1* gene were determined in genomic DNA isolated from the peripheral blood of 92 bariatric surgery cases and 91 nonobese control subjects. The rs1056836 (V4326L) polymorphism of the *CYP1B1* gene has 3 distinct genotypes: CC (homozygous normal), CG (heterozygous), and GG (homozygous mutant). The rs1056836 polymorphism in the *CYP1B1* gene is caused by a C/G change at base 4326.

Within the scope of this study, the genotype ratios for *CYP1B1* gene rs1056836 polymorphism were determined as 47 (51.1%) individuals with CC homozygous normal genotype, 37 (40.2%) individuals with CG heterozygous genotype and 8 (8.7%) individuals with GG homozygous mutant genotype in the case group intervened with bariatric surgery. In the control group, the number of individuals with CC homozygous normal genotype was 42 (46.2%), CG heterozygous genotype was 43 (47.3%) and GG homozygous mutant genotype was 6 (6.6%). When the genotype frequencies were statistically compared between the groups, no significant difference was observed (Table 3).

In the *rs1056836* polymorphism of the CYP1B1 gene, C is the wild-type allele and G is the risk (mutant) allele. The proportion of wild-type C allele was 131 (71.2%) in the case group and 128 (56.5%) in the control group. The rate of the risk allele G was 53 (28.8%) in the case group and 54 (29.7%) in the control group. When allele frequencies were statistically compared between the groups, no significant difference was observed (Table 3).

3.4. The effect of CYP1B1 gene rs1056827 and rs1056836 polymorphisms on anthropometric measurements and biochemical values

CYP1B1 gene rs1056836 polymorphism was analyzed in a group of 92 cases who underwent bariatric surgery. The anthropometric values of age, gender, body weight, height and body mass index and the biochemical parameters of TC, HDL-C, LDL-C, triglycerides, uric acid, vitamin B12, folic acid, CRP,

Table 1

Anthropometric measurements and biochemical parameter values of individuals in the case and control groups.

Parameters	Case (n = 92)	Control (n = 91)	*P*
Age	37.73 ± 12.49	50.77 ± 17.72	**.001**
Gender (F:M)	63 (%69.6):29 (%30.4)	40 (%43.9):51 (%56.1)	**.001**
Body weight (kg)	113.23 ± 19.58	69.00 ± 8.85	**.001**
Height (cm)	164.50 ± 9,89	165.57 ± 8.45	.432
BMI (kg/m^2)	41.68 ± 4.74	25.17 ± 2.4	**.001**
TC (mg/dL)	200.54 ± 32,57	192.48 ± 29.34	.171
HDL-C (mg/dL)	46.69 ± 10.13	46.22 ± 11.22	.843
LDL-C (mg/dL)	129.20 ± 29.51	121.36 ± 26.88	.052
TG (mg/dL)	121.26 ± 38.25	136.06 ± 50.28	.68
Uric acid (mg/dL)	5.94 ± 2.57	4.9 ± 1.76	**.005**
B12 (pg/mL)	471.83 ± 241.83	477.86 ± 262.59	.951
Folic acid (mcg)	8.02 ± 3.73	7.13 ± 3.04	.139
CRP (mg/L)	15.10 ± 22.85	24.36 ± 52.25	**.002**
Hemoglobin (g/dL)	13.28 ± 1.90	13.38 ± 2.28	**.001**

Bold values indicates statistical significance of 0.05.

The data are presented as mean ± standard deviation.

BMI = body mass index, CRP = C-reactive protein, F = female, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein, M = male, TC = total cholesterol, TG = triglycerides.

Table 2

Genotype frequencies of the *CYP1B1* gene rs1056827 polymorphism in the case and control groups.

Genotype	Case (n = 92)	Control (n = 91)	Total (n = 183)	*P*
GG homozygous normal	10 (10.8%)	7 (7.7%)	17 (9.3%)	.612
GT heterozygous	33 (35.9%)	45 (49.4%)	78 (42.6%)	.074
TT homozygous mutant	49 (53.3%)	39 (42.9%)	88 (48.1%)	.237
Allele				
G	53 (28.8%)	59 (32.4%)	112 (30.6%)	.184
T	131 (71.2%)	123 (67.6%)	254 (69.4%)	.612

and hemoglobin were analyzed by ANOVA test using SPSS v. 22.0 program.

The rs1056827 (A119S, G/T) polymorphism of the *CYP1B1* gene has distinct genotypes: GG (homozygous normal), GT (heterozygous), and TT (homozygous mutant). Body weight (116.16 ± 20.92), BMI (42.03 ± 5.58), uric acid (6.02 ± 2.77), vitamin B12 (486.58 ± 280.96), CRP (17.02 ± 28.91) and hemoglobin (13.50 ± 1, 76) levels were higher in TT genotype, while age (39.03 ± 14.17), HDL-C (48.64 ± 12.38) and folic acid (8.99 ± 4.42) levels were higher in GT genotype (Table 4). No abnormal values were found in the GG genotype, and although the levels of some parameters were found to be high, they were not statistically significant.

The *CYP1B1* gene rs1056836 (V4326L, C/G) polymorphism has 3 different genotypes: CC (homozygous normal), CG (heterozygous) and GG (homozygous mutant). The analysis showed that age (41.38 ± 11.25), LDL-C (134.30 ± 16.86), vitamin B12 (570.50 ± 234.01) and CRP (32.68 ± 53.42) levels were higher in the GG genotype, whereas body weight (115.04 ± 20.78), height (164.92 ± 8.51), BMI (42.07 ± 4.94) and hemoglobin (13.44 ± 1.79) levels were higher in the CG genotype. No abnormal values were found in the CC genotype (Table 5). *CYP1B1* gene rs1056836 (V4326L) polymorphism was not statistically significant on anthropometric measurements and biochemical parameter values.

4. Discussion

Obesity is a health problem characterized by abnormal fat accumulation due to increased consumption of high-energy foods and decreased physical activity. Over the past 3 decades, the significant rise in global obesity rates has been highlighted as a major public health issue in both developed and developing countries.[11] This increase is attributed to environmental factors, such as the consumption of high-energy foods and insufficient physical activity, as well as genetic predisposition.[12] Obesity is also known to be associated with various diseases, including type 2 diabetes, cardiovascular disorders, hypertension, osteoarthritis, and certain types of cancer.[13] The types of cancer associated with obesity include esophageal, thyroid, colon, kidney, liver, melanoma, multiple myeloma, rectum, gallbladder, leukemia, lymphoma, prostate cancer in men, and postmenopausal breast and endometrial cancer in women.[14] Studies emphasize that environmental factors, such as diet, physical activity, and education level, along with genetic factors, can influence obesity. However, the role of genetic factors in obesity has not been fully elucidated. Genome-wide association studies conducted on different populations have identified approximately 200 genetic variants associated with obesity, with only 3% of these variants thought to be related to BMI heritability.[5] Additionally, certain SNPs are reported to play a significant role in the obese human population.[6]

The cytochrome P450 (CYP) family, or CYP enzymes, metabolize xenobiotics such as steroids, lipid hormones, and drugs. The *CYP1B1* gene, a member of this family, encodes an extrahepatic CYP450 enzyme that activates many procarcinogens, including nitroaromatic hydrocarbons, arylamines, and polycyclic aromatic hydrocarbons.[15] *CYP1B1* plays a key role in the metabolism of androgen and estrogen substrates. Five distinct SNPs in the *CYP1B1* gene have been identified, resulting in amino acid substitutions: A119S, R48G, L432V, A443G, and N453S.[16] SNPs are genetic variations involving a single nucleotide change within the DNA sequence. These variations can lead to different phenotypes, predisposing individuals to certain diseases.[16] Studies suggest that *CYP1B1* may play an important role in adipogenesis and obesity.[17] The body weights, epididymal fat pad weights, and liver fat content of *CYP1B1*-null mice induced by a high-fat diet (HFD) were reported to be significantly lower compared to wild-type (non-mutated) mice.[18]

Table 3

Genotype frequencies of the *CYP1B1* gene rs1056836 polymorphism in the case and control groups.

Genotype	Case (n = 92)	Control (n = 91)	Total (n = 183)	*P*
CC homozygous normal	47 (51.1%)	43 (47.3%)	90 (49.2%)	.555
CG heterozygous	37 (40.2%)	42 (46.2%)	79 (43.1%)	.373
GG homozygous mutant	8 (8.7%)	6 (6.6%)	14 (7.7%)	.782
Allele				
C	131 (71.2%)	128 (70.3%)	259 (70.8%)	.509
G	53 (28.8%)	54 (29.7%)	107 (29.2%)	.302

Table 4

The effect of *CYP1B1* gene rs1056827 polymorphism on anthropometric measurements and biochemical parameters in the case group.

Parameters	GG (n = 10)	GT (n = 33)	TT (n = 49)	*P*
Age	36.20 ± 10.17	39.03 ± 14.17	37.16 ± 11.85	.742
Body weight (kg)	114.62 ± 26.47	108.47 ± 14.14	116.16 ± 20.92	.215
Gender (F:M)	5 (%7.9):5 (%17.2)	25 (%27.2):8 (%8.7)	33 (%35.9):16 (%17.4)	.298
Height (cm)	167.80 ± 15.66	161.93 ± 8.18	165.92 ± 9.16	.067
BMI (kg/m^2)	40.34 ± 3.10	41.58 ± 3.69	42.03 ± 5.58	.575
TC (mg/dL)	208.69 ± 42.04	195.32 ± 25.17	202.40 ± 34.38	.440
HDL-C (mg/dL)	40.01 ± 6.38	48.64 ± 12.38	46.92 ± 8.54	.060
LDL-C (mg/dL)	138.94 ± 34.53	123.84 ± 24.97	130.87 ± 31.13	.315
TG (mg/dL)	137.79 ± 62.36	114.21 ± 30.46	122.64 ± 36.52	.219
Uric acid (mg/dL)	5.96 ± 1.71	5.80 ± 2.54	6.02 ± 2.77	.933
B12 (pg/mL)	481.91 ± 175.05	446.89 ± 195.65	486.58 ± 280.96	.763
Folic acid (mcg)	6.59 ± 2.27	8.99 ± 4.42	7.66 ± 3.35	.127
CRP (mg/L)	9.58 ± 10.77	13.91 ± 13.50	17.02 ± 28.91	.605
Hemoglobin (g/dL)	13.21 ± 1.87	12.99 ± 2.12	13.50 ± 1.76	.491

The data are presented as mean ± standard deviation.

BMI = body mass index, CRP = C-reactive protein, F = female, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein, M = male, TC = total cholesterol, TG = triglycerides.

Table 5

The effect of *CYP1B1* gene rs1056836 polymorphism on anthropometric measurements and biochemical parameters in the case group.

Parameters	CC (n = 47)	CG (n = 37)	GG (n = 8)	*P*
Age	38.21 ± 11.49	36.32 ± 13.99	41.38 ± 11.25	.548
Body weight (kg)	112.24 ± 20.22	115.04 ± 20.78	110.75 ± 6.96	.759
Gender (F:M)	32 (%34.8):15 (%16.3)	25 (%27.2):12 (%13.0)	6 (%6.5):2 (%2.2)	.916
Height (cm)	163.98 ± 11.39	164.92 ± 8.51	164.50 ± 6.52	.863
BMI (kg/m^2)	41.59 ± 4.87	42.07 ± 4.94	40.44 ± 2.77	.672
TC (mg/dL)	204.79 ± 37.93	195.33 ± 25.89	199.71 ± 18.85	.413
HDL-C (mg/dL)	48.06 ± 11.24	46.18 ± 9.16	42.11 ± 5.88	.278
LDL-C (mg/dL)	131.72 ± 36.31	124.96 ± 20.69	134.30 ± 16.86	.515
TG (mg/dL)	122.61 ± 45.57	120.59 ± 30.72	116.46 ± 21.98	.908
Uric acid (mg/dL)	6.18 ± 2.61	5.91 ± 2.74	4.65 ± 0.67	.300
B12 (pg/mL)	452.93 ± 192.50	474.52 ± 295.30	570.50 ± 234.01	.449
Folic acid (mcg)	8.28 ± 3.85	7.77 ± 3.72	7.64 ± 3.43	.790
CRP (mg/L)	14.47 ± 21.19	12.09 ± 10.64	32.68 ± 53.42	.065
Hemoglobin (g/dL)	13.21 ± 1.97	13.44 ± 1.79	12.97 ± 2.36	.777

The data are presented as mean ± standard deviation.

BMI = body mass index, CRP = C-reactive protein, F = female, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein, M = male, TC = total cholesterol, TG = triglycerides.

Microarray data obtained from the livers of diet-induced obese *CYP1B1 KO* mice revealed that *CYP1B1* deletion significantly altered the expression of genes related to fatty acid homeostasis.[19] Another study showed that *CYP1B1* deficiency might reduce HFD-induced obesity and improve glucose tolerance.[20] However, it was noted that the absence of *CYP1B1* does not completely eliminate adipogenesis induced by adipogenic agents, suggesting that further investigation is needed to understand the role of *CYP1B1* in the regulation of obesity mechanisms.

One of the primary polymorphisms in the *CYP1B1* gene, rs1056827 (A119S, G/T), is localized in exon 2 and results from a guanine-to-thymine substitution. Another polymorphism, rs1056836 (V4326L, C/G), is localized in exon 3 and results in a leucine-to-valine substitution. In this study, we investigated for the first time the association of *CYP1B1* gene *CYP1B1*2* (rs1056827) and *CYP1B1*3* (rs1056836) polymorphisms with obesity in bariatric surgery patients in the Turkish population.

Anthropometric measurements, including age, sex, body weight, height, and BMI, as well as biochemical parameters such as TC, HDL-C, LDL-C, TG, uric acid, vitamin B12, folic acid, CRP, and hemoglobin, were analyzed in both the bariatric surgery-obesity group and the nonobese control group. Parameters such as age, sex, body weight, and BMI are significant factors associated with obesity. Among these, the mean age was found to be significantly higher in the control group compared to the obesity group. Regarding gender distribution, the proportion of females was 69.6% in the obesity group and 43.9% in the control group, suggesting a strong association between obesity and female gender. These results align with findings from previous studies in the literature.[21,22] Anthropometric measurements such as height, body weight, and BMI are important parameters associated with obesity. Among these, body weight and BMI were found to be significantly different between the obesity and nonobese groups ($P < .05$). In terms of biochemical parameters, only uric acid, CRP, and hemoglobin levels showed statistically significant differences between the groups ($P < .05$). A study conducted on 26,016 middle-aged and elderly individuals (>35 years) with metabolic syndrome in Taiwan reported that obesity was associated with high body fat, waist circumference, WHR, and inflammatory markers (CRP and neutrophil count).[23] In this study, a significant difference in CRP levels was also observed between the obesity and control groups. This result is thought to be due to the activation of systemic inflammation caused by the high waist-to-hip ratio associated with obesity, leading to increased release of inflammatory biomarkers. Hemoglobin concentration was found to differ significantly between obese and control groups ($P < .05$). While many studies have reported higher hemoglobin concentrations in obese groups, this study found higher hemoglobin concentrations in the control group. A 2018 study observed that although there was no significant difference in hemoglobin and ferritin levels, hemoglobin and ferritin concentrations were higher in obese and overweight individuals compared to those with normal weight, while serum iron levels were lower.[24] Another study in Turkey found lower hemoglobin, serum iron, and ferritin levels in obese children compared to children with normal weight.[25] When the groups were evaluated in terms of uric acid, the uric acid level in the obesity group was 5.94 ± 2.57 mg/dL, while this value was found to be 4.9 ± 1.76 mg/dL in the control group and a significant difference was found between the groups and a higher uric acid concentration was determined in the obese group. Studies have shown that uric acid is associated with diabetes, HT and coronary heart disease.[26,27] Uric acid elevation may be thought to mediate the development of obesity.

It is known that oxidative stress is associated with the development of obesity, a multifactorial disease. We investigated the association of rs1056827 (A119S, G/T) and rs1056836 (V4326L, C/G) polymorphisms of *CYP1B1* gene, one of the CYP enzyme family members catalyzing Phase I reactions that play an important role in xenobiotic mechanism, with obesity. The rs1056827 polymorphism has 3 different genotypes as GG (homozygous normal), GT (heterozygous) and TT (homozygous mutant) and the risky allele of this polymorphism is the T allele. Although the number of individuals with GT and TT genotypes in this polymorphism was higher in obesity patients who underwent bariatric surgery, it was not statistically significant between the groups. The rs1056836 polymorphism has 3 different genotypes, CC (homozygous normal), CG (heterozygous) and GG (homozygous mutant), and the risky allele of this polymorphism is the G allele. In this polymorphism, the highest rate was observed in individuals with CC homozygous normal genotype in both obesity group and nonobese control group. The association of these polymorphisms in the CYP1B1 gene with cancer has also been investigated in different studies in the literature.[28] When rs1056827 and rs1056836 polymorphisms in the *CYP1B1* gene were analyzed for the risk of development of different cancer types, it was reported that rs1056827 polymorphism was associated with breast, endometrium, prostate,[20] colon[29] and larynx[30] cancer.[15] reported that individuals with high BMI and the TT genotype have a higher risk of developing prostate cancer.[15] Regarding the rs1056836 polymorphism, it has been stated that individuals with the CG + GG genotypes are at a higher risk of developing breast cancer,[16,31] in their study involving 152 patients diagnosed with obesity who underwent bariatric surgery and xenobiotic metabolism, investigated the

expression of CYP1A1 and CYP1B1 isoenzymes using the immunohistochemistry method. They reported significant expressions of these enzymes in obese patients.[31] The primary reason for this is attributed to the role of these enzymes in the detoxification mechanism.

5. Conclusion

In conclusion, this study is the first in the literature to investigate the role of *CYP1B1* gene rs1056827 and rs1056836 polymorphisms in obesity. The main limitation of this study is that the case and control group participants were recruited from a single clinic. This research could serve as a pioneering study to better understand the effects of these polymorphisms on obesity by increasing the sample size in both the Turkish population and populations from different regions.

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