+45T>G single nucleotide polymorphism of adiponectin gene: Is it a factor in childhood obesity?

Childhood obesity

Tuba Kasap[1], Ömer Ateş[2], Samet Özer[1], Ali Gül[1], Resul Yılmaz[1], Ergün Sönmezgöz[1], Osman Demir[3], Emel Ensari[2]
[1]Department of Pediatrics, [2]Department of Medical Biology, [3]Department of Biostatistics,
Gaziosmanpaşa University Hospital, Tokat, Turkey

Abstract

Aim: Childhood obesity is increasing in incidence and is strongly associated with obesity in adulthood. Several studies to explain the role of genetics in the pathogenesis of obesity have been performed. The aim of this study was to investigate the relation between +45T>G single nucleotide polymorphism (SNP) and childhood obesity. Material and Method: 268 obese and 185 healthy (control) children and adolescents aged 6-17 years were enrolled. Laboratory tests including fasting glucose, insulin level, and lipid profile were drawn only from the obese participants. The +45T>G SNP in adiponectin gene was analyzed from the members of both groups by a polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP) method. Results: The genotype frequencies of the adiponectin gene for +45 locus in exon 2 were 77.9%, 19.1%, and 3% in obese subjects and 72.1%, 23.5%, and 4.4% in the control group for TT, TG, and GG respectively (p=0.357), with the allelic frequency of the G allele 12.5% in obese subjects and 16.1% in controls (p=0.129). When we compared different adiponectin genotypes, there wasn't any significant difference in frequencies of TT genotype (wild type) and non-TT (TG+GG) genotypes between the obese and control groups (p=0.162). Also, comparing GG genotype and non-GG (TG+TT) genotypes revealed no significant difference between the obese and control groups (p=0.439). Among obese subjects there were no significant relationships between different genotypes and clinical characteristics such as presence of hypertriglyceridemia, low high-density lipoprotein (HDL-C), hypertension, and insulin resistance. Discussion: In conclusion, in the present study, in a well-described obese and a control group of pediatric patients, we observed a lack of association between the +45T>G SNP and childhood obesity and its traits.

Keywords

Childhood Obesity; Adiponectin; Single Nucleotide Polymorphism

DOI: 10.4328/JCAM.5735 Received: 02.02.2018 Accepted: 11.03.2018 Published Online: 13.03.2018 Printed: 01.09.2018 J Clin Anal Med 2018;9(5): 376-80
Corresponding Author: Tuba Kasap, Department of Pediatrics, Gaziosmanpaşa University School of Medicine, Tokat, Turkey.
E-Mail: tubaserdar06@hotmail.com
ORCID ID: orcid.org/0030-0033-0366-5249

Introduction

Childhood obesity is increasing in incidence and is strongly associated with obesity in adulthood [1,2]. Because obese children are at risk of metabolic syndrome, cardiovascular diseases, and increased adult morbidity and mortality, childhood obesity is in fact a public health problem [3,4].

Childhood obesity reflects complex interactions of genetic, environmental, social, and behavioral factors. Increase in fast food consumption, alteration of nutritional components and food intake patterns, increased time on a television, computer, etc. and less time in active exercise may be associated with the increasing obesity rate in children. Other than these factors, genetics is an indisputably important factor for childhood obesity. The probability for a child with one obese parent to become an obese adult is three times higher than for those with nonobese parents [5,6]. For this reason, apart from advanced efforts to change eating behavior and to increase time on exercise, several studies to explain the role of genetics in the pathogenesis of obesity have been performed. In this context, adipokines and adipokine genes are being widely investigated. Adipokines are a variety of proteins secreted by adipocytes that are involved in the regulation of insulin sensitivity, lipid metabolism and energy balance, and metabolic homeostasis [7]. Some of the adipokines are leptin, adiponectin, TNF-alpha, IL-6, resistin, vaspin, visfatin, and omentin. Among these, the blood level of adiponectin has been found to be reduced in obese people compared with lean individuals [8]. Animal models and human studies support an important role for adiponectin in the pathophysiology of metabolic syndrome and most of its individual components, namely insulin resistance (IR), obesity, and dyslipidemia even during childhood and adolescence [9-11].

The gene encoding adiponectin is located in a locus on the third chromosome (3q27) which is close to the loci considered responsible for Type 2 diabetes and obesity [12]. Several researchers have searched the adiponectin gene for SNPs and have identified some of them; an estimated 30–70% of the variability in plasma adiponectin levels is explained by this genetic variation [12-16]. One of these SNPs in the adiponectin gene is T>G change at the 45th position; +45T>G SNP (rs2241766) in exon 2 which doesn't cause any change in amino acid sequence. There are different studies concluding different findings about the relation between this SNP and obesity [17,18].

In this study, +45T>G polymorphism in exon 2 of adiponectin gene was examined in obese and control groups of pediatric age as a gene that is thought to have a role in the development of obesity and its morbidities, such as hypertension, dyslipidemia, and insulin resistance.

Material and Method

Participants and study area

This study was a cross-sectional, case-control study. A total of 268 obese children and adolescents aged 6-17 years who were followed at the Hospital of the School of Medicine at Gaziosmanpaşa University, Tokat, Turkey, were enrolled in the study. Also 185 nonobese, healthy children aged 6-17 years who were being seen for other reasons were collected from outpatient pediatric clinics for the control group. The study protocol was in accordance with the Helsinki Declaration of the World Medical Association and ethics standards. Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa University School of Medicine (14-KAEK-204). Informed consent was obtained and the questionnaires used to gather information about the children were answered by the parents and family.

Weights were measured using a digital scale (Seca Corp., Chino, CA, USA). Measurements were made while the patients were barefoot and wearing light clothes. Height was measured using a portable stadiometer (Seca) together with weight. Body mass index (BMI) was calculated as weight in kg divided by height in meters squared (kg/m^2). The subjects were categorised as 'obese' if BMI was over 95 percentile and 'control' if the BMI was between 5-85 percentile, considering the sex-and age-specific growth curves and cutoff levels for Turkish children proposed by Neyzi et al. [19].

Laboratory tests

Laboratory tests including glucose, insulin levels, and lipid profiles were drawn only from the obese participants as fasting blood samples. Also, blood samples were separated from these patients for genetic analysis of +45T>G SNP in adiponectin gene. No laboratory tests except for genetic analyses were performed in the control group.

Serum fasting glucose, insulin, triglycerides (TGs), and high-density lipoprotein cholesterol (HDL-C) were measured by reagent kits from Roche Diagnostics adapted to the COBAS 6000 Autoanalyzer (Roche Diagnostics, Indianapolis, IN, USA).

Definition of hypertension, insulin resistance, and dyslipidemia

Blood pressure (BP) of patients was measured by a digital sphygmomanometer (OMRON 705IT, Omron Healthcare Co., Kyoto, JAPAN) and the mean of two measurements was recorded. Hypertension was considered if BP ≥ 95th percentile according to age, sex. and height [20].

The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated by the equation of HOMA-IR=Fasting insulin (μU/mL) x Fasting glucose (mg/dL) /405). The HOMA-IR cutoff point for diagnosis of insulin resistance was 3.16 [21].

Dyslipidemia was defined if TGs were >105 mg/dL in children < 10 years of age and > 136 mg/dL in children ≥ 10 years of age and/or HDL-C was < 35 mg/dL [22].

Genetic Analysis

Blood samples were collected from each subject, and DNA was extracted from peripheral blood samples using a GeneAll® Exgene™ Blood SV Genomic DNA Kit according to the manufacturer's instructions. The +45T>G SNP in adiponectin gene was analyzed by a polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP) method. PCR was performed in a total volume of 25 μL containing 25–50 ng of genomic DNA, 0.8 nmole/ μl of each primer, 1.5 mM MgCl2, 2.5 μl of 10× PCR buffer, 0.3 mM dNTP, and 1 U Taq DNA polymerase (Fermentas, Shenzhen, China). The PCR primers, PCR programme, product sizes, and restriction enzyme are shown in Table 1. The amplified products were run on a 3% agarose gel, stained with ethidium bromide, and visualized under ultraviolet (UV) light.

Statistical Analysis

Data are expressed as mean±standard deviation or frequency and percent. Independent sample t test was used to compare the continuous normal data between groups. Chi-square test was used to compare the categorical data between/among groups. A p-value <0.05 was considered as significant. Analyses were performed using SPSS 19 (IBM SPSS Statistics 19, SPSS, Inc., an IBM Co., Somers, NY).

Results

In this study the adiponectin gene +45T>G variant was genotyped in obese and nonobese groups of pediatric patients. Clinical and laboratory characteristics of the study participants are shown in Table 2.

The genotype frequencies of adiponectin gene were 77.9%, 19.1% and 3% in obese subjects and 72.1%, 23.5% and 4.4% in the control group for TT, TG, and GG respectively (p=0.357), with the allelic frequency of the G allele 12.5% in obese subjects and 16.1% in controls (p=0.129) (Table 3). There was no significant difference between obese and control groups according to genotypic or allelic frequencies. Genotype frequencies were in Hardy-Weinberg equilibrium.

When we compare different adiponectin genotypes, there wasn't any significant difference in frequencies of TT genotype (wild type) and non-TT (TG+GG) genotypes between obese and control groups (p=0.162) (Table 4). Also comparing GG genotype and non-GG (TG+TT) genotypes revealed no significant difference between obese and control groups (p=0.439) (Table 5). Among obese subjects there were no significant relations between different adiponectin genotypes and clinical characteristics such as presence of hypertriglyceridemia, low HDL-C, hypertension, and insulin resistance (Table 6). Also there were

Table 1. PCR primers, PCR programme, product size, and restriction enzyme for the +45T>G SNP in adiponectin gene

Polymorphism	Primers	RFLP Enzyme	Product Size	PCR Programme
Adiponectin +45T>G	F: 5'-GCA GCT CCT AGA AGT AGA CTC TGC TG-3' R:5'-GCA GGT CTG TGA TGA AAG AGG CC-3'	Sma I	372 bp T; 372bp G;209+163bp	94°C 5 min 94°C 30s 60°C 30s 37 cycle 72°C 30s 72°C 7 min

Table 2. Clinical and laboratory characteristics of study participants

	Obese (n=268)	Control (n=185)
Age	11.61±2.83	10.74±3.36
Gender(F/M)	163/105	101/84
Length (cm)	150.76±15.17	143.56±17.84
Weight (kg)	65.9±19.96	38.99±14.8
BMI (kg/m^2)	27.93±4.39	18.1±3.18
HDL-C (mg/dL)	48.19±12.41	
TGs (mg/dL)	111.29±64.42	
Insulin (uIU/mL)	19.08±12.39	
Glucose (mg/dL)	88.21±12.01	
HOMA-IR	4.13±3.09	
Hypertension	93(40.3)	
IR	142(56.3)	
Low HDL-C	27(10.4)	
Hypertriglyceridemia	113(44.0)	

Data are shown as mean±standard deviation or frequency, percentage. BMI: Body mass index (kg/m2), HDL-C: High-density lipoprotein, TGs: Triglycerides, HOMA-IR: The homeostasis model assessment of insulin resistance index, IR: Insulin resistance.

Table 3. Genotypic and allelic distributions of adiponectin gene in obese and control groups

	GROUP				
Genotype	Obese n (%)	Control n (%)	x^2	p	OR (% CI)
TT	208 (77.9)	132 (72.1)	2.060	0.357	-
TG	51 (19.1)	43 (23.5)			
GG	8 (3)	8 (4.4)			
Allele					
T	467 (87.5)	307 (83.9)	2.303	0.129	0.746 (0.51-1.09)
G	67 (12.5)	59 (16.1)			

Table 4. Adiponectin genotype (TT and non TT) distributions in obese and control groups

TT		Adiponectin genotypes n(%)		x^2	p	OR (% CI)
		TG+GG				
Group	Obese	208(77.9)	59(22.1)	1.958	0.162	0.734 (0.47-1.13)
	Control	132(72.1)	51(27.9)			

Table 5. Adiponectin genotype (GG and non GG) distributions in obese and control groups

GG		Adiponectin genotypes n(%)		x^2	p	OR (% CI)
		TG+TT				
Group	Obese	8(3)	259(97)	0.599	0.439	0.675 (0.24-1.83)
	Control	8(4.4)	175(95.6)			

Table 6. Adiponectin genotype and allele distributions based on clinical characteristics

TT		Adiponectin genotype (%)			Allele (%)	
		TG	GG	T	G	
Hypertension	No	105(58)	28(63.6)	5(83.3)	238(86.2)	38(13.8)
	Yes	76(42)	16(36.4)	1(16.7)	168(90.3)	18(9.7)
x^2;p		1.891; 0.388			1.746; 0.186	
Dyslipidemia	No	97(49.2)	26(52)	6(75)	220(85.3)	38(14.7)
	Yes	100(50.8)	24(48)	2(25)	224(88.9)	28(11.1)
x^2;p		2.091; 0.352			1.481; 0.224	
IR	No	87(44.2)	19(41.3)	4(50)	193(87.7)	27(12.3)
	Yes	110(55.8)	27(58.7)	4(50)	247(87.6)	35(12.4)
x^2;p		0.252; 0.882			0.002; 0.963	
Low HDL-C	No	183(91)	43(86)	6(75)	409(88.1)	55(11.9)
	Yes	18(9)	7(14)	2(25)	43(79.6)	11(20.4)
x^2;p		2.969; 0.227			3.156; 0.076	
High total cholesterol	No	175(88.4)	47(94)	8(100)	397(86.3)	63(13.7)
	Yes	23(11.6)	3(6)	0(0)	49(94.2)	3(5.8)
x^2;p		2.313; 0.315			2.614; 0.106	
High TGs	No	108(54.5)	29(58)	6(75)	245(85.7)	41(14.3)
	Yes	90(45.5)	21(42)	2(25)	201(88.9)	25(11.1)
x^2;p		1.420; 0.492			1.205; 0.272	

HDL-C: High-density lipoprotein, TGs: Triglycerides, IR: Insulin resistance.

no significant relationships between the mean of quantitative variables and different genotypes of adiponectin (Table 7).

Table 7. The mean of quantitative variables based on different genotypes of adiponectin

	BMI	HOMA-IR	HDL-C	TGs	Insulin	FG
TT	24.40±6.27	4.15±3.21	48.57±11.93	113.96±66.14	19.27±12.78	88.22±12.35
TG	23.22±6.13	4.26±2.78	47.46±14.06	105.06±60.98	18.95±11.31	89.14±10.69
GG	24.08±5.63	2.85±1.52	43.63±14.63	92.71±33.08	13.47±6.57	85.19±9.16
p	0.269	0.484	0.489	0.481	0.431	0.671
TT	24.4±6.27	4.15±3.21	48.57±11.93	113.96±66.14	19.27±12.78	88.22±12.35
TG+GG	23.34±6.04	4.05±2.67	46.93±14.07	103.36±57.87	18.13±10.87	88.6±10.51
p	0.123	0.831	0.377	0.271	0.551	0.828
GG	24.08±5.63	2.85±1.52	43.63±14.63	92.71±33.08	13.47±6.57	85.19±9.16
TG+TT	24.14±6.25	4.17±3.13	48.35±12.36	112.17±65.11	19.21±12.49	88.4±12.02
p	0.969	0.235	0.291	0.401	0.198	0.455

BMI: Body mass index (kg/m2), FG: Fasting glucose (mg/dL), HDL-C: High-density lipoprotein cholesterol (mg/dL), HOMA-IR: The homeostasis model assessment of insulin resistance index, TGs: Triglycerides (mg/dL).

Discussion

Adiponectin, which is one of the adipokines, is known to have an important role in the pathophysiology of obesity and its comorbidities such as insulin resistance (IR), hypertension, and dyslipidemia. In the present case-control study, significant association was not found between +45T>G SNP of adiponectin gene and childhood obesity or its comorbidities. In the literature, there are very different results in this context. Some studies have shown significant association between +45T>G SNP of adiponectin gene and obesity [17,23-25] whereas other studies have suggested an absence of such an association [18,26,27]. For instance, in their case-control study about obesity and polymorphisms, Bouatia-Naji et al. [18] did not find any evidence of association between +45T>G SNP and childhood obesity and their results about allelic frequencies of this SNP in obese children were similar to our results. In another case-control study that was performed on obese school children and adolescents, Orellana et al. [28] didn't find any significant difference in the frequency of +45T>G SNP in childhood obesity. Ukkola et al. [29] also found this SNP in equal frequencies among obese and control subjects. On the other hand there are some studies which have found the opposite. For instance, Wu et al. [17] found this SNP (G allele) to be associated with increased risk of obesity in children. Also in the study of Stumwoll et al. [24] the G allele was found to be significantly associated with increased obesity risk. Furthermore, interestingly, there are some other studies which found the G allele to be associated with decreased obesity risk [23,25]. However, all of these conflicting diverse results are not surprising since the studies have examined populations that are very different in ethnicity, age, health condition, and sample size.

In our study there was no association between +45T>G SNP of adiponectin gene and obesity traits such as IR, hypertension, or dyslipidemia. There are also diverse results about this relation in the literature. In some studies the G allele was found to be associated with higher LDL [17] and total cholesterol levels [17, 29], fasting glucose [30, 31], and HOMA-IR [17, 32, 33]. For example, Petrone et al. [30] reported that the 45G carriers showed higher fasting and 2nd hour glucose levels compared with non-carriers in a population of overweight/obese children. However, there are studies that have concluded that the G allele in +45T>G SNP of adiponectin gene is associated with lower fasting insulin levels and lower HOMA-IR score [34]. Finally, similar to our study, there have been some studies which found no association with dyslipidemia, FG, insulin sensitivity, HOMA-IR, or HT [35-37]. The reasons for this discrepancy, again, may be related to variation across studies in ethnic background, environmental factors, sample size, and other factors such as inclusion criteria of the studies.

Our study has some limitations. One of them is lack of adiponectin level measurements in either group. In some other studies, it has been mentioned that an estimated 30–70% of the variability in plasma adiponectin levels is explained by genetic variations [12,16]. The question of how a silent mutation just like adiponectin +45T>G SNP results in a change of plasma level has not been fully elucidated, but it has been shown that this mutation may alter RNA splicing or stability, suggesting an allele-specific differential expression of adiponectin [38]. Also it is obvious that searching for an association between an SNP and a complex disease like obesity that includes diverse genetic and environmental interactions could not be a simple issue.

In conclusion, in the present study, in a well-described obese and a control group of the Turkish pediatric population, we observed a lack of association between the +45T>G SNP and childhood obesity and its traits.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study 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. No animal or human studies were carried out by the authors for this article.

Funding

None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Ells LJ, Hancock C, Copley VR, Mead E, Dinsdale H, Kinra S, et al. Prevalence of severe childhood obesity in England: 2006-2013. Arch Dis Child. 2015; 100(7):631-6.

2. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000; 894:1-253.
3. Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa heart study. Pediatrics. 2005; 115(1):22-7.
4. van Emmerik NM, Redners CM, van de Veer M van Buuren S, van der Baan-Slootweg OH, Kist-van Holthe JE, et al. High cardiovascular risk in severely obese young children and adolescents. Arch Dis Child. 2012; 97(9):818-21.
5. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. N Engl J Med. 1997; 337(13):869-73.
6. Maes HH, Neale MC, Eaves LJ. Genetic and environmental factors in relative body weight and human adiposity. Behav Genet. 1997; 27(4):325-51.
7. Cao H. Adipocytokines in obesity and metabolic disease. J Endocrinol. 2014; 220(2):T47-59.
8. Oh DK, Ciaraldi T, Henry RR. Adiponectin in health and disease. Diabetes Obes Metab. 2007; 9(3):282–9.
9. Sheng T, Yang K. Adiponectin and its association with insulin resistance and type 2 diabetes. J Genet Genomics. 2008; 35(6):321–6.
10. Whitehead JP, Richards AA, Hickman IJ, Macdonald GA, Prins JB. Adiponectin-a key adipokine in the metabolic syndrome. Diabetes Obes Metab. 2006; 8(3):264–80.
11. Punthakee Z, Delvin EE, O'loughlin J, Paradis G, Levy E, Platt RW, et al. Adiponectin, adiposity, and insulin resistance in children and adolescents. J Clin Endocrinol Metab. 2006; 91(6):2119–25.
12. Lindsay RS, Funahashi T, Krakoff J, Matsuzawa Y, Tanaka S, Kobes S, et al. Genome-wide linkage analysis of serum adiponectin in the Pima Indian population. Diabetes. 2003; 52(9):2419–25.
13. Takahashi M, Arita Y, Yamagata K, Matsukawa Y, Okutomi K, Horie M, et al. Genomic structure and mutations in adipose-specific gene, adiponectin. Int J Obes Relat Metab Disord. 2000; 24(7):861–8.
14. Hara K, Boutin P, Mori Y, Tobe K, Dina C, Yasuda K, et al. Genetic variation in the gene encoding adiponectin is associated with an increased risk of type 2 diabetes in the Japanese population. Diabetes. 2002; 51(2):536–40.
15. Vasseur F, Helbecque N, Dina C, Lobbens S, Delannoy V, Gaget S, et al. Single nucleotide polymorphism haplotypes in the both proximal promoter and exon 3 of the APM1 gene modulate adipocyte secreted adiponectin hormone levels and contribute to the genetic risk for type 2 diabetes in French Caucasians. Hum Mol Genet. 2002; 11(21):2607–14.
16. Comuzzie AG, Funahashi T, Sonnenberg G, Martin LJ, Jacob HJ, Black AE, et al. The genetic basis of plasma variation in adiponectin, a global endophenotype for obesity and the metabolic syndrome. J Clin Endocrinol Metab. 2001; 86(9):4321–5.
17. Wu J, Yan WJ, Mo J, Yang HB, Wang ZZ, Lei MX, et al. Association of adiponectin gene polymorphism with obesity in children. Zhongguo Dang Dai Er Ke Za Zhi. 2011; 13(7):539-42.
18. Bouatia-Naji N, Meyre D, Lobbens S, Séron K, Fumeron F, Balkau B, et al. ACDC/adiponectin polymorphisms are associated with severe childhood and adult obesity. Diabetes. 2006; 55(2):545–50.
19. Neyzi O, Günöz H, Furman A, Bundak R, Gökçay G, Darendeliler F, et al. Weight, height, head circumference and body mass index references for Turkish children. Çocuk Sağlığı ve Hastalıkları Dergisi. 2008; 51: 1-14.
20. Falkner B, Daniels SR. Summary of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Hypertension. 2004; 44(4):387-8.
21. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005; 115(4):500-3.
22. Sangun Ö, Dündar B, Köşker M, Pirgon Ö, Dündar N. Prevalence of metabolic syndrome in obese children and adolescents using three different criteria and evaluation of risk factors. J Clin Res Pediatr Endocrinol. 2011; 3(2):70-6.
23. Menzaghi C, Ercolino T, Di Paola R, Berg AH, Warram JH, Scherer PE, et al. A haplotype at the adiponectin locus is associated with obesity and other features of the insulin resistance syndrome. Diabetes. 2002; 51(7):2306–12.
24. Stumvoll M, Tschritter O, Fritsche A, Staiger H, Renn W, Weisser M, et al. Association of the T-G polymorphism in adiponectin (exon 2) with obesity and insulin sensitivity: interaction with family history of type 2 diabetes. Diabetes. 2002; 51(1):37–41.
25. Sutton BS, Weinert S, Langefeld CD, Williams AH, Campbell JK, Saad MF, et al. Genetic analysis of adiponectin and obesity in Hispanic families: the IRAS Family Study. Hum Genet. 2005; 117(2-3):107–18.
26. Krízová J, Dolinková M, Lacinová Z, Sulek S, Dolezalová R, Housová J, et al. Adiponectin and resistin gene polymorphisms in patients with anorexia nervosa and obesity and its influence on metabolic phenotype. Physiol Res. 2008; 57(4):539-46.
27. Yu Z, Han S, Cao X, Zhu C, Wang X, Guo X. Genetic polymorphisms in adipokine genes and the risk of obesity: A systematic review and meta-analysis. Obesity (Silver Spring). 2012; 20(2):396-406.
28. Orellana G, Sapunar J, Sáez K, Aguayo C, Calvo C, Radojkovic C, et al. Association between adiponectin gene polymorphisms and obesity in school age children from Hualpén, Chile. Rev Med Chil. 2012; 140(10):1245-52.
29. Ukkola O, Ravussin E, Jacobson P , Sjöström L, Bouchard C. Mutations in the adiponectin gene in lean and obese subjects from the Swedish obese subjects cohort. Metabolism. 2003; 52(7):881–4.
30. Petrone A, Zavarella S, Caiazzo A, Leto G, Spoletini M, Potenziani S, et al. The promoter region of the adiponectin gene is a determinant in modulating insulin sensitivity in childhood obesity. Obesity (Silver Spring). 2006; 14(9):1498-504.
31. Ruchat SM, Loos RJ, Rankinen T, Vohl MC, Weisnagel SJ, Després JP, et al. Associations between glucose tolerance, insulin sensitivity and insülin secretion phenotypes and polymorphisms in adiponectin and adiponectin receptor genes in the Quebec Family Study. Diabet Med. 2008; 25(4):400–6.
32. Nakatani K, Noma K, Nishioka J, Kasai Y, Morioka K, Katsuki A, et al. Adiponectin gene variation associates with the increasing risk of type 2 diabetes in non-diabetic Japanese subjects. Int J Mol Med. 2005; 15(1):173-7.
33. Li LL, Kang XL, Ran XJ, Wang Y, Wang CH, Huang L, et al. Associations between 45T/G polymorphism of the adiponectin gene and plasma adiponectin levels with type 2 diabetes. Clin Exp Pharmacol Physiol. 2007; 34(12):1287-90.
34. Melistas L, Mantzoros CS, Kontogianni M, Antonopoulou S, Ordovas JM, Yiannakouris N. Association of the +45T>G and +276G>T polymorphisms in the adiponectin gene with insulin resistance in nondiabetic Greek women. Eur J Endocrinol. 2009; 161(6):845-52.
35. Jang Y, Chae JS, Koh SJ, Hyun YJ, Kim JY, Jeong YJ, et al. The influence of the adiponectin gene on adiponectin concentrations and parameters of metabolic syndrome in non-diabetic Korean women. Clin Chim Acta. 2008; 391(1-2):85–90.
36. Panagopoulou P, Stamna E, Tsolkas G, Galli-Tsinopoulou A, Pavlitou-Tsiontsi E, Nousia-Arvanitakis S, et al. Adiponectin gene polymorphisms in obese Greek youth. J Pediatr Endocrinol Metab. 2009; 22(10):955-9.
37. Vozarova de Courten B, Hanson RL, Funahashi T, Lindsay RS, Matsuzawa Y, Tanaka S, et al. Common polymorphisms in the adiponectin gene ACDC are not associated with diabetes in Pima Indians. Diabetes. 2005; 54(1):284–9.
38. Yang WS, Tsou PL, Lee WJ, Tseng DL, Chen CL, Peng CC, et al. Allele-specific differential expression of a common adiponectin gene polymorphism related to obesity. J Mol Med (Berl). 2003; 81(7):428-34.

How to cite this article:
Kasap T, Ateş Ö, Özer S, Gül A, Yılmaz R, Sönmezgöz E, Demir O, Ensari E. +45T>G single nucleotide polymorphism of adiponectin gene: Is it a factor in childhood obesity? J Clin Anal Med 2018;9(5): 376-80.