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The Interaction of Peroxisome Proliferator-Activated Receptor- γ (PPAR γ) Pro12Ala Polymorphism and Dietary Fat Intake among Turkish Patients with Metabolic Syndrome: A Cross Sectional Study

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Abstract

Background: The metabolic syndrome is a complex disorder which occurs as a result of the interaction between genetic and environmental factors. The interaction between the peroxisome proliferator-activated receptor gamma (PPARγ) Pro12Ala polymorphism and dietary fats has been proposed to act in the pathogenesis of syndrome. This study aimed to verify whether dietary nutrient intake interacts with the PPARγ Pro12Ala polymorphism to modulate the features of the syndrome.

Methods: A total of 150 patients with metabolic syndrome participated. All subjects underwent a clinical, anthropometrical, biochemical and nutritional assessment and analysis of Pro12Ala polymorphism of PPARγ genotype.

Results: The polymorphism was detected in 14% of the sample (1.3% AlaAla homozygote and 12.7% AlaPro heterozygote). Biochemical indicators of lipid profile, glucose and liver function did not differ significantly with PPARγ genotype ($p>0.05$). Amongst the anthropometrical measurements, only lean body mass was significantly different with PPARγ genotype ($p=0.032$). There was no evidence that the association of either individual macronutrients (carbohydrates, protein, fat) or type of fatty acids (saturated, monounsaturated, polyunsaturated) with metabolic syndrome were modified by PPARγ Pro12Ala genotype ($p>0.05$ for all).

Conclusions: The results suggest that PPARγ Pro12Ala polymorphism cannot modulate the association between dietary fat intake and components of the metabolic syndrome.

Keywords: Metabolic syndrome; PPARγ Pro12Ala polymorphism; dietary fatty acids

Introduction

The metabolic syndrome has become one of the major public-health challenges worldwide due to its increased prevalence over the last years. It is a complex disorder characterized by abdominal obesity, insulin resistance, dyslipidemia and hypertension (Alberti et al.) [1]. The development of the metabolic syndrome involves a complex interaction of lifestyle behaviours, such as unhealthy diet and genetic factors(Alberti et al.; Siani) [1,2]. Understanding the science of gene-diet interactions, in other words nutritional genomics, is important for health professionals in order to recognise its implications for clinical practice in the metabolic syndrome (Ryan-Harshman et al.) [3].

Among the genetic factors potentially involved in the aetiology of the metabolic syndrome, the gene encoding for peroxisome proliferator-activated receptor gamma (PPARg), a transcription factor that regulates glucose and lipid metabolisms, has attracted a lot of attention (Roche et al.; He) [4,5]. PPARγ is located on chromosome 3 and has four different mRNA isoforms: PPARγ1, PPARγ2, PPARγ3 and PPARγ4. While the other isoforms encode the same protein, PPARγ2 contains an additional exon of 28 aminoacids at the N-terminus. A C/G mutation at codon 12 of this exon leads to the substitution Proline>Alanine (Pro12Ala). This amino acid substitution results in the Pro12Ala polymorphism, which constitutes three different genotypes: Pro12Pro, Pro12Ala and Ala12Ala genotypes. Many studies were conducted to clarify the relationship between this single nucleotide polymorphism and the regulations of glucose and lipid metabolisms. Since this amino acid position is involved in insulin-mediated transcriptional activation, the substitution of alanine for proline could cause a change in the protein structure and might result in a decrease in PPARγ2 activities (Meirhaeghe et al.) [6].

Several studies have found that people with Ala allele of PPARγ2 have a reduced risk of type 2 diabetes (Tai et al.; Altshuler et al.) [7,8] and cardiovascular disease (Doney et al.) [9] as well as a lower body mass index (BMI) (Gonzalez Sanchez et al.; Kadowaki et al.) [10,11]. However, other studies have found an increased risk of type 2 diabetes (Lindi et al.) [12] and a higher BMI in people with Ala12Ala variant (Mirzaei et al.) [13]. Some studies have failed to detect any association (Pischon et al.; Mancini et al.) [14,15].

The inconsistent results suggest the potential roles of other genetic or environmental factors which might influence the possible association (Luan et al.; He) [16]. Since fatty acids are natural ligands of PPARγ2, it has been suggested that the association between PPARγ2 Pro12Ala polymorphism and the components of the metabolic syndrome might be modified depending on the length of the chain and/or the degree of saturation of dietary fatty acids (Robitaille et al.; Memisoglu et al.; Franks et al.; AlSaleh et al.; Garaulet et al.) [17-21]. However, the results of the studies on the PPARγ2 Pro12Ala polymorphism-dietary fatty acid interaction are also contradictory (Stumvoll et al.) [22]. It has been suggested that the strength of the association seems to depend on the population and the ethnic groups studied (Scacchi et

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al.; Ek et al.) [23,24]. To the best of our knowledge, no results from a Turkish population have yet been reported. Therefore, this study aimed to examine if the potential interaction between PPARγ2 Pro12Ala polymorphism and dietary fatty acids intake modulates the features of the metabolic syndrome in a Turkish population.

Methods

Subjects

A total of 150 patients with the metabolic syndrome (125 female and 25 male with a mean age of 53.3±6.98 years, range 18-65 years) were recruited from the Endocrinology Unit, Hacettepe University Hospitals, Ankara, Turkey. The study endocrinologist diagnosed all cases according to the definition made by the International Diabetes Federation (IDF) (Alberti et al.) [1]. The inclusion criteria were 1) attending routine outpatient visits, 2) aged 18-65 years, 3) meeting IDF criteria for the metabolic syndrome. Patients with liver and kidney diseases, cancer, mental and psychological disorders were excluded from the study, as were pregnant and lactating women. This study was approved by the local ethics committee of Hacettepe University (HEK06/54) and informed consent was obtained from the participants.

Study design

A cross-sectional and observational study design was used. All participants underwent a routine physical examination by the endocrinologist, followed by biochemical, anthropometrical and nutritional assessments and the analysis of Pro12Ala polymorphism of PPARγ2.

Biochemical assessment and blood pressure: After a 10-h fasting, glucose, triglycerides, total cholesterol, High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Very Low Density Cholesterol (VLDL-C), Apolipoprotein A (Apo A-1) and B (Apo B), and lipoprotein-a levels were measured on fresh plasma at the biochemistry laboratory. Plasma glucose concentration was determined by the glucose oxidase method (Olympus AU2700). Plasma total cholesterol, triglyceride, HDL-C, LDL-C and VLDL-C concentrations were measured by using enzymatic calorimetric kits with intra- and interassay CV of <10% (Roche Diagnostics GmbH, Mannheim, Germany). Plasma Apo A-1 and Apo B levels were determined by immunonephelometric methods with the Behring Nephelometer II (Dade Behring, Marburg, Germany). Serum C-reactive protein levels were measured using the nephelometric method (Siemens BNTM II). Plasma insulin levels were assayed by chemiluminiscent immunoassay kits (Roche Diagnsotics GmbH, Mannheim, Germany) with intra- and inter-assay CVs of ≤4.3 and ≤3.4% respectively at the nuclear medicine laboratory. Insulin resistance was assessed with Homeostatic Model Assessment (HOMA) calculated as follows: HOMA= [Fasting insulin (μU/ml) x fasting glucose (mg/dl)/22.5 (Katsuki et al.) [25]. Systolic (SBP) and Diastolic Blood Pressure (DBP) were measured in duplicate by using a sphygmomanometer (Erka Perfect-Aneroid Sphygmomanometer) and the results were averaged.

Anthropometrical assessment: Body weight and height were measured with participants wearing light clothing and no shoes using a calibrated digital scale (Seca 220 Scale, Germany). The measurements were taken in duplicated and the mean was recorded. Body mass index (BMI) was calculated by dividing the weight (in kilograms) by the square of the height (in metres). The cut-off point of 30 kg/m^2 defined obesity according to the current WHO classification (WHO) [26]. Using an inflexible tape, waist circumference was measured at the level of the umbilicus, and hip circumference was measured at the widest part of the hip region with participants wearing light clothing. Abdominal obesity was defined with waist circumference: ≥80 cm for women and ≥94 cm for men according to IDF definition (Alberti et al.) [1]. The waist and hip circumference measurements were taken in duplicated and the mean was recorded. The waist-to-hip ratio was calculated. Body composition (fat mass and lean mass) was analysed using the Tanita UM Series Body Composition Analyser. All measurements were taken by the study dietitian.

Nutritional assessment: Dietary intake was investigated through the use of a 24-dietary recall by the study dietitian. Total, saturated (SFA), Monounsaturated (MUFA) and Polyunsaturated (PUFA) fatty acid intakes were calculated using a computer program (BeBIS, Nutrition Information System, Istanbul, Turkey Version 6).

Other lifestyle factors: The details of socio-demographic characteristics, family and medical history, and other lifestyle habits such as physical activity, smoking and alcohol consumption were collected by the dietitian using a questionnaire during the face-to-face

1	Pro/Pro Homozygotes (n=129)	Ala Allele Carriers (n=21)	p
Age (year; mean ± SD)	53.4 ± 7.17	52.6 ± 5.85	0.579
Sex (n of Male/Female)	21/108	4/17	0.756
Allele frequency (n;%)	129 (86)	21 (14)	0.755
Presence of diabetes (n;%)	99 (76.7)	14 (66.6)	0.471
Presence of obesity (n;%)	106 (82.1)	18 (85.7)	1.000
Presence of hyperlipidemia (n;%)	77 (60.0)	15 (71.4)	0.434
Presence of hypertension (n;%)	100 (77.5)	17 (80.9)	1.000
Dietary intake (% of total energy; mean ± SD)			
Total fat	33.7 ± 8.3	32.6 ± 9.5	0.580
Saturated fat	10.4 ± 3.39	10.5 ± 4.87	0.925
Monounsaturated fat	11.5 ± 4.09	10.8 ± 3.88	0.519
Polyunsaturated fat	9.7 ± 5.05	9.2 ± 5.64	0.406
Current smokers (n;%)	24 (18.6)	4 (19.0)	0.633
Alcohol consumers (n;%)	18 (14.0)	2 (9.5)	0.921
Physical inactivity (n;%)	110 (85.3)	21 (100.0)	0.170

Data are mean ± SD or n (%).

p was analysed by student t-test (independent samples test) for age and dietary intake, and by chi-square tests for other variables.

Table 1: General characteristics of participants.

interview with each participant. The questionnaire was developed by the researchers. The content validity of the questionnaire was measured by a pilot study involving 28 participants who were eligible for the study population. Based on the comments and question clarifications posed by these respondents, some questions were reworded, and the response options were altered. The physical activity levels of the participants were evaluated using a questionnaire validated from World Health Organization Global Physical Activity Questionnaire (WHO) [27].

Genetic analyses: Genomic DNAs were isolated from buccal swabs using the MN DNA isolation kit (Macherey Nagel-Nucleospin, GERMANY). Following the DNA extraction, samples were diluted to 2.0-2.5ng/µl concentration in nanopure water and 384-well PCR reaction plates were prepared for all samples with 2 µl DNA per well.

The amplification of the polymorphic site and hME reaction: Sequenom RealSNP software was used to design sequence specific PCR primers (F//AGCGCAAGTGTTATGGGTGAAACTCTGGGAG & R//AGCGCAAGTGTCCCCA ATAGCCGTATCTG) and extension probe (GGGAGATTCTCCTATTGAC) for Pro12Ala (C/G) variation of PPARγ2 gene. PCR and extension primers were prepared with a concentration of 1 µm and 10µm respectively. After PCR reactions of the polymorphic site, amplicons were subjected to post PCR cleanup in a total volume of 7µl to remove unincorporated dNTPs, and the cleaned PCR products were used as templates for the locus-specific primer extension (homogeneous mass extend=hME primer) reactions. The final products were treated with a cation exchange resin per well to remove salts (SpectroCLEAN resin). This step was a standard step of genetic analysis, and it is necessary for the accuracy of mass spectrometry. All the procedures above were performed according to the manufacturer's protocol of Sequenom MassARRAY platform. Positive (sample with known Pro12Ala variation) and no-template controls were included in every plate to check quality and to confirm that there was no contamination.

The analysis of hME products on MALDI-TOF based MS: A small volume of products was arrayed from 384-well plates onto 384-sample SpectroCHIPs, using Nanodispencer system (Sequenom Inc). The target chips were inserted into the MALDI-TOF mass spectrometer of the MassARRAY Compact System (Sequenom Inc.), and the mass of the unextended and extended primers were determined. The analysis was performed using the SpectroTYPER software.

Statistical analyses: The results were given as mean and standard deviation (SD) or in proportions. The main characteristics of genotype groups were compared using Student's t-test for continuous variables and Pearson's chi-squared test (χ^2) for categorical variables. The models were adjusted for age, gender, smoking, physical activity, medication, dietary energy, total and saturated fat intakes. The χ^2 goodness-of-fit test was used to assess the deviation from the Hardy-Weinberg equilibrium of the genotypic frequency by calculating the expected frequencies of genotypes. Multivariate analysis was conducted by linear regression, with the metabolic syndrome components as the outcome variables; the independent variables included in the model were the Pro12Ala polymorphism and calculated dietary total fat, SFAs, MUFAs and PUFAs intakes (the percentage of the total energy intake). Odds ratios (ORs) and 95% CIs for PPARg2 Pro12Ala polymorphism (Ala and Pro alleles) and dietary intake of total fat, SFAs, MUFAs, PUFAs were estimated using logistic regression analysis. The model was adjusted for age and gender. All statistical analyses were conducted using SPSS for Windows, version 15.0, and p value ≤ 0.05 (two tailed) was considered significant.

Results

The prevalence of the PPARγ Pro12Ala polymorphism was 86% for Pro12Pro (n=129), 12.7% for Pro12Ala (n=19), and 1.3% for Ala12Ala (n=2). Since the Ala12Ala genotype had a low frequency, all analyses were conducted comparing Pro homozygotes (86%) with Ala allele carriers (14%). The genotype distribution was in Hardy-Weinberg equilibrium (p>0.713). The presence of obesity, type 2 diabetes, hypertension or hyperlipidemia did not significantly differ depending on the distribution of Pro12Ala polymorphism of PPARγ2 Diet and other lifestyle factors such as physical activity, smoking or alcohol consumption were found similar among the genotype groups (Table 1).

Table 2 summarizes the biochemical and anthropometrical parameters in genotype groups. The parameters of lipid profile apart from HDL cholesterol and apolipoprotein A, and fasting glucose level have a tendency to be slightly higher in Ala allele carriers compared with Pro/Pro homozygotes. In contrast, HOMA values and systolic and diastolic blood pressures were found slightly lower in Ala allele carriers than in Pro/Pro homozygotes. However, none of these differences were found statistically significant (p>0.05). Amongst the anthropometrical measurements, weight, BMI, body lean mass and waist circumference were slightly higher in Ala allele carriers compared with Pro homozygotes. However, only body lean mass was significantly higher in Ala allele carriers (p=0.032).

The prevalence of five the metabolic components defined by IDF was

	Pro Allele	Ala Allele	p*
Biochemical parameters			
Total cholesterol (mg/dl)	193.4 ± 48.70	203.8 ± 45.23	0.334
HDL-C (mg/dl)	50.6 ± 10.52	50.3 ± 14.82	0.655
LDL-C (mg/dl)	116.9 ± 41.72	123.6 ± 38.46	0.447
VLDL-C (mg/dl)	34.3 ± 22.73	37.3 ± 26.57	0.908
Triglyceride (mg/dl)	171.0 ± 112.44	186.6 ± 132.85	0.854
Apo A-1 (mg/dl)	135.6 ± 22.50	135.9 ± 35.48	0.736
Apo B (mg/dl)	108.1 ± 32.65	112.7 ± 35.00	0.749
Glucose (mg/dl)	142.2 ± 55.40	148.7 ± 79.87	0.583
Insulin (µu/ml)	14.7 ± 11.00	14.4 ± 6.83	0.605
HOMA	4.7 ± 4.00	4.0 ± 3.27	0.520
CRP	0.6 ± 0.50	0.5 ± 0.34	0.444
Blood pressures			
SBP (mmHg)	138.0 ± 18.90	133.8 ± 13.22	0.382
DBP (mmHg)	85.9 ± 10.54	81.4 ± 11.08	0.138
Anthropometrical parameters			
Body weight (kg)	83.8 ± 13.76	89.0 ± 14.08	0.135
BMI (kg/m^2)	34.1 ± 4.83	35.4 ± 5.92	0.244
Fat mass (kg)	33.4 ± 9.05	35.4 ± 8.01	0.302
Lean mass (kg)	50.2 ± 8.46	53.6 ± 9.69	0.032*
Waist circumference (cm)	101.8 ± 10.10	105.3 ± 10.88	0.171
WHR	0.9 ± 0.08	0.9 ± 0.08	0.751

*Data are mean ± SD. It was analysed by linear regression model to eliminate the influences of other independent variables apart from alleles. Therefore, values were adjusted for age, sex, smoking, physical activity level, BMI, dietary energy, total and saturated fat intake and medication (statins for dyslipidemia; acarbose, sulfonylurea, metformin, glitazone, beta blocker and insulin for diabetes diuretics, ACEI and ARB for hypertension).

**HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; VLDL-C: Very Low Density Cholesterol; Apo A-1: Apolipoprotein A-1; Apo B: Apolipoprotein B; HOMA: Homeostatic Model Assessment; CRP: C-Reactive Protein; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BMI: Body Mass Index; WHR: Waist-to-Hip Ratio.

Table 2: Biochemical markers, blood pressure and anthropometrical measurements according to PPARγ2 genotype**.

evaluated. Since abdominal obesity is a prerequisite for the diagnosis of the syndrome, all participants were abdominally obese. Therefore, a model of abdominal obesity was not analysed. The impaired glucose metabolism (presence of type 2 diabetes or glucose intolerance or high glucose levels), high levels of serum triglycerides, low levels of serum HDL cholesterol and high blood pressure were obtained respectively in 82.7%, 74.7%, 77.3% and 86% of the study population. The prevalence of none of the components differed significantly between genotypes ($p>0.05$ for all) (Data not shown). The interaction between PPARγ[2] Pro12Ala and dietary fat intake, including total fat, SFAs, MUFAs and PUFAs intakes, on the prevalence of the metabolic syndrome components was verified, and no significant association of either total fatty acid or subtypes of fatty acid intakes with the components of the metabolic syndrome modified by PPARg2 Pro12Ala polymorphism was detected ($p>0.05$ for all) (Table 3).

Discussion

PPARg2 is one of the most promising candidate genes for the metabolic syndrome due to its critical role in glucose and lipid metabolism. Previous studies suggested that the Ala variant is associated with moderately reduced PPARγ2 activity, which may lead to a lower BMI, increased insulin sensitivity and improved lipid profile (Deeb et al.; Altshuler et al.; He,; Gonzalez-Sanchez et al.) [5,8,10,28] In this study, the polymorphism was detected in 14% of the study sample, and the Ala variants did not have a lower BMI, a better insulin sensitivity or improved lipid profile. Only, the lean body mass was significantly higher in Ala variants. Furthermore, no association between either individual macronutrients or type of fatty acids and the components of the metabolic syndrome was modified by PPARγ2 Pro12Ala genotype.

The association between PPARg2 genotype and BMI was explained by the reduced adipocytes differentiation in the Ala variants. However, the suggested association failed to appear in many other studies as well as this study (Beamer et al.; Gonzalez-Sanchez et al.; Kao et al.; Kim et al.) [10,29-31]. Furthermore, the Ala allele was associated with a higher BMI, waist circumference, and fat mass in the Quebec Family Study (Robitaille et al.). Tonjes et al. Masud and Ye [17,32,33] reported an association of the Ala allele with higher BMI only in obese persons. Higher BMI in Ala variants was not found statistically significant in this study, probably due to a smaller study sample compared with previous studies (Robitaille et al.; Tonjes et al.; Masud and Ye) [17,32,33]. Similarly, the previous studies that examined the potential association between insulin resistance and PPARg2 Pro12Ala genotype found inconsistent results (Altshuler et al.; Gonzalez-Sanchez et al.; Deeb et al.; Mancini et al.) [8,10,15,28]. In terms of insulin resistance, the findings of this study were parallel with the studies that found no significant difference at plasma fasting glucose level, plasma fasting insulin level, HOMA values or prevalence of diabetes between genotypes (Mancini et al.; Kao et al.) [15,30]. Among the lipid profile, the Ala12 allele was associated with higher HDL cholesterol and lower total triglycerides levels in previous studies (Tai et al.; Gonzalez-Sanchez et al.) [7,10]. This study failed to show any significant association between PPARγ Pro12Ala genotype and lipid profile. Beamer et al. and Kim et al. [29,31] who used a similar study design also found no significant difference at the parameters of lipid profile by genotype. The potential association between PPARγ Pro12Ala genotype and blood pressure was examined infrequently in the previous studies. Kao et al. [30] showed that the diastolic and systolic blood pressures were slightly lower in Ala allele carriers, even if the differences were not statistically significant. These findings were in parallel with the results of this study.

The role of fatty acid intake in the development of the metabolic syndrome is well known. Recently, research has shown that not everyone responds to the same extent to dietary fatty acid intake (Robitaille *et al.*) [17]. (Deeb *et al.* [28] hypothesised that PUFAs might be more effective stimulators of adipogenesis in Pro homozygotes rather than Ala carriers because PUFAs seem to be preferred by PPARγ2 more than SFAs due to being natural ligands of PPARs. Luan et al. [16] Showed that low dietary PUFAs intake was associated with higher BMI in Ala allele carriers than that in Pro homozygotes. This was the first study to report a gene-diet interaction with PPARγ2 Pro12Ala polymorphism and suggested that Ala allele carriers who ingest SFAs are more susceptible to the metabolic syndrome than Pro homozygotes. Pisabarro et al. [34] showed a similar association between trans-fatty acid intake and risk of type 2 diabetes in Ala allele carriers. Furthermore, Memisoglu et al. [18] reported an interaction between the intake of MUFAs, BMI and Pro12Ala polymorphism of PPARγ. In addition to BMI, insulin sensitivity was also associated with Pro12Ala polymorphism of PPARγ2 and dietary fatty acid intake (Scacchi et al.; Soriguer et al.; Garaulet et al.) [21,23,25,35]. Previous studies also suggested varied associations between dietary fatty acid intake and plasma total, HDL, LDL cholesterol or triglyceride levels according to PPARγ2 Pro12Ala genotype (Robitaille et al.; AlSaleh et al.; AlSaleh et al.) [17,20,36].This study failed to show any association of the Pro12Ala polymorphism with dietary fatty acid intakes on the prevalence of the metabolic syndrome components similar to the studies conducted by (Kao et al. and Kim et al.) [30,31]. The inconsistent results of different studies could be explained by the differences in study sampling, the analytical methods of the biomarkers or the genetic backgrounds of the participants. Furthermore, this study assessed the gene-diet interaction in terms of only one single nucleotide polymorphism. However, the presence of other gene-gene or gene-environment interactions

	High triglycerides level (>150 mg/dl)		Low HDL-C level (<40 mg/dl in males and <50 mg/dl in females)		High blood pressure (SBP≥130 mmHg or DBP ≥ 85 mmHg)		Presence of type 2 DM or Presence of glucose intolerance or High glucose level (≥100 mg/dl)	
	Pro Allele	**Ala Allele**	**Pro Allele**	**Ala Allele**	**Pro Allele**	**Ala Allele**	**Pro Allele**	**Ala Allele**
Total fat (g)	0.99 (0.94-1.03)	0.92 (0.81-1.05)	1.01 (0.96-1.06)	0.87 (0.75-1.01)	1.03 (0.96-1.09)	0.76 (0.00-0.)	0.97 (0.91-1.03)	0.96 (0.86-1.08)
SFA (g)	0.99 (0.88-1.11)	0.94 (0.74-1.20)	1.07 (0.94-1.22)	0.89 (0.72-1.10)	0.96 (0.82-1.11)	135.7 (0.00-0.)	0.93 (0.81-1.07)	1.06 (0.85-1.33)
MUFA (g)	1.00 (0.90-1.10)	0.75 (0.54-1.05)	0.98 (0.89-1.09)	0.79 (0.59-1.05)	1.04 (0.91-1.18)	0.92 (0.00-0.)	0.92 (0.82-1.03)	1.02 (0.77-1.34)
PUFA (g)	0.97 (0.90-1.05)	0.97 (0.80-1.17)	1.01 (0.93-1.10)	0.87 (0.70-1.09)	1.07 (0.95-1.20)	0.81 (0.00-0.)	1.02 (0.92-1.13)	0.78 (0.57-1.06)

1: Data are OR (% 95 CI).

2: It was analysed by logistic regression analyses and all models were adjusted for age and gender.

3: Since abdominal obesity is the main criteria for diagnosis of metabolic syndrome according to IDF criteria, all participants had abdominal obesity and a model of abdominal obesity was not analysed.

4: $p>0.05$ for each parameter.

Table 3: The association of dietary fatty acids with the metabolic syndrome components by Genotypes PPARγ[1-4].

that might have potential roles in the development of the metabolic syndrome should also be considered.

Since this study was the first to examine a gene-diet interaction in a Turkish population, it was planned as a pilot study that might provide a basis for these types of studies in Turkey. However, the study had some limitations, and the main limitation was the small sample size. It is relevant to note that the participants were patients who regularly attended the endocrinology clinic, and were prescribed a diet low in total and saturated fat as a part of their treatment. Most participants were not fully compliant with the prescribed diet; however, the average total and saturated fat intakes did not exceed the recommended amounts too much. Therefore, the modifying effect of the Pro12Ala variation on the relationship between dietary fat intake and the presence of the metabolic syndrome components may not be evident for a normal total and saturated fat intake. Furthermore, the difficulty in accurately assessing fat intake based on a 24-hour dietary recall might be another explanation for not confirming the previous findings. The major pitfalls of this method are recall bias and errors in the estimate of portion size in the visual inspection of pictures.

In conclusion, this study supports the inconsistent results concerning the role of PPARγ2 Pro12Ala genotype in the association between the components of the metabolic syndrome and dietary intakes. Our findings do not support the hypothesis that the Pro12Ala polymorphism of the PPARγ2 gene plays a major role in the development of the metabolic syndrome. The role of a combined gene-environment effect in the etiology of the metabolic syndrome needs to be further explored in large study populations from different ethnic backgrounds.

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Besides, everyone is experiencing “Emergency mood” almost every day and most of the time. Emergency mood is “stress” in other words. When in stress, Cortisol, the stress hormone, is released in blood. This can be affecting many mechanisms in the body. It will cause blood sugar imbalance, impair cognitive performance, suppress thyroid function, decrease bone density, increase blood pressure, increase fat in belly, cause exhaustion, increase estrogen, increase inflammation and will lower immune system.

When we eat in stress, digestion will decrease, calorie burning will decrease, and nutrient excretion will increase. Thus Cortisol and insulin hormones signal fat storage and stop building muscles. Therefore, the body will have sugar crisis, which will be craving more sugar and more energy as a natural feedback, and the easiest way is chocolate and sweets.

To lower stress and its effects on body weight; first, avoid making big steps in one time. Big steps won’t be reached in short times, which will cause stress. Second, ignore any cause of stress in your life. Everybody is susceptible to stress situations in life, but learning to ignore everyday problems is the best way. Mindfulness can change how you think and deal with these situations. (Try closing your eyes 10 minutes every day to relax and forget about conflicts). Third, start reality thinking about what makes you in difficult situations. Fourth, when you feel stressed, set goals to control the stress factors that can be controlled. Fifth, make decisions about the changes and how you will implement them. And last, avoid eating when you are stressed or passing through a stress situation. Instead, try to have walk (this will decrease Cortisol and increase serotonin, happy hormone) or talk to a close person, which will help you lower stress and try to find solutions.

Stress can be controlled by a simple small steps, but don’t let it control you and your health, specially your weight.

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