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Original articles

Nutritional status among women with preeclampsia and healthy pregnant women

Gülhan Samur[1], Özlem Özpak Akkuş[2*], Gözde Ede[1], Aylin Ayaz[1], Aslı Akyol, Melih Akkuş[3], Nuri Danışman[4]*

[1]Hacettepe University, Nutrition and Dietetics Department, Sıhhıye, Ankara, Turkey - E-mail: gsamur@hacettepe.edu.tr; [2]Keçiören Education and Research Hospital; [3]Hakkari Government Hospital; [4]Zekai Tahir Burak Women's Health Education and Research Hospital, Turkey

Summary. *Aim:* Pregnancy-onset hypertension and proteinuria is defined as preeclampsia (PE). PE affects 2% to 8% of all pregnancies and causes both maternal and perinatal morbidity and mortality. The aim of the present study was to compare the nutritional status of women with PE with healthy pregnant. *Methods:* This research was carried out at local women health care, education and research hospital in Ankara, Turkey. Thirty pregnant women who were being followed up with the diagnosis of preeclampsia and 30 healthy pregnant women as a control group involved in the study. All participants were given an introduction to the research and a questionnaire regarding their nutritional status and habits. Anthropometric measurements and blood samples were taken. *Results:* Weight gain during pregnancy, gestational age and fetal birth weight were found to be significantly lower in preeclamptic pregnant women than healthy pregnant women ($p<0.001$). On the other hand, pre-pregnancy BMI was significantly higher in the preeclamptic group ($p<0.001$). Women with PE had higher blood pressure, fasting blood glucose concentration, serum total cholesterol, triglyceride and homocystein levels compared to healthy pregnant women ($p<0.05$). Average daily energy, carbohydrates, fiber, vitamin B_6 intakes were significantly different between preeclamptic and healthy pregnant women ($p<0.05$). There were no statistically significant differences among the groups of the micronutrients except for vitamin B_6. *Conclusion:* Further research that examines the effects of nutritional habits and nutritional supplementation on development of preeclampsia is needed in order to prevent hypertensive disorders in pregnancy.

Key words: preeclampsia, pregnancy, nutrition, dietary factors

Introduction

Preeclampsia is the most common medical complication of pregnancy. It affects nearly 2-8% of all pregnancies. It is still one of the major factors for maternal and neonatal mortality despite improvements in antenatal and neonatal care (1). Studies up to date have focused on pathophysiology, prevention and treatment of the disease. Although symptoms of preeclampsia are well-understood, the exact mechanisms involved in the etiology of the disease are largely unknown (2-5).

Studies have shown that endothelial damage, immunological dysfunction, endocrine abnormalities, genetic and nutritional elements may play a role in the development of preeclampsia (3, 6-8). Uteroplacental development in preeclamptic pregnancies has been shown to be insufficient (3-4, 9). Local ischemia of the spiral arteries that supply blood to the placenta and uteroplacental ischemic damage causes accumulation of oxidized products, cytokines and activated leukocyte secretions which leads to endothelial damage (5, 10). Additionally, maternal factors such as chronic hy-

*Equal contribution

pertension, insulin resistance, dyslipidemia, diabetes and adiposity have been shown to play a key role in the development of preeclampsia (5, 11). Currently, endothelial cell activation is considered as the underlying pathophysiology of preeclampsia (11). Free radicals are very active and tissue damaging compounds which occurs as a result of lipid peroxidation in metabolism. Under normal circumstances, these compounds are removed by organism's antioxidant mechanisms. However, lack of balance between oxidant and antioxidant molecules may trigger harmful effects of free radicals and contribute to the development of diseases. In preeclamptic patients ascorbic acid and vitamin E levels, which are the most important components of the antioxidant system, were decreased (7,11-12). In addition, free fatty acid and triglycerides were increased two fold compared to healthy pregnant women. Increase in triglycerides and free fatty acids were aberrant even weeks or months before the disease is clinically apparent (5,10,13). In preeclamptic patients low density lipoprotein (LDL)-cholesterol increases whilst cardio-protective high-density lipoprotein (HDL)-cholesterol decreases (10).

Dietary factors can be determinative in the progress of the mechanisms that are mentioned above. Therefore, nutritional habits can be considered as an important risk factor in the development of preeclampsia (5,8). Maternal nutritional status during pregnancy has been investigated as a potential treatment target in the prevention of preeclampsia. Poor dietary quality in mid-pregnancy, including energy, micronutrient and macronutrient intake, has been implicated in increased risk for preeclampsia (14). A large body of evidence has shown that some nutrients can improve endothelial function, either by reducing oxidative stress or by modifying certain inflammatory responses (5, 11). Micronutrients including folate, sodium, calcium, potassium, iron, copper, and zinc represent potential etiologic and treatment targets for preeclampsia prevention (5, 14). Maternal micronutritional status in pregnancy may influence placental development. Some studies have shown that excess energy (high carbohydrates and high fat diet) intake or insufficient nutrient intake during pre-pregnancy and pregnancy periods may be associated with the increased risk of preeclampsia (7-8, 10, 15). However, there are almost no studies that show a definite relationship. This study aimed to investigate the relationship between development of preeclampsia and nutritional status of pregnant women in Ankara, Turkey.

Methods

Subjects

This research was carried out at local women health care, education and research hospital in Ankara, Turkey. The preeclampsia group was composed of 30 pregnant women from Ankara who had hospitalized with preeclampsia diagnosis at perinatology service. The control group was composed of 30 healthy pregnant women who had been visiting the hospital for routine control. The healthy pregnant women who were equally matched with the patient group for age and general status were recruited. Eligibility criteria included aged at least 19 years and at least 16 completed weeks of pregnancy. On determination of eligibility, women were invited to participate in the study at the time of their initial prenatal care visit. The presence of any of the following conditions was considered as exclusion criteria for all the participants: pregestational hypertension, chronic hypertension and systemic diseases which could cause hypertension (such as renal diseases, autoimmune diseases, endocrine diseases, cancer or mental illness). Informed consent was obtained from each participant before the study. Hacettepe University's ethics committee approved the study and after obtaining consent from each participant, their information, blood and urine samples were collected. Preeclampsia diagnosis criteria were as follows: high blood pressure (BP≥140/90 mmHg) and increased protein excretion in 24 hours urine test (≥300 mg/24 hours) or ≥+1 proteinuria with dipstick test after 20 weeks of gestation (1).

Questionnaire and nutritional assessments

Data were collected from the patients during a facetoface interview with qualified dieticians. In the interview, a questionnaire was used to determine the general features (age, gender, educational status and occupation) physical activity level, food consumption frequency and diet habits of the pregnant women. Participants' dietary intake was assessed using food frequency questionnaire (FFQ). The FFQ included 65 food items traditionally consumed in Turkey. Foods were classified into the following food categories: milk and dairy products, meat and meat products, fruits, vegetables, breads and cereals, beverages, and desserts. Intake frequencies for the food items consisted of eight categories ranging from never/once a month to more than one per day. Trained interviewers asked participants how often they had consumed one portion of each food item during the entire previous trimester. To compute the total amount of food intake per day, the reported frequency of consumption for each food item was multiplied by the portion size and then total food intake was converted to nutrient intake based on the food's nutrient profile. Standardized food recipes for Turkey (16) and BEBIS program (17) which is a food composition database for nutrient estimation were used to determine average daily energy and nutrient intake for each participant. These values were compared with the recommended daily allowance values (The Dietary Guidelines for Turkey 2014) (18) to determine the energy and nutrient requirement meeting status and the requirement meeting percentages were calculated. For each woman enrolled in the study a complete clinical history was recorded before the delivery. All physical measurements were obtained by trained dieticians were taken with women wearing light clothes and without shoes. Body weight and height were taken from pregnancy records. After pre pregnancy body mass index (BMI: weight-kg/height-m^2) were calculated.

Biochemical parameters

Blood samples were drawn in fasting conditions (8h), from the antecubital vein. Plasma was separated by centrifugation and then frozen at -30°C and stored until analysis. Fasting blood glucose and lipid profile (high-density lipoprotein [HDL], low-density lipoprotein [LDL], very-low-density lipoprotein [VLDL] and triglycerides [TG]), were determined by an enzyme colorimetric test and homocystein, folic acid and vitamin B_{12} levels were measured immuno chemiluminescent method by using Immulite 2500 autoanalyser and commercial kits in Education and Research Hospital biochemistry laboratory.

Statistical analyses

SPSS (Statistical Package for Social Sciences Inc., Chicago, IL, United States) for Windows 17.0 program was used to analyze the data. Descriptive statistical methods (standard deviation, minimum, maximum and mean) were used for the evaluation of the data. Student t test was used to compare the quantitative data (19). As the data did not exhibit normal distribution, the median and interquartile range values were used to conduct statistical analyses of the daily dietary energy and nutrient intakes and however, the mean and SD values are also presented. The MannWhitney U test was used for statistical comparison of the groups. Spearman's correlation test was used to analyse correlations between the parameters, including the correlation between energy and nutrient intake, regression analysis was performed for the associated parameters. Results were evaluated with a confidence interval of 95% and significance level of $p<0.05$.

Results

Table 1 describes the general features and clinical characteristics of pregnant women. The average age of women across all groups was 27.42±5.05 years. The gestational age was greater in healthy pregnant women than women with PE (38.1 ±2.89 weeks vs 34.6 ±3.33 weeks; $p<0.0001$). General features of pregnant women indicated that age and years of education, was found to be higher in healthy pregnant women ($p>0.05$) (Table 1). Weight gain during pregnancy, gestational age and fetal birth weight were found to be significantly lower in preeclamptic pregnant women than healthy pregnant women ($p<0.001$). On the other hand, pre-pregnancy BMI was significantly higher in the preeclamptic group ($p<0.001$) (Table 1).

Women with PE had higher blood pressure (diastolic and systolic) ($p<0.001$) and fasting blood glucose concentration ($p<0.05$) compared to healthy pregnant women (Table 1). When the lipid profile of groups analyzed, there was no differences in serum LDL-cholesterol and VLDL- cholesterol levels between preeclamptic and healthy pregnant. It was observed that women with PE had lower HDL-cholesterol levels compared to healthy pregnant women. Additionally,

Table 1. General features and clinical characteristics of pregnant women

General features and clinical characteristics	Preeclamptic Pregnant (n=30)	Healthy Pregnant (n=30)	P-value
	Mean±SD	Mean±SD	
Age(years)	26.17±6.0	28.7±4.1	0.300[a]
Years of education	8.9±0.7	9.0±0.8	0.920[a]
Gestational age (week)	34.6 ±3.33	38.1 ±2.89	0.000[a] **
Pre-pregnancy BMI (kg/m^2)	25.1±4.0	23.2±1.6	0.020[a]*
Weight gain during pregnancy (kg)	10.3±2.9	13.3±2.5	0.000[a] **
Fetal birth weight (g)	2166 ± 692	3222 ± 674	0.000[a] **
Diastolic pressure (mmHg)	98.0±8.1	69.6±8.5	0.000[a] **
Systolic pressure (mm Hg)	158±12.9	112.6±10.8	0.000[a] **
Fasting blood glucose (mg/dL)	88.2±10.0	80.5±13.9	0.045[a] *
T. Cholesterol (mg/ dL)	288.8±5.86	247.6±6.17	0.007[a]*
LDL (mg/ dL)	205.0±132.7	196.0±155.0	0.403[b]
HDL (mg/ dL)	61.2±16.61	72.1±14.18	0.008*[b]
VLDL (mg/dL)	57.0±25.9	57.0±23.9	0.666[b]
TG (mg/ dL)	277.0±138.0	268.0±102.2	0.032*
Homocystein (μmol/L)	7.6 ±3.32	6.1±3.07	0.027*[a]
Folic acid (ng/mL)	12.6±3.6	13.9±8.4	0.025[b]
B_{12} (pg/mL)	180.0±87.6	200.0 ±60.5	0.633[b]

**p<0.05, ** p<0.001 between preeclamptic women and pregnant control women. [a]Mann Whitney U-test, [b]Independent two-sample t-tests; p<0.05. Results expressed as mean±standard deviation. BMI, body mass index; HDL, high-density lipoprotein; LDL, low-densitylipoprotein; VLDL, very-low density lipoprotein.*

it was noted that women with PE had higher total cholesterol and triglyceride levels compared to healthy pregnant (p<0.05). (Table 1). The mean plasma homocysteine levels were found to be 7.7±3.3 μmol/L and 6.1±3.1 μmol/L in preeclampsia and control groups, respectively (p<0.05; Table 1).

It was observed that women with PE had lower folic acid (12.6±3.6 ng/mL, p<0.05), and vitamin B_{12} levels (180.0±87.6 pg/mL, p>0.05) compared to healthy pregnant women (folic acid 13.9±8.4 ng/mL and B_{12} 200.0 ±60.5 pg/mL) (Table 1).

Daily average dietary energy and nutrient intakes and requirement meeting percentages are shown in Table 2. It was found that women with PE had higher energy and carbohydrate intake compared to healthy pregnant (p<0.05). PE women met 85.3% of their daily energy requirement, whereas control group met 81.5% of their energy requirement. Protein and fat intake were lower among women with PE than in healthy pregnant women but the difference was not statistically significant (p>0.05). Total dietary fiber intakes were significantly lower in preeclamptic group than controls. The daily average dietary fibre intakes were 20.25.3g (met 72.3% of daily fiber requirement) and 26.78.4g (met 95.6 % of daily fiber requirement) in preeclampsia and control groups, respectively (Table 2).

There were no statistically significant differences among the groups of the micronutrients except for vitamin B_6 (Table 2).

Table 3 lists results from logistic regression that was performed in order to determine which factors remain associated with PE development. After the adjustment of the nutritional variables for gestational age and BMI, it was observed that diet energy intake, carbohydrates and fiber intake were associated with PE development.

Discussion

Maternal nutritional status during pregnancy has been investigated as a potential treatment target

Table 2. Daily dietary energy, nutrient intakes and requirement meeting percentages

Energy and Nutrients*	Preeclamptic Pregnant (n=30)		Healthy Pregnant (n=30)		
	Mean ± SD	**RDA %**	**Mean ± SD**	**RDA %**	**P-value**
Energy (kcal)	1955.8±288.1	85.3	1783.0±340.4	81.5	0.039*
Total Protein (g)	66.4±10.3	87.9	67.2±14.3	89.1	0.896
Total Carbohydrate (g)	253.3±37.3	NC	227.3±45.2	NC	0.019*
Total Lipid (g)	64.7±24.5	108.0	71.9±18.7	116.0	0.216
SFA (g)	27.3±10.1	120.2	30.4±9.6	130.5	0.221
MUFA (g)	23.3±10.7	85.4	26.4±9.0	94.6	0.280
PUFA (g)	10.4±5.8	92.7	11.6±4.4	99.8	0.394
Total Fiber (g)	20.25.3	72.3	26.7±8.4	95.6	0.001*
Retinol (μg)	372.1±162.0	142.1	568.5±821.7	162.7	0.204
Vit E (μg)	12.1±5.4	61.9	10.52.4	50.4	0.142
Vit B_1 (mg)	0.9±0.3	63.4	0.9±0.2	64.4	0.834
Vit B_2 (mg)	1.5±0.8	105.5	1.40.3	104.8	0.905
Niacin (mg)	11.6±4.9	64.4	9.8±3.5	54.7	0.118
Vitamin B_6 (mg)	1.2±0.3	66.4	1.6±0.5	82.7	0.006*
Folic Acid (μg)	315.5±68.9	53.8	323.2±87.4	52.6	0.704
Vit B_{12} (μg)	2.4±1.5	93.4	2.71.7	107.2	0.385
Vit C (mg)	138.9±69.0	154.3	127.5±73.0	141.8	0.084
Sodium (mg)	3793.1±120.7	NC	3426.4±108.0	NC	0.052
Calcium (mg)	868.1±253.0	66.7	912.9±232.5	70.2	0.481
Iron (mg)	11.1±2.6	41.5	11.7±2.9	43.2	0.515

**Dietary Guidelines for Turkey, RDA; recommended daily allowance, **p<0.05; Results expressed as mean±standard deviation. SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids, NC,not clear.*

Table 3. Logistic regression to determine which factors are associated with preeclampsia development

Variables	Odss Ratios (OR)	95% Confidence Interval (CI)	P
Body Mass Index (>25.0 kg/m²)	2.33	1.31-2.50	0.004*
Dietary intake			
Energy (kcal/day)	1.21	0.72-2.01	0.001*
Carbohydrate (g/day)	1.47	1.04–2.08	0.032**
Fiber (g/day)	1.11	1.01-1.23	0.035
***p<0.01, **p<0.05			

in the prevention of preeclampsia. The risk factors for preeclampsia include obesity, dyslipidemia, insulin resistance and other factors that are also risk factors for atherosclerosis. For many years diet has been suggested to play a role in the development of preeclampsia (5, 10, 14). Associations between nutrition and preeclampsia have been investigated in several studies and have shown increased risk of preeclampsia with high consumption of energy, added sugar (sugar-sweetened soft drinks), PUFA, and decreased risk of preeclampsia with high consumption of milk and high intake/sufficient status of vitamin D (8, 20-27).

In this study we compared the nutritional status of women with preeclampsia and healthy pregnant women from Ankara in Turkey. The results of this study showed that women with PE had lower gestational age and fetal birth weight, higher fasting blood glucose concentration as well as a higher BMI compared to healthy pregnant women. It was found that women with PE had higher dietary energy,carbohydrate intake and lower fiber intake compared to healthy pregnant. Also, results from the logistic regression showed that energy, carbohydrate and fiber were associated with the development of PE. The present study is of particular importance as, to the best of our knowledge, it is the first study investigating the association between nutritional status and preeclampsia risk in pregnant women in Turkey.

Several observational studies (21, 22), report that obesity or high body mass index (BMI) prior to pregnancy increases the risk of preeclampsia and gestational hypertension and similar pattern was also observed in our study. Brennand and et al. reported that obese women with excessive weight gain during pregnancy had higher preeclampsia prevalence compared to the obese women with poor weight gain or the obese women with adequate weight gain (22). In this study, healthy pregnant women had gained more weight compared to preeclamptic women. This result conflicts with literature but the lower mean gestational age in the preeclamptic women than control could be the reason for this. On the other hand, pre-pregnancy BMI was significantly higher in the preeclamptic group ($p<0.001$). Also it was demonstrated that higher prepregnancy body mass index (BMI) is associated with an increased risk of PE (OR 2.33, $p<0.05$).

Improved dietary quality has also been associated with a decreased risk of preeclampsia (24-30). We did not identify significant differences in macronutrient and micronutrient intake except energy, carbohydrate and fiber intake in women who developed PE compared with controls. A large case-control study which examined fat, protein and energy intakes of preeclamptic women indicated that the intake of these nutrients were lower. Sucrose and polyunsaturated fatty acids were identified as energy-rich nutrients significantly associated with energy intake and preeclampsia (24). Conversely, other studies showed no difference between preeclamptic pregnant women and healthy pregnant women in energy intake (25-27). In this study, mean daily energy and carbohydrates intake of the preeclamptic pregnant women was significantly higher than the healthy pregnant women ($p<0.05$). Our findings were consistent with others who identify differences in energy intake as predictors of preeclampsia. In a multicenter case-control study of Latin American women, dietary intake was determined using food frequency questionnaires among women with preeclampsia and normotensive controls. Although energy intake was increased in the preeclampsia group, increased dietary intake of carbohydrates was the only macronutrient predictive of preeclampsia (26). The gestational timing of macronutrient intake in late pregnancy may confound accuracy of measures because of the presence of disease. Findings from this study may have been influenced by the late gestational timing of dietary intake measures. Also these findings suggests that energy components rather than total energy, may be more influential in the prediction of preeclampsia.

In a prospective study it was reported that no difference was determined between the groups for fatty acid and nutrient intake between 16 weeks of gestation and 32 weeks of gestation in healthy versus preeclamptic pregnancies (25). Current study indicated that healthy pregnant women consumed more total lipid intake than preeclamptic pregnant women but this difference was statistically insignificant ($p>0.05$).

Maternal plasma lipids are significantly elevated during pregnancy. Women who develop preeclampsia experience even more dramatic lipid changes (5). In several studies were demonstrated reduced HDL and increased triacylglycerols and LDL cholesterol in women with PE (26, 29-32). According to findings of our study women with PE had higher concentrations of total cholesterol and triglycerides than control subjects ($p<0.05$). The HDL cholesterol concentrations were lower in women with PE than in control subjects ($p<0.05$). On the other hand we found that women with PE had lower LDL levels compared to healthy pregnant controls ($p>0.05$). In similar another study Reyes et.al. explained that lower LDL concentrations in women with PE are the result of increased LDL oxidation rate (26). High energy diets and dietary fatty acids composition can lead to dyslipidemia, especially postprandial hypertriglyceridemia in pregnant women with PE (5, 10, 26, 30).

In a prospective study by Clausen et al. (24) reporting higher risk of preeclampsia development in pregnant women with high polyunsaturated fatty acid consumption; rate of preeclampsia was 1.6 when the dietary energy intake from omega-6 fatty acids were <5.2% whilst the rate of preeclampsia risk was 2.3 when the dietary energy intake from omega-6 fatty acids were >7.5% (24). With regards to the effects on decreasing platelet aggregation and improving vasodilatation, omega-3 fatty acids are suggested to have an important role on preventing preeclampsia (30-32). Fatty acid composition of the dietary fat is very important as well as the dietary intake amount. Fatty acid composition of the dietary fat intake should include <7% saturated fatty acid (SFA), 15% monounsaturated fatty acid (MUFA) and 8-10% polyunsaturated fatty acids (28). In this study, dietary intake of SFA, MUFA, PUFA were higher in the healthy pregnant women group compared to the preeclamptic pregnant women but these differences were insignificant.

The clinical data on the role of fiber in pregnancy, however, are quite limited (30, 32-33). More well-designed cohort studies and clinical trials that assess the relationship between fiber intake prior to or during pregnancy and the risk of PE are needed to further explore the role of fiber as well as of obesity, insulin resistance, and dyslipidemia in the development of PE (5).

Qui et al. (32) reported 0.28 fold decreased risk of preeclampsia in high fiber consuming pregnant women (≥21 g daily) compared to the low fiber consuming pregnant women (<12 g daily). Although there are studies suggesting no relationship between fiber intake and preeclampsia (34). In this study fiber intake of the preeclamptic pregnant women were lower than the healthy pregnant women and this difference was statistically significant ($p<0.05$). After the adjustment of the nutritional variables for gestational age and BMI, it was observed that dietary fiber intake were associated with PE development (OR= 1.11, $p<0.05$).

Folate may reduce the risk of developing PE by improving endothelial function at both the placental and systemic levels or by lowering homocysteine, a risk factor for PE (27, 35-38). Sanchez et al. (35) demonstrated that while women who had lower plasma folic acid levels had 1.6 times increased risk of preclampsia, no relationship was found between low vitamin B_{12} and increased preeclampsia risk. Nevertheless there are studies reporting no relationship between folic acid intake and preeclampsia status (25, 27). In our study dietary folic acid and vitamin B_{12} intake and its serum levels of preeclamptic pregnant women was lower compared to the healthy pregnant women. When we evaluate these results with Turkish Recommended Daily Allowances Guide, their food intake was found to be similar and the mentioned differences were found to be statistically insignificant.

This study has some limitations. The important limitation include the small sample size of participants. The small sample size may have contributed to the failure to establish significant differences between dietary intake group means. The inconsistent findings for the influence of maternal micronutrient, macronutrient, and energy intake as a predictor of preeclampsia may be the result of other factors such as metabolic processes and bodymass index that have the potential to alter measures of maternal nutritional status. We used FFQ to assess the nutritional status of participants. Misreporting is a serious error in all dietary assessment methods. Recall bias, and lack of accuracy of the participants self-reported estimations of their habitual dietary intakes must be considered. Due to the design of the study, causality cannot be determined, only associations between the dietary factors and the development PE can be formulated.

Conclusion

There are limited studies that have shown the effects of nutrition on prevention and treatment of preeclampsia. In most studies, controversial and conflicting results were found about the nutritional factors which were taken as part of the diet and/or supplements. In these studies, the relationship between early or late period preeclampsia risk development and nutrient factor supplements and related cofactors could not be enlightened due to the lack of detailed food intake records during pregnancy. In order to prevent gestational hypertension disorders more studies should be done on the effects of nutritional habits and supplements.

The present study is of particular importance as, to the best of our knowledge, it is the first study investigating the association between nutritional status and preeclampsia risk in pregnant women in Turkey.

Additional research is needed to establish a strong causal relationship between dietary factors and preeclampsia and to describe the incidence preeclampsia. As the number of studies on this subject is limited, the results of the present may provide useful information for future studies.

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Correspondence:
Gülhan Samur, Assoc.Prof, PhD,
Hacettepe University, Nutrition and Dietetics Department
06500 Sıhhıye, Ankara, Turkey
Tel.: +90 312 311 96 49
Fax: +90 312 309 13 10
E-Mail: gsamur@hacettepe.edu.tr