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Original Article

Vitamin D deficiency in adolescent pregnancy and obstetric outcomes

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ABSTRACT

Objective: The aim of this study was to evaluate the rates of vitamin D deficiency in adolescent pregnants and its influence on the obstetric outcomes.
Materials and methods: A total of 300 singleton pregnant women aged between 14 and 20 years, were divided into three groups according to their gestational weeks (100 pregnant adolescents from each trimester). Randomly selected 300 singleton pregnant women older than 20 years of age with the similar gestational ages were designed as the control group at the same time period. We divided serum 25(OH)D levels into three categories deficiency, inadequacy and adequate levels according to the Endocrine Society guidelines. Serum 25(OH)D levels were also evaluated according to age, seasons and gestational periods. Adverse obstetric outcomes were recorded.
Results: Overall, 86% of the subjects were found to have deficient 25(OH)D levels (<20 ng/ml). The levels indicated an inadequate state in 72 subjects (12%) and only 12 (2%) women had adequate 25 (OH) D levels. Among adult pregnant women the rates of deficient, inadequate and adequate levels were 88.3%, 11%, and 0.7% respectively. Among adolescent pregnant women these rates were 83.7%, 13%, and 3.3% respectively. The lowest 25(OH)D levels occurred during the winter while the highest levels were detected during the summer in both groups. Calcidiol, 25(OH)D, was a significant predictor for preterm delivery (AUC = 0,909; $p < 0,001$) and also for SGA (AUC = 0,915; $p < 0,001$). Maternal age was another significant predictor for SGA (AUC = 0,787; $p < 0,001$) and preterm delivery (AUC = 0,785; $p < 0,001$).
Conclusion: We found a high incidence of 25(OH)D deficiency in Turkish pregnant women. Adolescent age and low 25(OH)D levels are significant risk factors for PTD and SGA. Effective prophylaxis programs for vitamin D deficieny and/or fortification of foods with vitamin D are essential in pregnant women especially in the winter season.

Introduction

In recent years, there has been increased interest in the potential role of vitamin D for prevention of non-skeletal disorders, in addition to its effects on bone health. Disorders that complicate pregnancy, such as gestational diabetes mellitus (GDM), preeclampsia, preterm delivery (PTD), and fetal growth abnormalities are in this wide range [1–3]. Intake of vitamin D supplements during pregnancy has been reported to decrease adverse pregnancy outcomes [4,5]. However, other studies have not found the same association [6,7].

In many countries, vitamin D deficiency is a major public health problem [8]. Vitamin D deficiency is common in pregnant women in Turkey [9–13]. According to a study from İstanbul performed by Alagöl et al. 66.6% of reproductive age women have had low vitamin D levels [9]. Pehlivan et al. reported the rate of mothers who had a vitamin D value below 16 ng/ml was 94.8% [10]. Ergür et al. reported that 18.6% of the mothers and 2.9% of the neonates had normal vitamin D levels [11]. In İzmir, a sunny region of Turkey, vitamin D deficiency rate (<10 ng/ml) was reported as 50.4% among pregnant women [12]. Finally Gür G et al. reported that vitamin D deficiency (≤20 ng/ml) in pregnant women and their infants was 62.6% and 58.6%, respectively [13].

Adolescent pregnancy is a serious public health issue because of its association with increased risks of adverse obstetric and perinatal outcomes such as maternal mortality, PTD, small for

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gestational age (SGA), preeclampsia and neonatal death [14–19]. In adolescent pregnant women, vitamin D status is of particular significance to optimize calcium (Ca) absorption for skeletal growth and maintenance, effects on pregnancy, and short- and long-term effects in the offspring [20]. Serum level of calcidiol, 25- hydroxyvitamin D [25(OH)D], is used as the most accurate way of determining vitamin D deficiency and sufficiency but there is no consensus yet on the cut-off point values. The Endocrine Society defines deficiency as serum 25(OH)D < 20 ng/ml (50 nmol/L), while both The Institute of Medicine (IOM) and the National Osteoporosis Society agree that serum 25(OH)D level for bone health <12 ng/ml (30 nmol/L) indicates deficiency [21,22].

According to The American College of Obstetricians and Gynecologists (ACOG), there is not sufficient evidence to recommend routine screening for vitamin D deficiency in all pregnant women; also, there is no optimal serum vitamin D level during pregnancy [23]. IOM recommends intake of 600 IU/D, and the Endocrine Society suggests intake of 600-2000 IU/D vitamin D for pregnant women [21,24].

This study aims to determine the rate of vitamin D deficiency in adolescent pregnancy and its influence on the obstetric outcomes.

Materials and methods

This is a hospital based, cross-sectional, observational study. The Medical Research Ethics Board of Dr. Zekai Tahir Burak Women Health and Research Hospital approved the study. The study was implemented at Dr. Sami Ulus Women and Children's Health and Research Hospital between January 2012 and December 2014.

A total of 300 singleton pregnant women, age 14–20 years, were divided into three groups according to their gestational weeks (100 pregnant adolescents from each trimester). Further, 300 randomly selected singleton pregnant women older than 20 years of age with similar gestational ages were designed as the control group for the same time period. Written informed consent was obtained from all participants.

Gestational age was calculated from the mothers last menstrual period and confirmed by first-trimester obstetric ultrasound. Women who had chronic metabolic diseases impacting 25(OH)D metabolism, such as liver or kidney disease or thyroid disorders, were excluded from the study. Demographic characteristics including age, gravidity, parity, obstetric and medical history, body mass index (BMI), time spent outdoors, clothing type (closed = all body parts except face and hands are covered with clothes, or not), and the gestational week at the time of blood sampling were recorded. Adverse obstetric outcomes were defined as PTD, preeclampsia, GDM, cesarean delivery, and SGA. PTD was defined as delivery before 37 weeks' gestation, and LBW was birth weight less than 10 percentile according to gestational age.

Blood samples taken from an antecubital vein and serum 25(OH)D concentrations were measured using enzyme-linked immunosorbent assay (ELISA). Serum 25(OH)D status was evaluated in three categories following Endocrine Society guidelines: <20 ng/ml, deficient; 20–29,9 ng/ml, inadequate; and ≥30 ng/ml, adequate levels. The seasons for sample collection were defined as spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February).

SPSS (Statistical Package for Social Sciences) 20. 0 was used for statistical analysis. The results were presented as means, standart deviations, or number and percentage of pregnant women. T-test, repeated measures, and ANOVA for independent samples, chi-square test, and Fisher's exact test were used for comparisons between groups. Correlation analyses were used to calculate the degree of association, and multinominal logistic regression analyses were used to determine adjusted associations. ROC curve was used to determine the predictive value of tests and to calculate cut-off points. P value lower than 0.05 was accepted as statistically significant.

Results

A total of 600 pregnant women (300 study group and 300 control group) were recriuted for this study. The demographic characteristics of the pregnant women are seen in Table 1. There was a statistically significant difference between the groups for the mean of ages ($p < 0.05$), while there were no significant differences between the groups for gravidity, parity, BMI, clothing type, educational levels, and time spent outdoors ($p > 0.05$).

The mean serum 25(OH)D concentrations of adolescents and the control group according to season are seen in Table 2. The deficiency rate of 25(OH)D for all pregnant women was 86%, while the rate of inadequency was 12%, and the rate of adequate values was 2%. Among adolescent pregnant women, these rates were 83,7%, 13% and 3.3%, respectively.

There was a significant difference between serum 25(OH)D levels according to season ($p < 0.001$) within the groups. The lowest vitamin D levels occurred during the winter, while the highest levels were detected during the summer in both groups.

Serum 25(OH)D levels of all participants (both study and control groups) according to age, seasons and gestational age are seen in Table 3. There was a significant difference between serum 25(OH)D status according to the season ($p = 0{,}000$) and educational level. However, there were no significant differences between serum 25(OH)D according to age and gestational age ($p > 0.05$).

Table 1
Demographic characteristics.

		Study group	Control group
Age	Mean (min–max)	18.43 ± 1.30 (14–20)	28.67 ± 5.38 (21–43)*
Gradividity	Mean (min–max)	1 (0–6)	2 (1–6)
Parity	Mean (min–max)	0 (0–3)	0 (0–4)
BMI	Mean (min–max)	24.1 ± 4.0 (15.6–40.4)	24.9 ± 5.4 (15.5–41.9)
Educational level	None	34 (11.3%)	20 (6.6%)
	primary school	82 (27.3%)	90 (30.0%)
	secondary	145 (48.3%)	154 (51.3%)
	high	37 (12.3%)	33 (11.0%)
	university	2 (0.7%)	3 (1.0%)
Closed wear	Yes	102 (35.8%)	100 (33.3%)
	No	178 (64.2%)	200 (66.7%)
Time spent outdoors (minutes/per day)	Mean (min–max)	69.4 ± 65.7 (0–360)	70.6 ± 67.6 (0–360)

* p < 0,05, BMI: Body Mass Index, Closed wear: all the body parts except face and hands are covered with clothes.

Table 2
Serum vitamin D levels according to maternal age and seasons.

Maternal age	Season	Vitamin D levels		Deficient (<20 ng/ml)	Inadequency (20–29,9 ng/ml)	Adequate (≥30 ng/ml)
≤20	Spring (n = 68)	Mean (min–max)	16.2 (13.9–46.8)	67 (95.5%)	1 (4.5%)	–
	summer (n = 78)	Mean (min–max)	20,8 (10.1–69.4)	32 (41.0%)	36 (46.2%)	10 (12.8%)
	Autumn (n = 82)	Mean (min–max)	11.5 (10.1–37.2)	81 (98.8%)	1 (1.2%)	–
	Winter (n = 72)	Mean (min–max)	8.9 (2.4–40.3)	71 (98.6%)	1 (1.4%)	–
≥21	Spring (n = 70)	Mean (min–max)	14.8 (14–22.3)	70 (98.6%)	1 (1.4%)	–
	summer (n = 85)	Mean (min–max)	18,8 (11.4–52.0)	53 (62.4%)	30 (35.2%)	2 (2.4%)
	Autumn (n = 78)	Mean (min–max)	12.7 (11.8–22.6)	76 (97.4%)	1 (1.3%)	–
	Winter (n = 67)	Mean (min–max)	10,4 (7.1–28.5)	66 (98.5%)	1 (1.5%)	–

Obstetric outcomes according to age are seen in Table 4. There were statistically significant differences between the two groups (study and control) for PTD, SGA, and preeclampsia ($p < 0,05$). Maternal age was a significant predictor for SGA (AUC = 0,787; $p < 0,001$) (Fig. 1). Optimal cut off value was obtained at 19,5 years, with 67% sensitivity and 80% specificity. Additionally, maternal age was significant predictor of preterm delivery (AUC = 0,787; $p < 0,001$) (Fig. 2). Optimal cut off value was obtained at 19,5 years, with 66,1% sensitivity and 79,7% specificity.

There was a significant difference for preeclampsia rates between groups ($p = 0,000$), and being older was a risk factor for preeclampsia.

Calcidiol was a significant predictor of preterm delivery (AUC = 0,909; $p < 0,001$) (Fig. 2). Optimal cut off value was obtained at 10,95 ng/ml with 82,5% sensitivity and 91,5% specificity.

Table 5 demonstrates the obstetric outcomes according to cut off values of 25(OH) D while Table 6 shows the obstetric outcomes according to cut off values of 25(OH)D for all maternal ages. There were statistically significant differences between the groups according to having 25(OH)D levels below or higher than 10,9 ng/ml for SGA and PTD in both age groups (study and control) ($p = 0,000$).

Whether all pregnants considered according to cut off values of 25(OH)D there was a statistically significant relation between the groups to having 25(OH)D levels below or higher than 10,9 ng/ml for GDM, PTD and SGA.

Calcidiol was also a significant predictor for SGA (AUC = 0,915; $p < 0,001$) (Fig. 1). Optimal cut-off value was obtained at 10,85 ng/ml, with 84,4% sensitivity and 90% specificity.

Optimal cut off values of 25(OH)D levels predicting PTD and SGA according to gestational ages and seasons are seen in Table 7.

Table 3
25(OH)D levels according to age, season, gestational age, and educational level (n = 600).

	25(OH)D levels (mean) (ng/ml)	P
Age[a]		
≤20	15.40 ± 7.91	0.115
≥21	14.93 ± 4.70	
Season[b]		
Spring (1)	15.71 ± 2.93	0,000
Summer (2)	21.95 ± 7.50	(1–2,3,4)
Autumn (3)	12.44 ± 2.39	(2–3,4)
Winter(4)	9.85 ± 3.32	(3–4)
Gestational week[b]		
1. Trimester	14.28 ± 5.25	
2. Trimester	15.50 ± 6.61	0.075
3. Trimester	15.73 ± 7.41	
	25(OH)D levels (median [Min-Max])	
Educational level[c]		
None	14,30 [7,90–28,50]	
primary school	13,05 [2,40–37,20]	
secondary	14,60 [6,22–69,40]	0.022
high	13,70 [6,80–57,00]	
university	10,30 [9,10–13,00]	

[a] t test.
[b] ANOVA.
[c] Kruskal Wallis H analyses were used.

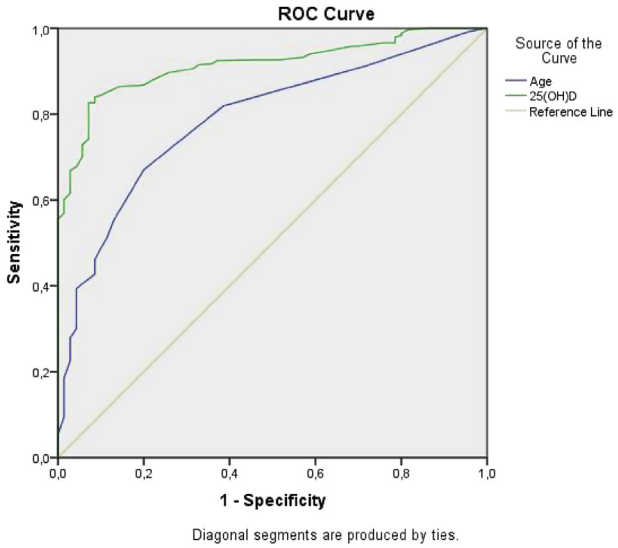

Fig. 1. ROC curve of age and 25(OH)D to predict SGA.

Table 4
Obstetric outcomes according to maternal ages.

Ages	GDM		PTD		SGA		Preeclampsia		Cesarean	
	no	yes	No	yes	no	Yes	no	yes	no	yes
≤20 n (%)	290 (96.6)	10 (3.4)	249 (82.8)	51 (17.2)	239 (79.6)	61 (20.4)	290 (96.6)	10 (3.4)	199 (66.3)	101 (33.7)
≥21 n (%)	285 (95.2)	15 (4.8)	292 (97.3)	8 (2.7)	292 (97.3)	8 (2.7)	250 (83.4)	50 (6.6)	195 (65)	105 (35)
P	0.311		0.000		0.000		0.000		0.35	

GDM: Gestational Diabetes Mellitus, PTD: Preterm Delivery, SGA: Small for Gestational Age.

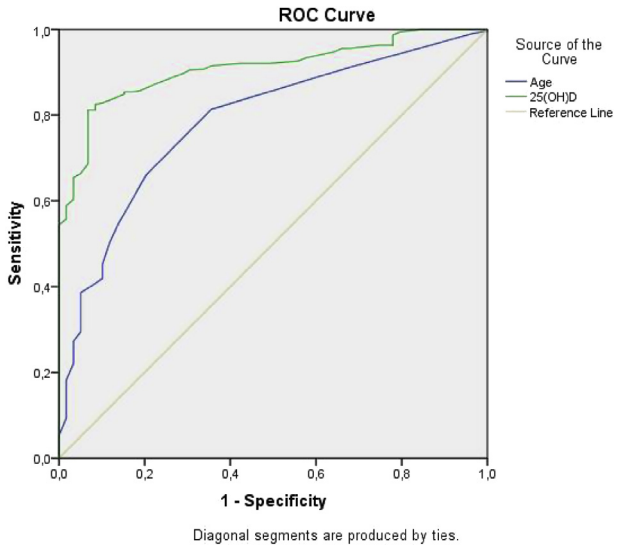

Fig. 2. ROC curve of age and 25(OH)D to predict PTD.

Calcidiol level was significantly correlated with mean time spent outdoors (r = 0,093, p = 0,028). There were no statistically significant correlations between 25(OH)D levels, age (r = 0,046, p = 0,265) and BMI (r = −0,084, p = 0,056).

Multinominal lojistic regression analyses were used to determine adjusted associations. Serum 25(OH)D levels were not independently associated with any of the factors studied, including gravidity, parity, educational level and clothing type.

Discussion

This study revealed that 86% of pregnant women were deficient in vitamin D (25(OH)D < 20 ng/ml). This rate was 83,7% in the adolescent pregnancy group. Only 2% of all pregnant women had adequate 25(OH)D.

The highest 25(OH)D values were in the third trimester, while the lowest values were in the first trimester. This is an expected result because during pregnancy, serum vitamin D levels increase 50–100% over the nonpregnant state during the second and third trimesters to facilitate the availability of extra calcium required for fetal skeletal growth [25,26].

There were statistically significant associations between low serum 25(OH)D levels and SGA and PTD, with cut-off values 10,85 ng/ml and 10,95 ng/ml, respectively. There were also significant correlations between the serum 25(OH)D levels for each trimester seperately, and SGA and PTD with similar cut off values (Table 7). Calcidiol influences fetal growth by regulating human chorionic gonadotropin expression and secretion in human syncytiotrophoblast and increasing placental steroid secretion [27,28]. Calcidiol also plays a part in fetal glucose usage through its role in glucose/insulin metabolism [29].

It can directly influence skeletal muscle and bone development through calcium homeostasis and transport [30,31]. Therefore, in the case of 25(OH)D deficiency, SGA is an expected result.

Although the etiology of PTD has not exactly been explained yet, infection is a significant cause, and 25(OH)D deficiency is a potential risk factor for vaginal and pelvic infection [32].

Turkey is a country that experiences four true seasons, and the results of this study suggest that season is a strong predictor of serum 25(OH)D concentrations in pregnant women. The mean levels of vitamin D during the summer season were significantly higher than levels measured during the winter season, The 25(OH)D levels in the winter season were statistically significant predictor for PTD and SGA while there was no relationship between 25(OH)D levels and PTD or SGA in the summer. Therefore, vitamin D supplementation during pregnancy is necessary, especially in the winter, to prevent adverse obstetric outcomes.

There were no significant differences between serum 25(OH)D levels according to age, and adolescent years were not a potential risk factor for 25(OH)D deficiency during pregnancy.

Nevertheless, pregnancy in adolescence brings a high risk of adverse obstetric outcomes [33]. There were no significant difference of the 25(OH)D mean serum level between adolescents and adults, and both were far below the adequate levels. Therefore the cause of adverse obstetric outcomes might depend on both young age and low vitamin D levels in adolescent group. Despite being at adolescent ages is a potential risk factor for adverse obstetric outcomes adult women who has lower 25(OH)D levels than 10.9 were also at risk for PTD and SGA (Table 5). Therefore low vitamin D levels at any maternal age is a risk for adverse obstetric outcomes (Table 6).

Serum 25(OH)D levels and poor obstetric outcomes (GDM, SGA, PTD, Preeclampsia) were not independently associated with any of the factors studied, including gravidity, parity, and clothing type. There was a significant correlation between 25(OH)D levels and mean time spent outdoors during the day.

Women who graduated from secondary school had significantly higher 25(OH)D levels (p < 0,05). However, we can not say that there is a correlation between educational level and 25(OH)D levels. There was also no association between BMI and 25(OH)D levels. This might be because all the 25(OH)D values were low.

Although it is thought that 25(OH)D deficiency may be associated with preeclampsia, GDM, and cesarean delivery, we did not

Table 5
Obstetric outcomes according to cut off values of 25(OH) D.

Ages ≤ 20	GDM		PTD		SGA		Preeclampsia		Cesarean	
	no	yes	no	yes	no	yes	no	yes	no	yes
25(OH)D < 10.9 n	98	1	52	47	43	56	96	3	66	33
Actual risk %		1		47.5		56.6		3		33.3
25(OH)D ≥ 10.9 n	192	9	197	4	196	5	194	7	133	68
Actual risk %		4.5		2		2.5		3.5		33.8
P	0,174		0000		0,000		0836		0,943	
Ages ≥ 21										
25(OH)D < 10.9 n	47	–	41	6	40	7	38	9	35	12
Actual risk %		0		12.8		14.9		19.1		25.5
25(OH)D ≥ 10.9 n	238	15	251	2	252	1	212	41	160	93
Actual risk %		5.9		0.8		0.4		16.2		36.8
P	0.140		0.000		0.000		0.670		0.304	

GDM: Gestational Diabetes Mellitus, PTD: Preterm Delivery, SGA: Small for Gestational Age.

Table 6
Obstetric outcomes according to cut off values of 25(OH) D for all maternal ages.

All ages	GDM		PTD		SGA		Preeclampsia		Cesarean	
	no	yes	no	yes	no	yes	no	yes	no	yes
25(OH)D < 10.9 n	145	1	93	53	84	62	134	12	101	45
25(OH)D ≥ 10.9 n	430	24	448	6	447	7	406	48	293	161
P	0.029		0.000		0.000		0.505		0.498	

GDM: Gestational Diabetes Mellitus, PTD: Preterm Delivery, SGA: Small for Gestational Age.

Table 7
Optimal cut off values of 25(OH)D levels predicting PTD and SGA according to gestational ages and seasons.

	PTD			SGA		
	Cut off (ng/ml)	Sensitivity (%)	Specificity (%)	Cut off (ng/ml)	Sensitivity (%)	Specificity (%)
1.Trm	10.9	81.2	95.5	11.03	80.9	96
2.Trm	10.6	88.8	84.2	10.75	89.7	87.5
3.Trm	10.95	81.8	94.4	10.95	82.6	90.5
Spring	NS			NS		
Summer	NS			NS		
Autumn	11.08	84.1	78.6	11.08	86.4	78.9
Winter	9.35	62.5	58.1	9.45	60	61.2

find any association between 25(OH)D levels and adverse obstetric outcomes except preterm delivery and small birth weight. However, there was a significantly increased GDM ratio at the levels of 25(OH)D above 10.9 ng/ml for all pregnant women. However there was no significant difference in groups separately for GDM according to 25(OH)D levels. Therefore this result may be an incidental finding.

There are several reports on vitamin D status across different regions and populations.

Andıran et al. reported 46% of the Turkish mothers had serum 25(OH)D concentrations below 10 ng/ml [34]. In a study from Pakistan, 45% of mothers had serum 25(OH)D levels <10 ng/ml [35]; in another study, this rate was 80% [36]. However, it is reported that only an estimated 7% of American pregnant or lactating women are at risk for vitamin D deficiency (25(OH)D < 15 ng/ml) [37,38]. This may be due to having regular vitamin D-fortified foods other than the supplements prescribed during pregnancy.

Contrary to our results, Xiao et al. found the vitamin D levels in younger pregnant women were lower than they were in the older pregnant women in a Chinese population [39]. Black et al. and Xiao et al. also found a strong relationship between season and serum 25(OH)D levels [39,40]. However in a study from Turkey, lower education and economic levels were found to predict lower vitamin D status of mothers [34]. In a study from Holland, suboptimal maternal vitamin D status and low education level were reported as determinants of SGA [41]. Previous studies suggested that BMI is inversely correlated with serum 25(OH)D levels [42,43]. However, we did not find any association between BMI and 25(OH)D levels in our study, similar to Ganmaa et al. [36]. This might be because of all the 25(OH)D values were low.

A potential limitation of this study was having a homogenous study population for education and economic level and vitamin D status. There were only 12 pregnant women among 600 with adequate vitamin D levels, and a great percentage (86%) of the pregnant women had vitamin D deficiency (<20 ng/ml). This is an interesting result for our country because vitamin D is mostly synthesized in the skin under the influence of sunlight, and Turkey is a country which experiences four seasons and has a sunny environment. Despite these results we did not find increased risk for adverse obstetric outcomes such as GDM, preeclampsia, and increased cesarean ratios, as expected for this low vitamin D status.

Conclusion

Despite the country's sunny environment, there is a high incidence of 25(OH)D deficiency in Turkish pregnant women. Adolescent age and low 25(OH)D levels are significant risk factors for PTD and SGA. Therefore, effective prophylaxis programs for vitamin D deficieny and/or fortifying foods with vitamin D are essential to prevent vitamin D deficiency and its obstetric outcomes in pregnant women, especially in the adolescents and in the winter season.

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Conflict of interest

All authors (Fatma Doğa Öcal, Zehra Aycan, Gülşah Dağdeviren, Nuray Kanbur, Tuncay Küçüközken, Orhan Derman) declare that they have no potential financial and non-financial conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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