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The Correlation Between Vitamin D Levels and Thyroid Functions in Early Pregnancy

Özlem Dülger[1*], Zeynep Oğul[2], Sinem Dinmez[2]

[1]Obstetrics and Gynecology, Karamanoglu Mehmetbey University, Karaman, Turkey
[2]Midwifery, Fenerbahce University, Istanbul, Turkey

ABSTRACT

Vitamin D deficiency (serum vitamin D <10 ng/ml) and thyroid dysfunctions are prevalent issues globally, particularly during pregnancy. Evidence suggests a potential link between thyroid function and vitamin D levels. This study aims to investigate the correlation between serum vitamin D levels and thyroid functions in women during the first trimester of pregnancy.

The study was conducted retrospectively at a University Education and Research Hospital's pregnancy clinic, covering data from August 2023 to March 2024. The sample group consisted of first-trimester pregnant women who attended routine pregnancy check-ups and had complete vitamin D levels and thyroid function tests (n=185). The sociodemographic data form and blood serum level assessment forms were used as data collection tools. The data were analyzed using descriptive statistics and correlation analysis.

The average age of the pregnant women participating in our study was 27.6±4.9 years, and the Body Mass Index (BMI) was 25.4±4.8 (overweight). The mean number of pregnancies was 1.13±0.3, and the gestational week was 8.19±1.8. Of the participants, 35 had subclinical hypothyroidism, 37 had thyroiditis, and 113 had normal thyroid functions. The study identified 36 women with normal/adequate vitamin D levels (≥20 ng/ml), 113 with vitamin D insufficiency (10–20 ng/ml), and 36 with vitamin D deficiency (<10 ng/ml). The correlation analysis revealed no significant relationship between the thyroid function tests and vitamin D levels of the pregnant women. It was determined that vitamin D levels do not affect thyroid gland function in the first trimester.

Keywords: First trimester**,** Vitamin D, Deficiency, Pregnancy, Thyroid hormones

Introduction

Pregnancy enhances the activation and production of steroid hormones, with the breakdown of thyroxine-binding globulin (TBG), resulting in increased levels of TBG, free tetraiodothyronine (T4), and free triiodothyronine (T3)(1). As a result, thyroid dysfunction is among the most prevalent endocrine disorders impacting women of reproductive age. Thyroid disorders not only impact fertility and pregnancy outcomes but may potentially affect the development of the infant nervous system and elevate the occurrence of congenital problems. Pregnancy hyperthyroidism occurs in approximately 0.2% of cases, whereas hypothyroidism is more prevalent at 2.5% (2). It is acknowledged that the assessment of thyroid functions varies by trimester (3). Several hormonal and metabolic changes during each trimester lead to complicated influences on maternal thyroid physiology (4).

Women of reproductive age have an elevated incidence of thyroid disorders, including chronic thyroiditis, thyroid dysfunctions, Hashimoto's hypothyroidism, and Graves' disorder, necessitating an analysis of factors influencing thyroid function tests. Thyroid hormone receptors and vitamin D receptors are identical steroid hormone receptors involved in the production of various genes, and any alterations in these structural genes increase the susceptibility to autoimmune disorders, that involve autoimmune diseases of the thyroid like Hashimoto's and Graves' disease (5).Vitamin D concentrations have been found to be diminished in instances of autoimmune thyroiditis; Vitamin D insufficiency is increasing, and vitamin D intake can reduce thyroid antibody levels and decrease autoantibody levels with treatment (temd.org.tr).

Vitamin D deficiency is widespread globally, about one billion individuals in developing nations are facing this lack of supply(6). Vitamin D insufficiency is more prevalent in Asian nations

***Corresponding Author:** Ozlem Dulger, Karamanoglu Mehmetbey University, School of Medicine. Department of Obstetrics and Gynecology
e-mail: ozlem_dulger@yahoo.com.tr, Mobile phone: +90 532 606 43 80, Fax number: +90 338 226 33 51
ORCID ID: Özlem Dülger: 0000-0003-0400-1513, **Zeynep Oğul:** 0000-0003-1298-330X, **Sinem Dinmez:** 0000-0002-4055-1830
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and Middle Eastern countries than in other regions ; in Turkey, the prevalence is about 49%, which is comparable to that of other Middle Eastern nations (7).The demand for vitamin D rises during pregnancy, with a natural increase in serum vitamin D levels detected in the second and third trimesters. Vitamin D deficiency throughout pregnancy is prevalent among high-risk populations, including vegetarians, individuals with limited sun exposure, and those with darker skin colours. In light of these results, the purpose of this research is to add to the knowledge by examining the association between vitamin D levels and thyroid functions in pregnant women during the first few weeks of pregnancy.

Materials and Methods

This study was conducted retrospectively using data from 185 pregnant women who visited the Karaman Education and Research Hospital obstetrics clinic for regular pregnancy check-up between August 2023 and March 2024. Permissions for the study were obtained from the Fenerbahçe University Non-Interventional Research Ethics Committee on 20.02.2024, decision number 27.2024fbu, and from the Karaman Education and Research Hospital on 20.03.2024, decision number 8. The study population consisted of 347 pregnant women who attended the clinic for first-trimester pregnancy check-ups. The sample group included pregnant women in their first trimester who had both thyroid function tests, measured vitamin D levels, and had no known pre-existing conditions before pregnancy. The exclusion criteria are outlined below (Figure 1).

The data collection tools used in this study included a sociodemographic data form and a blood serum levels form (for thyroid function tests and vitamin D levels). The sociodemographic data form consisted of questions regarding the woman's age, weight, height, Body Mass Index (BMI), gestational week, gravida, parity, abortion, and curettage. The calculation of the gestational week was based on the last menstrual period (LMP). If the woman did not know her LMP, the gestational week was determined by comparing ultrasound reports. The Blood Serum Levels Form included the pregnant women's vitamin D levels and thyroid function tests (TSH, T3, T4, TPO, TG) during the first trimester. Before data collection began, the necessary legal permissions were obtained, and it was ensured that data collection adhered to the Personal Data Protection Law, with a commitment that the data would be used solely for scientific purposes.

Blood samples obtained from pregnant women during their first prenatal visit (first trimester) were evaluated. To determine the relationship between vitamin D and autoimmune thyroid diseases in pregnancy, levels of thyroid antibodies (TPO and TG) and Free T4, Free T3, TSH, and 25(OH)D were analyzed. Blood samples were taken from all pregnant women after at least 8 hours of fasting. The collected blood samples were transferred to the Karaman Education and Research Hospital laboratory. The blood samples were centrifuged to obtain serum and stored at 4°C. Free T3, Free T4, TSH, TPO, and TG levels were measured by Snibe (Maglumi X8, China). The quantitative analysis of vitamin D was conducted using the Snibe (Maglumi X8, China) competitive immunoluminometric assay, following a standard curve reviewed by two qualified reviewers according to standard clinical procedures. According to the Turkish Endocrinology Society Clinical Practice Guidelines, vitamin D levels of 20 ng/ml and above are defined as normal/adequate, levels between 10–20 ng/ml as vitamin D insufficiency, and levels below 10 ng/ml as vitamin D deficiency (temd.org.tr).

Statistical Analysis: The data obtained in the study were analyzed using the SPSS (Statistical Package for Social Sciences) for Windows 22.0 software. Descriptive statistical methods such as numbers, percentages, means, and standard deviations were used to evaluate the data. Differences in the proportions of categorical variables between independent groups were analyzed using Chi-Square tests. One-way ANOVA tests were used to compare quantitative continuous data among diagnostic groups. Pearson correlation analysis was applied to analyze the continuous variables of the study.

Results

The pregnant women in our study were categorized into three groups: subclinical hypothyroidism, thyroiditis, and normal thyroid function. There were 35 women diagnosed with subclinical hypothyroidism, 37 with thyroiditis, and 113 with normal thyroid functions. The pregnant women's average age, weight, and height were 27.6±4.9 years, 66.8± 13.6 kg, and 1.62 meters, respectively. The Body Mass Index (BMI) of the pregnant women was determined to be 25.4±4.8, indicating that they were overweight.

Table 1: Sociodemographic Characteristics of Pregnant Women

Variables		Subclinical Hypothyroidism		Thyroiditis		Normal Thyroid Function		Total		
		n	%	n	%	n	%	n	%	
BMI	Underweight	0	%0.0	3	%8.1	5	%4.4	8	%4.3	
	Normal Weight	16	%45.7	18	%48.6	53	%46.9	87	%47.0	
	Overweight	11	%31.4	10	%27.0	36	%31.9	57	%30.8	
	Obese	8	%22.9	6	%16.2	19	%16.8	33	%17.8	X2=9.381 p=0.496
Number of Pregnancies	1	16	%45.7	19	%51.4	50	%44.2	85	%45.9	
	2	15	%42.9	7	%18.9	28	%24.8	50	%27.0	
	3 or more	4	%11.4	11	%29.7	35	%31.0	50	%26.9	X2=15.076 p=0.129
Number of Births	0	21	%60.0	20	%54.1	60	%53.1	101	%54.6	
	1	12	%34.3	9	%24.3	33	%29.2	54	%29.2	
	2	2	%5.7	7	%18.9	15	%13.3	24	%13.0	
	3	0	%0.0	1	%2.7	5	%4.4	6	%3.2	X2=4.940 p=0.552
Number of Miscarriages	0	28	%80.0	28	%75.7	88	%77.9	144	%77.8	
	1 or more	7	%20.0	9	%24.3	25	%22.2	41	%22.2	X2=4.430 p=0.619
Number of Curettages	0	34	%97.1	36	%97.3	113	%100.0	183	%98.9	
	1	1	%2.9	1	%2.7	0	%0.0	2	%1.1	X2=3.177 p=0.204

Chi-Square Analysis; One-Way ANOVA

Table 2: Results of Thyroid Tests and Vitamin D Levels by Groups

Groups	Subclinical Hypothyroidism		Thyroiditis		Normal Thyroid Function		F	p
	Mean	SD	Mean	SD	Mean	SD		
TSH	2.937	1.497	2.398	2.882	1.300	1.061	15.483	0.000
Free T3	2.997	0.334	2.794	0.349	2.929	0.289	4.125	0.018
Free T4	1.224	0.129	1.167	0.127	1.188	0.122	1.804	0.168
TPO	2.906	4.129	393.617	336.044	9.719	72.426	82.649	0.000
TG	14.710	17.168	273.644	372.677	28.922	98.994	26.967	0.000
Vitamin D Level	14.202	4.824	16.941	7.732	16.196	7.388	1.508	0.224

One-Way ANOVA

The average number of pregnancies among the women was 1.13±0.3, and the average gestational week was 8.19±1.8. There were no significant differences in BMI, the number of pregnancies, births, miscarriages, and curettages among the subgroups of pregnant women categorized by thyroid function (Table 1).

Vitamin D levels of 20 ng/ml and above are defined as normal/adequate, levels between 10–20 ng/ml as vitamin D insufficiency, and levels below 10 ng/ml as vitamin D deficiency. For non-skeletal effects, it is preferable for vitamin D levels to be above 30 ng/ml. In our study, there were 36 pregnant women (19%) with vitamin D

Table 3: The Relationship Between Thyroid Functions and Vitamin D in Pregnant Women

		BMI	Vitamin D	TSH	T3	T4	TPO	TG
Vitamin D	r	-0.166*	1.000					
	p	0.024	0.000					
T4	r	-0.107	-0.027	-0.142	0.272**	1.000		
	p	0.151	0.715	0.059	0.000	0.000		
TPO	r	-0.013	0.066	0.462**	-0.210**	-0.173*	1.000	
	p	0.860	0.382	0.000	0.005	0.021	0.000	
TG	r	0.080	-0.055	0.097	0.062	0.009	0.450**	1.000
	p	0.284	0.458	0.194	0.405	0.907	0.000	0.000

*<0.05; **<0.01; Pearson Correlation Analysis

levels of 20 ng/ml and above (normal/adequate), 116 (62%) with levels between 10–20 ng/ml (vitamin D insufficiency), and 36 (19%) with levels below 10 ng/ml (vitamin D deficiency). Additionally, the results of the Chi-square analysis showed no significant differences in vitamin D levels among the pregnant women categorized by thyroid function (X^2=3.697; p=0.157>0.05).

Upon examining Figure 2, it is evident that 81% of pregnant women have insufficient or deficient vitamin D levels.

In our study, the results of the one-way ANOVA showed that the TSH, T3, TPO, and TG measurements significantly differed among the groups of pregnant women with subclinical hypothyroidism, thyroiditis, and normal thyroid function (p=0.000<0.05). The differences in TSH and T3 measurements are attributed to pregnant women with subclinical hypothyroidism, while the differences in TPO and TG measurements are due to pregnant women with thyroiditis. The pregnant women's T4 and vitamin D levels did not show significant differences among the groups (p>0.05)(Table 2).

In our study, a very weak negative correlation (r=-0.166, p=0.024<0.05) was found between vitamin D and BMI in pregnant women. As BMI increases, vitamin D levels decrease. A weak positive correlation (r=0.272, p=0.000<0.05) was identified between the T4 and T3 thyroid hormones. As the T4 hormone level increases, the T3 hormone level also increases.

Among the pregnant women in our study, a weak positive correlation was found between thyroid autoimmunity tests, specifically between TPO and TG (r=0.45, p=0.000<0.05) and between TPO and TSH (r=0.462, p=0.000<0.05). As TPO antibody levels increase, TG antibody and TSH hormone levels also increase. Additionally, a very weak negative correlation was identified between TPO and T3 (r=-0.21, p=0.005<0.05) and between TPO and T4 (r=- 0.173, p=0.021<0.05). As TPO antibody levels increase, T3 and T4 hormone levels decrease (Table 3).

When examining the relationship between thyroid function tests and vitamin D levels among pregnant women, no significant correlation was found between thyroid function status and serum vitamin D levels.

Discussion

Maternal vitamin D deficiency and insufficiency are frequently observed during pregnancy and

are considered significant global public health issues. A high prevalence of vitamin D deficiency among pregnant women has been observed. These rates vary based on ethnic background and sun exposure (9). In Turkey, the prevalence of vitamin D deficiency (<10 ng/ml) among pregnant women and women of reproductive age ranges from 46% to 80%, attributed to insufficient vitamin D intake, covering, and inadequate sun exposure due to lifestyle factors (10). In our study, a significant proportion (81%) of pregnant women were found to have insufficient and deficient levels of vitamin D (Figure 2). There is increasing evidence of the relationship between insufficient vitamin D levels and adverse pregnancy outcomes, including preeclampsia, small for gestational age (SGA), gestational diabetes mellitus (GDM), and preterm birth (11).

In our study, a very weak negative correlation (r=-0.166, p=0.024<0.05) was found between vitamin D and BMI in pregnant women. As BMI increases, vitamin D levels decrease (Table 3). Various findings in the literature relate to the relationship between vitamin D and BMI. Similar to our findings, Christoph et al. (12) conducted a study with first-trimester pregnant women and

Fig. 1. Flowchart of Sample Selection Criteria

found that individuals with higher BMI were associated with lower serum levels of vitamin D. In contrast, another study concluded that there was no correlation between vitamin D, thyroid functions, and BMI (13).

A weak positive correlation ($r=0.272$, $p=0.000<0.05$) was found between pregnant women's T4 and T3 thyroid hormones. As the T4 hormone level increases, the T3 hormone level also increases (Table 3). Thyroid function tests are frequently conducted during pregnancy. TSH, free T3, free T4, and thyroid antibodies (thyroid peroxidase (TPO) and thyroglobulin (TG)) are the most commonly requested tests to diagnose thyroid disease (14). The physiological changes in thyroid function parameters such as TSH, free T4, and T3 become more complex during pregnancy. In the first 8-10 weeks of pregnancy (first trimester), the mother's serum TSH hormone decreases significantly due to the stimulatory effect of human chorionic gonadotropin (hCG) on the thyroid gland (15). Generally, for every 10,000 IU/L increase in hCG, TSH decreases by 0.1 mU/L. Therefore, serum TSH concentrations in women during pregnancy are lower than pre-pregnancy levels (16). The free T4 level peaks around 10-12 weeks of gestation and then decreases until delivery, while free T3 concentrations increase throughout pregnancy (17). Thus, our study's findings align with the literature.

In our study, a weak positive correlation was found between TPO and TG ($r=0.45$,

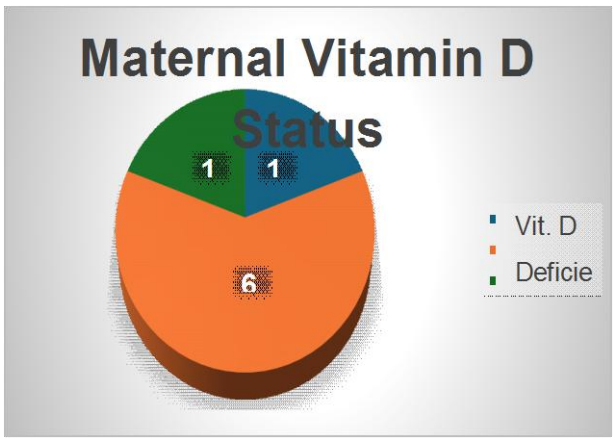

Fig. 2. Vitamin D levels of Pregnant Women

$p=0.000<0.05$) and between TPO and TSH ($r=0.462$, $p=0.000<0.05$) in pregnant women. As TPO antibody levels increase, TG antibody and TSH hormone levels also increase (Table 3). While the measurement of thyroid antibodies (TPO and TG) does not provide definitive information about thyroid function status, the presence of these antibodies (positive results) has significant implications for pregnancy (18). The incidence of subclinical hypothyroidism (high TSH and normal or low-normal T4) affects at least 2% of the female population. These women typically have no clinical symptoms and are often asymptomatic.

Approximately 5% of women with subclinical thyroid dysfunction in the European region remain undiagnosed (19). In 50-60% of cases, even in iodine-sufficient areas, autoimmune thyroid disease (positive TPOAb or thyroglobulin antibodies, TgAb) is present (20).

Thyroid peroxidase antibodies (TPOAb), a marker of thyroid autoimmunity, are the most significant risk factor for thyroid dysfunction during pregnancy. Women who are TPOAb positive have higher TSH concentrations, lower free T4 concentrations, and a higher risk of thyroid dysfunction during pregnancy compared to TPOAb-negative women. TPOAb positivity is independently associated with an increased risk of miscarriage and preterm birth (21). It is well known that subclinical hypothyroidism during pregnancy is associated with adverse fetal and obstetric outcomes, including miscarriages, pregnancy-related anemia, preeclampsia, placental abruption, postpartum hemorrhage, preterm birth, low birth weight, and increased neonatal respiratory distress (22).

In this study, a significant positive correlation was found between TPO levels and TG and TSH levels ($r=0.462$). This finding is consistent with

previous studies that have identified a positive correlation between high TPO antibody levels and TSH (23). The increase in TG and TSH levels with elevated TPO levels in our pregnant participants aligns with the literature, indicating a higher risk of adverse fetal and maternal outcomes during pregnancy.

In our study, a very weak negative correlation was found between TPO and T3 ($r=-0.21$, $p=0.021<0.05$) and between TPO and T4 ($r=-0.173$, $p=0.021<0.05$). As TPO antibody levels increase, T3 and T4 hormone levels decrease. The significant correlations between thyroid hormones T3 and T4 with anti-TPO highlight the role of thyroid antibodies in thyroid diseases (23). For example, TPO antibodies are positive in approximately 10% of women during early pregnancy (24), indicating a relationship between thyroid autoimmunity and adverse obstetric outcomes such as infertility, miscarriage, and preterm birth (21). A recent meta-analysis demonstrated that high TPO antibody levels in pregnant women are significantly associated with an increased risk of preterm birth and miscarriage (25).

Our study's results underscore the importance of investigating thyroid auto-antibodies in relation to elevated thyroid hormone levels. Recent meta-analysis evidence has shown a consistent relationship between vitamin D deficiency during pregnancy and an increased risk of low birth weight. Preventing maternal vitamin D deficiency could be a crucial public health strategy to reduce the risk of low birth weight (26). The literature reveals that the vitamin D receptor (VDR) is expressed in immune cells, regulating their proliferation and leading to thyroid damage, indicating a relationship between vitamin D and thyroid disease (27).

Our study found no significant correlation between thyroid function status and serum vitamin D levels in pregnant women (Table 3). Previous studies in the literature also support these findings. Musa et al. (13) demonstrated no clear relationship between thyroid function 25(OH) and vitamin D in pregnant women. Zhao et al. (28) showed no significant relationship between serum vitamin D levels and thyroid parameters. Nizar et al. (29) found no significant correlation between vitamin D levels and thyroid function in pregnant women in Oman and Jordan. Still, they noted a relationship between higher vitamin D concentrations (>30 ng/ml) and lower TSH levels. Similarly, studies in Northern China also indicate no clear relationship between vitamin D levels and thyroid parameters (30).

In conclusion, despite the high prevalence of vitamin D deficiency among pregnant women in our study, no significant relationship was found between vitamin D deficiency and thyroid function in the first trimester. Further research with larger sample sizes is recommended to clarify the role of the relationship between vitamin D and thyroid functions.

Ethical Approval: Permissions for the study were obtained from the Fenerbahçe University Non-Interventional Research Ethics Committee on 20.02.2024, decision number 27.2024fbu, and from the Karaman Education and Research Hospital on 20.03.2024, decision number 8.

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