

The effect of ultraviolet index measurements on levels of vitamin D and inflammatory markers in pregnant women

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Background: Hypovitaminosis D is a risk factor for infertility and several adverse pregnancy outcomes. These negative effects of vitamin D deficiency may be due to inflammatory processes. T lymphocytes play a key role in the formation of immune response by producing some cytokines. Vitamin D is known to have significant effects on T lymphocytes and T regulator cells. The most significant determinant of vitamin D in the human body is sun exposure. The most important indicator determining the sun exposure in a region is the ultraviolet index (UVi). We tried to determine the effect of UV changes on vitamin D values during pregnancy and possible effects on inflammatory markers in a single region. **Methods:** The vitamin D serum values and blood count values of pregnant patients at the time of first admission were recorded in the months of April to September (AS) and October to March (OM). The daily UVi values of the Izmir region were obtained. These daily values were averaged according to the two groups. As inflammatory markers, the Neutrophil-Lymphocyte ratio (NLR), Platelet-Lymphocyte ratio (PLR), Monocyte-Lymphocyte ratio (MLR), mean platelet volume (MPV) and erythrocyte volume distribution (RDW) values were calculated from the blood count. **Results:** The UVi mean value was found to be 8 for AS and 3 for OM. There was a significant difference in the mean vitamin D values for the AS (42 patients) and OM (40 patients) periods. A predisposition to inflammatory processes was determined for the OM period in terms of the inflammation markers examined between the two groups. Our study showed lower levels of RDW and MPV and similar values for NLR, PLR and MLR according to the UVi values. **Discussion:** Vitamin D plays role in many systems as a hormone, a vitamin or an immunomodulator after activation in the skin tissue. Besides its known benefits to the musculoskeletal system, adequate serum vitamin D values reduce the risk of certain types of cancer, mental disorders, infectious diseases, cardiovascular diseases, type 2 diabetes mellitus, autoimmune disorders and adverse pregnancy outcomes. Additionally, lower UVi may be associated with lower vitamin D values in pregnant women and increased inflammatory markers in complete blood count. As a result, in order to avoid adverse pregnancy outcomes, the UVi values of regions may be useful for determining replacement of vitamin D during or before pregnancy.

Keywords

Vitamin D; Ultraviolet index; Inflammatory processes; Pregnancy

1. Introduction

Vitamin D deficiency is common in many societies, and there is a large gap between the recommended daily vitamin D needs and the dietary intake of vitamin D in the general population. Although vitamin D is primarily important for musculoskeletal health, there are substantial data suggesting that it may also be important for fertility, pregnancy outcomes and breastfeeding. Observational studies have shown that vitamin D deficiency is a risk factor for reduced fertility and various adverse pregnancy outcomes, and it is associated with low vitamin D content in breastmilk. Additionally, there are studies emphasizing the importance of vitamin D-rich nutrition and vitamin D supplementation in preventing gestational diabetes, which is an important problem in pregnancy [1–3].

Vitamin D is a secosterol produced in the skin from sun exposure or obtained from foods that naturally contain vitamin D, including cod liver oil and oily fish, foods enriched with vitamin D and supplements. During exposure to sunlight, 7-dehydrocholesterol (7DHC) in the skin is converted to pre-vitamin D₃. Approximately 60% of 7DHC is found in the epidermis, and more than 90% of the pre-vitamin D₃ that is produced is in the epidermis. Once formed, vitamin D₃ is ejected out of the keratinocyte membrane and absorbed into the dermal capillary bed by the vitamin D binding protein (D-BP). Vitamin D that is ingested is absorbed into chylomicrons, which are released into the lymphatic system, then enters the venous blood, where it binds to D-BP and transported to the liver. Vitamin D₂ and vitamin D₃ are 25-hydroxylated by liver to create the major circulating vitamin D metabolite, 25-OH-D, which is used to identify a patient's vitamin D status. This metabolite undergoes further hydroxylation by 25-OH-D-1 α -hydroxylase in the kidneys to form the secosteroid hormone 1 α -25-dihydroxy-vitamin D (1,25-OH-2D). 1,25-OH-2D performs many of its functions by regulating gene transcription through a nuclear vitamin D receptor (VDR). It binds to the nuclear VDR, which binds the retinoic acid X receptor to form a heterodimeric complex that binds to specific nucleotide sequences in the DNA known as vitamin D response elements. Once connected, various tran-

scription factors bind to this complex, resulting in up or down regulation of the activity of the gene [2–5].

Meta-analyses of randomized controlled trials (RCTs) have documented that physiological vitamin D supplementation during pregnancy is safe and maintains skeletal health by improving vitamin D and calcium status. Moreover, vitamin D supplementation in pregnant women is often necessary to achieve an adequate vitamin D status as recommended in dietary vitamin D guidelines. Vitamin D levels during pregnancy are not only dependent on oral supplements and diet, but variables such as maternal sunlight exposure, degree of skin pigmentation, latitude, lifestyle and body mass index (BMI) may also affect vitamin D levels. In addition, diseases that can lead to parathyroid hormone disorders can also affect vitamin D levels. It is common knowledge that, if a woman has vitamin D deficiency during pregnancy, her fetus will also have it [2, 3, 6].

During the year, the seasons that play the main role in a person's exposure to sunlight. It is the ultraviolet index (UVi) that plays the main role in the seasons. UVi depends on many variables such as how the sun shines on the earth, time zone in calendar and time, altitude of the geographic location, degree of cloud coverage and proximity to coasts. People's behavior may also be determinant in being affected by UVi. These factors include how people dress, time spent outside the home and use of sunscreen [2, 3, 7].

There are also reliable biological pathways that support utilization of UV during pregnancy, regardless of the vitamin D pathway. For example, clinical studies have shown that sunlight, especially ultraviolet A (UVA), has direct effects on vascular health and lowers blood pressure through the release of nitric oxide (NO) from the skin. Exposure to UVA for 20 minutes causes a reduction in the mean systolic arterial pressure of 3.5 mmHg and diastolic blood pressure of 4.9 mmHg in healthy adults [8–10]. In animal samples, the beneficial effects of UVA exposure on the immune system and metabolic systems have been confirmed. One study found that, when exposed to UV rays, mice fed high-fat diets weighed 40% lower and had less fasting glucose, insulin and glucose intolerance [9, 10]. Researchers attributed this to the increased release of NO from the skin due to UV rays. NO has important roles in mitochondrial biogenesis in brown adipose tissue and also in modulation of insulin and glucose transport within the body.

Many recent studies have suggested that inflammatory processes may be the basis of many diseases and also poor pregnancy outcomes [11–14]. The Neutrophil-Lymphocyte ratio (NLR) is one of the most popular inflammatory markers because it can be easily calculated from the complete blood count, and higher levels may be associated with poor obstetric results such as preeclampsia, gestational diabetes or HELLP syndrome [15, 16]. Furthermore, hypovitaminosis D is a risk factor for infertility and several adverse pregnancy outcomes [11]. These negative effects of vitamin D deficiency may be due to inflammatory processes [13, 17]. Vitamin D is known

to have significant effects on T lymphocytes and T regulator cells. It regulates the differentiation and activity of CD4+ T cells, resulting in a more balanced Th1/Th2 response that limits development of self-reactive T cells preventing inflammation and autoimmunity. In animal models, deep analysis of immune responses has been attempted. Mice deficient in vitamin D showed a decreased expression of angiogenin 4, an antibacterial protein that acts by minimizing the invasion of tissues by enteric bacteria. This leads to higher levels of bacteria in the colon epithelium. This deregulation is related with tissue inflammation in inflammatory bowel diseases and, accordingly, vitamin D could protect from this inflammation by inducing the antibacterial protein angiogenin 4. Additionally, vitamin D helps to promote innate immune responses by preventing tissue damage associated with excessive inflammation [6, 13, 18, 19].

Our aim in this study is to determine the effect of UVi changes on vitamin D values measured at the beginning of pregnancy and their possible effect on inflammatory markers in the blood in the region of Izmir in Turkey.

2. Materials and methods

We designed a progressive cross-sectional study and planned two time zones according to the sun exposure of the Izmir city located on the Aegean coast. The vitamin D serum values (routinely checked by the Provincial Hıfızlıha Laboratory at the beginning of pregnancy) and blood count values of pregnant patients at the time of first application (it was confirmed that they were not receiving vitamin D supplementation) were recorded in the months of April to September (AS) and October to March (OM) in the Izmir region (the last menstrual dates were taken as a basis for the determined time periods). The demographic data of all patients were recorded (Table 1). Informed consent was obtained from each patient who participated in the study. The daily UVi values of the Izmir region were obtained from the General Directorate of Meteorology. These daily values were averaged according to the two groups. As inflammatory markers, the Neutrophil-Lymphocyte ratio (NLR), Platelet-Lymphocyte ratio (PLR), Monocyte-Lymphocyte ratio (MLR), mean platelet volume (MPV) and erythrocyte volume distribution (RDW) values were calculated from the blood count.

The SPSS 25 (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp., Armonk, NY, USA) statistical package program was used to analyze the data. The variables are expressed using mean standard deviation, percentage and frequency values. The variables were evaluated after checking the preconditions for normality and homogeneity of variances (Shapiro Wilk and Levene's Tests). While analyzing the data, *t*-test for 2 independent groups (Student's *t*-test) was used for comparison of two groups, and Mann Whitney-U test was used if the prerequisites were not met. For the significance level of the tests, $p < 0.05$ and $p < 0.01$ values were accepted. According to the methods of comparing the means

Table 1. Baseline demographic and clinical characteristics of our study population.

	April to September (AS) period (n = 42)	October to March (OM) period (n = 40)	p value
Age (Mean value)	29.357 (20–38)	28.600 (24–33)	0.447
Number of pregnancies (Median value)	1 (1–3)	1 (1–2)	0.999
Body mass index (BMI)	22.771	23.6725	0.762
Previous history of smoking	6*	8*	
Additional disease	7 [^]	4 [^]	

* 6–12 pieces per day.

[^] hypothyroidism, hyperthyroidism, arrhythmia, migraine.

Table 2. Comparison of the two pregnancy groups according to vitamin D and inflammation markers.

	April to September (AS) period	October to March (OM) period	p value
	(UVi mean value: 8)	(UVi mean value: 3)	
	n = 42	n = 40	
Vitamin D serum value	18.56 ± 6.91	15.33 ± 6.54	0.030
NLR	3.53 ± 1.68	4.14 ± 1.87	0.120
RDW	13.92 ± 2.07	15.58 ± 2.55	0.002
PLR	114.05 ± 40.01	124.92 ± 32.64	0.181
MLR	0.29 ± 0.14	0.26 ± 0.11	0.406
MPV	9.92 ± 2.11	7.51 ± 1.67	0.001

NLR, Neutrophil-Lymphocyte ratio; RDW, Erythrocyte volume distribution; PLR, Platelet-Lymphocyte ratio; MLR, Monocyte-Lymphocyte ratio; MPV, Mean platelet volume.

of two independent groups, the required sample size was determined as at least 80 subjects in total, with at least 40 subjects in each group. In this case, it was determined that the power of the test was obtained as approximately 80.16%.

3. Results

The mean of the daily UVi values of the Izmir region according to the two groups was calculated. The UVi mean value was found to be 8 for AS and 3 for OM. There was a significant difference in the mean vitamin D values for the AS (42 patients) and OM (40 patients) periods (18.56 ± 6.91; 15.33 ± 6.54; *p* value: 0.030). A predisposition to inflammatory processes was determined for the OM period in terms of the inflammation markers examined between the two groups (NLR: 3.53 ± 1.68; 4.14 ± 1.87; *p* value: 0.120, RDW: 13.92 ± 2.07; 15.58 ± 2.55, *p* value: 0.002, PLR: 114.05 ± 40.01; 124.92 ± 32.64; *p* value: 0.181, MLR: 0.29 ± 0.14; 0.26 ± 0.11; *p* value: 0.406, MPV: 9.92 ± 2.11; 7.51 ± 1.67; *p* value: 0.001) (Table 2).

4. Discussion

Studies showing the negative effects of inflammation on pregnancy have already been conducted. Disruptions in the cytokine balance may cause various problems during pregnancy such as spontaneous abortion, preterm birth, preeclampsia and intrauterine growth restriction. T lymphocytes play a key role in the formation of immune response by producing some cytokines. Vitamin D is known to have significant effects on T lymphocytes and T regulator cells [13, 17].

In our study, we evaluated the effect of UVi on the values of vitamin D and inflammatory markers in the complete blood count in pregnant women at the beginning of pregnancy. First of all, the vitamin D levels were correlated with the UVi values. Secondly, some inflammatory markers such as RDW and MPV were also correlated with the UVi and vitamin D levels.

It is common knowledge that sun exposure has an important role in vitamin D production. It depends on very much on the lifestyle of people, and its measurement is hard and subjective. Nevertheless, measurement of UVi is a routine process in meteorology institutions, and the acquired data are measurable, objective and predictable. Vitamin D deficiency is very common in pregnancy, and vitamin D supplementation is recommended by guidelines [20, 21]. The results of the patients in our study showed the values at the beginning of pregnancy before the start of vitamin D replacement. At this point, the UVi values of regions may be useful for determining replacement of vitamin D during or before pregnancy.

Vitamin D plays role in many systems as a hormone, a vitamin or an immunomodulator after activation in the skin tissue. Besides its known benefits to the musculoskeletal system, some observational studies suggest that serum 25-OH-D levels higher than 28 to 32 ng/dL reduce the risk of certain types of cancer, mental disorders, infectious diseases, cardiovascular diseases, type 2 diabetes mellitus, autoimmune disorders and adverse pregnancy outcomes [2, 4, 22–26]. Therefore, UVi values or associated vitamin D levels may have an effect on the inflammatory indices in complete blood count.

In our study, we also evaluated some inflammatory markers based on the UVi values. There are studies about the utility of some complete blood count inflammatory indices such as NLR and RDW [27, 28]. Our study showed lower levels of RDW and MPV and similar values for NLR, PLR and MLR according to the UVi values. In addition, other factors that can cause inflammation in the body such as various infections, autoimmune diseases, cancer, and even stress should be kept in mind.

The strengths of the study were a different and objective look at sun exposure and a prospective structure. Most other studies in the literature have examined vitamin D values at the end of pregnancy, at birth and in the postpartum period. Our study emphasized vitamin D values in the first trimester of pregnancy and also in patients who were not receiving any supplementation. However, the limitations of the study can be considered as being conducted in a single region, the number of patients not including a large population and the difficulty of standardization of human behaviors regarding daily sun exposure.

In conclusion, lower UVi may be associated with lower vitamin D values in pregnant women and increased inflammatory markers in complete blood count. An increase in inflammatory processes may also trigger adverse pregnancy outcomes. As a result, in order to avoid adverse pregnancy outcomes, the UVi values of regions may be useful for determining replacement of vitamin D during or before pregnancy. Further investigation with larger series may contribute to the literature.

Author contributions

All the work was done by SB. The author read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Baskent University Institutional Review Board and Ethics Committee. Approval number: KA20-352. Informed consent was obtained from all patients.

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Conflict of interest

The author declares no conflict of interest.

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