

Maternal Vitamin D Deficiency and Insufficiency - Prevalence and Effective Factors

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Abstract

Objective: We aimed to reveal the prevalences of vitamin D deficiency and severe deficiency in pregnant women who applied for routine examination in our study.

Methods: Between January 2015 and January 2018, 635 healthy pregnant women who applied to our clinic for the first trimester routine pregnancy examination were included in the study. The age, place of residence, season in which the material was taken, 25 - OH vitamin D levels were reached. Vitamin D level under 10 ng/ml was accepted as severe deficiency, 10 - 30 ng/ml insufficiency and 30 - 100 ng/ml normal.

Results: Vitamin D deficiency was detected in 58.1 % and severe deficiency was found in 36.9 %, while vitamin D levels were normal in only 5 % of the patients. Vitamin D levels were significantly lower in the 35 years old group (95.8 % - 90.9 %) ($p = 0.03$). There was no statistical correlation between the place of residence and vitamin D (94.6 % - 95.7 %) ($p = 0.529$). We found abnormal vitamin D results in winter and autumn season (98 % - 99.4 % versus 89.4 % - 93.3 %) ($p = 0,000$).

Conclusion: We observed that vitamin D deficiency and severe deficiency, which have serious maternal and neonatal effects, are quite common in our society (95 %). We are in the belief that how much decrease in negative maternal and perinatal outcomes have been observed with the 'Vitamin D Supplement Programme in Pregnancy' hold by T.C. Ministry of Health, via using 1200 IU vitamin D perday from 12 week of pregnancy until postpartum 6th month, by cross-sectional studies and if the first 6 year results are in positive direction, deficiency must be replaced according to age, season, and the geographic region with more effective methods.

Key words: Vitamin D, pregnancy, prevalence

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Introduction

Vitamin D is one of the fat-soluble vitamin and is first named in 1920. It is nowadays known as a steroid hormone, not a classical vitamin because it can be synthesized endogenously in the appropriate biological medium, Although it is known that the most important effect is on calcium-phosphorus metabolism and bone mineralization, it is also known to be associated with cancer (such as breast, ovarian, endometrium, gastrointestinal tumors, lymphoma), cardiovascular diseases, metabolic syndrome (hypertension and diabetes), infectious diseases, autoimmune diseases (multiple sclerosis, arthritis), musculoskeletal diseases (osteoarthritis), which are associated with many health problems

(Barrett and McElduff, 2010; Iyidir and Altınova 2012).

Vitamin D is known to be synthesized in the skin by the effects of ultraviolet (UV) rays in 90 - 95 %. Dietary intake of fatty fish species, fish oil and vitamin D-containing preparations have little effect on vitamin D levels in the body (Fidan et al., 2014). Ergocalciferol (vitamin D2) is derived from plant-derived ergosterol, and 7 - dehydrocholesterol (provitamin D3) is cholecalciferol (vitamin D3). Due to its biomolecular structure, the biological activity of vitamin D2 is 3 to 10 times lower than that of vitamin D3. Vitamin D, formed by epidermis with UV effect, binds to vitamin D binding peptide (DBP) and transported to the liver. In the liver by 25 alpha hydroxylation is converted to 25 - OH vitamin D (calcidiol). Although 25 - OH vitamin D is not biologically active, it is very important to show the level of vitamin D in the body thanks to its long half - life of 2 - 3 weeks. The 25 - OH vitamin D is converted to 1,25 - OH vitamin D (calcitriol), a biologically active form, by passing through the circulation and undergoing 1 alpha hydroxylation in the kidney under parathormone (PTH) control. 1,25 - OH vitamin D has a half - life of 4 - 6 hours and can not be used for measurement. Parathormone, hypocalcemia/phosphatemia, increases active metabolite conversion (Bikle, 2007; Meer et al., 2011; Mallah et al., 2011).

In order for fetal bone mineralization to take place in a healthy way during pregnancy, comprehensive adaptations to vitamin D and hence calcium metabolism occur. Approximately 25 - 30 grams of calcium passes through the fetus during pregnancy. Mother does that calcium balance which in favor of fetus by increasing calcium absorption from the mouth (the most important effect), by increasing the kidney calcium uptake and by increasing calcium mobilization from the bone. In pregnancy placenta, amnion, umbilical cord, decidua, breast and fetal parathyroid secrete PTH-related peptide (PTHrP) and the amount increases as pregnancy progress. Renal calcitol synthase increases with estrogen, prolactin, human chorionic somatotropin in addition to PTHrP (Kovacs and Kronenberg, 1997; Kent et al., 1991; Kovacs and Kronenberg, 2006).

Maternal vitamin D has been shown to be effective in fetal bone development as well as in dental, neuronal and fetal growth. In addition, normal vitamin D levels have been shown to reduce the incidence of diabetes (Pludowski et al., 2013).

We have seen in recent years that vitamin D deficiency has been studied in more detail in terms of causing severe maternal and neonatal problems, and in many health policies, strategies to prevent deficiency of maternal vitamin D (Kiely and Hemmingway, 2017).

We aimed to emphasize the importance of determining the prevalence of maternal vitamin D deficiency and its treatment

Methods

Ordu Provincial Health Directorate and Ordu University Medical Faculty Training and Research Hospital Clinical Practice Ethics Committee approvals were obtained (Date:26/04/2018, Number: 2018-87). Between January 2015 and January 2018, 635 healthy pregnant women who applied to the obstetrics clinics for the first trimester routine pregnancy examination were included in the study. Those who have chronic disease and / or metabolic disease, who use drugs effective on bone metabolism, are excluded from the study. Patients' age, place of residence, 25 - OH vitamin D levels obtained using Architect System, and the season in which the material was received were obtained from our hospital registry system.

25 - OH vitamin D level was < 10 ng/ml, severe deficiency, 10 - 30 ng/ml insufficiency and 30 - 100 ng/ml were normal. Patients were divided according to age groups as under and over 35; according to residence site as rural and urban; and to the season in which materials obtained as spring, summer, autumn and winter.

Statistical analysis of the data was performed using the SPSS 20 program. Student's t-test was used to compare numerical data, chi-square and Fisher Exact test were used to compare continuous data. A P value < 0.05 was considered statistically significant.

Results

The mean age of pregnancies was 28.9 ± 5.34 (18 - 40). 66.8 % of the patients were urban, and 33.2 % were living in the rural area.

25 - OH vitamin D insufficiency and severe deficiency were found to be 58.1 % (369/635) and 36.9 % (234/635) respectively, while only 5 % (32/635) of the patients was normal for vit D levels. Vitamin D insufficiency, severe deficiency and normal prevalences is shown in Table 1.

Table 1: Vitamin D insufficiency, severe deficiency and normal prevalences.

Insufficiency	369/635	58.1 %
Severe Deficiency	234/635	36.9 %
Normal	32/635	5 %

Patients were divided into two groups as < 35 years and > 35 years according to age groups. The abnormal 25 - OH vitamin D results were found to be 95.8 % in the < 35 age group and > 90.9 % in the 35 years' age group. 25 - OH vitamin D level was significantly lower in the < 35 years' age group (p = 0.03). Abnormal vitamin D ratio -age related is shown in Table 2.

Table 2: Abnormal vitamin D ratio - age related

Age group	Abnormal patient number	Abnormal patient ratio
<35	503	95.8 %
>35	100	90.9 %

The rate of abnormal 25 - OH vitamin D values in urban and rural population was found to be close to each other (94.6 % - 95.7 %). There was no statistical correlation between the place of life and 25 - OH vitamin D values (p = 0.33). Abnormal vitamin D ratio - residence related is shown in Table 3.

Table 3: Abnormal vitamin D ratio - residence related

Place of residence	Abnormal patient number	Abnormal patient ratio
Urban	401	94.6 %
Rural	202	95.7 %

The abnormal 25 - OH vitamin D results were ranked according to the seasons as follows; Summer 89.4 % - Spring 93.3 % - Winter 98 % - Autumn 99.4 %. We found that abnormal 25 - OH vitamin D results were more common in winter and autumn (p = 0,000). Abnormal vitamin D ratio - season related is shown in Table 4.

Table 4: Abnormal vitamin D ratio - season related

Season	Abnormal patient number	Abnormal patient ratio
Summer	147	89.4 %
Spring	154	93.3 %
Winter	144	98 %
Autumn	158	99.4 %

Discussion

Maternal vitamin D deficiency; composes the risk of vitamin D deficiency in neonates and also risk for infantile rickets. It is also emphasized that pregnancy is a critical period and fetal effects continue all the life time when the effects of vitamin D on fetal bone and neuronal development is taken into account. Complications such as low birth weight, skeletal problems, neonatal hypocalcemia, immunodeficiency, and type 1 diabetes in the newborn can occur in the newborn while poor results such as maternal sub/infertility, preclampsia, gestational diabetes and increased cesarean rate occur due to lack of vitamin D in the mother.

Vitamin D measurement is biochemically challenging. Different results can be obtained with different methods of analysis, with more than 10 %. Immunoassay (radio, manual, automated) and LC-MS / MS (liquid chromatography-tandem mass spectrometry) are the most widely used methods. It is possible to perform healthier prevalence studies by standardizing the methods used worldwide (Ferrari et al., 2017).

We have taken the thresholds for our study according to a report published by the Ministry of Health in 2011. According to this report, 25 - OH D levels of 30 ng / ml are considered as threshold values in adults, which are not considered to cause parathyroid hormone elevation. Values between 10 and 30 ng / ml are considered to be inadequate and values below 10 ng / ml are considered to be severe.

The average maternal vitamin D concentration ranged from 5.2 to 52 ng / mL (13 to 130 nmol / L) according to a review, which included studies from 1959 to 2014. Globally, vitamin D deficiency is present in 54% of cases (threshold value of 20 ng / mL) and severe vitamin D deficiency is in 18 % (threshold value of 10 ng / mL) (Rajneeta et al., 2016).

In the study of USA, Australia, Middle East and South Asia, where the threshold values were 30 ng / ml for failure and 20 ng / ml for severe deficiency, the prevalence of vitamin D severe deficiency was 26-98%, while the prevalence of insufficiency was 66-100% (Daphna, 2011). These data show how much the thresholds affect the prevalence.

The results of a meta-analysis of 121 studies conducted between 1962 and 2009 were published by the World Health Organization in six geographical regions (Asia, Europe, Africa, Latin America, North America and Australia). According to the report, the prevalence of vitamin D deficiency

in the world (at a cut-off value of 30 ng / mL) ranges from 2 to 97 %. Regionally, it is found that the severe deficiency is a more important problem in Asia (18 - 48 %) and the Middle East (9 - 80 %) (Mithal et al., 2009).

As many studies exist in Turkey related to vit D levels containing children, adolescent, postmenopausal patients, we found no studies demonstrating the prevalence D deficiency.

In all studies, it is possible to reach the conclusion that vitamin D deficiency is more common in some regions but it is a worldwide health problem and affects the pregnant / newborn population more frequently (Mithal et al., 2009; Daphna, 2011; Rajneeta et al., 2016).

In our study, vitamin D insufficiency was found in 58.1 % and severe deficiency was found in 36.9 %. Normal vitamin D levels were detected in only 5 % of the patients. These data show that our threshold value and the proportion of studies conducted in our region are close to each other, and maternal vitamin D deficiency is a very important public health problem.

Geographical factors are very effective in vitamin D metabolism. Many factors affect the efficiency of the sun's rays, such as cloud density, ozone layer density, air pollution level, altitude, time / duration of sun exposure, and social clothing style. In the North American study, it has been shown that 5 to 15 minutes of sunshine every other day, face and arms exposed to the sun are important to meet the need for vitamin D (Hollick, 1996). On the one hand, modern business life, urbanization and industrialization are obstacles to the duration and quality of exposure to the sun. On the other hand, the conservative society that condemns women to their homes and the low socioeconomic level also affect the production of vitamin D in a poor way (Cidem et al., 2013).

In our study, the incidence of abnormal vitamin D in the urban and rural population was found to be close to each other (94.6 % - 95.7 %). There was no statistically significant correlation between the place of life and vitamin D levels ($p = 0.529$). So that points out the importance of other contributor factors like personal factors.

Seasonal differences with geographical factors are also important. In the north and south of 33 degrees' latitude, it is shown that there is no vitamin D synthesis due to the oblique angle of incidence of sun rays in winter. The closer to the equator region, the seasonal difference disappear (Wacker and Hollick, 2013). As in many studies, a recently

published Chinese study has also shown that vitamin D deficiency is more frequent in winter and autumn (Yuan-Hua et al., 2018). In our study, we also tried to reveal the correlation between vitamin D and seasons. The incidence of vitamin D deficiency was as follows in the seasons; summer 89.4 % - spring 93.3 % - winter 98 % - autumn 99.4 %. We have also found that vitamin D deficiency is seen higher in winter and autumn, as in other studies. ($p = 0, 000$)

Depending on personal factors such as dark skin pigmentation, advanced age (> 70), malabsorption (such as cystic fibrosis, Crohn's disease, gluten enteropathy), liver / kidney disease and topical sun cream (especially > 30 factors), vitamin D levels differ (Dror and Allen, 2010). We investigated the effect of age on vitamin D levels in our study. Vitamin D deficiency was found to be 95.8 % in the < 35 age group and $> 90.9\%$ in the 35 years' age group. Thus, in the < 35 years' age group, we found significantly more vitamin D deficiency ($p = 0.03$).

The review published in 2014 does not fully support routine vitamin D supplementation in pregnancy. It is argued that routine vitamin D monitoring in pregnancy is more accurate in providing support to patients with low levels (Weinert and Silveiro, 2015). In studies dealing with dietary regulation other than vitamin D support, it has been shown to be useful to question dietary habits and to take note of body mass index during early prenatal referral (Milman et al., 2016).

In addition, many organizations recommend routine vitamin D supplements without regard to vitamin D levels. The American College of Obstetricians and Gynecologists (ACOG), the Endocrine Society, and the Institute of Medicine (IOM) recommend 600 IU / day vitamin D for pregnancy (Institute of Medicine, 2011; Holick et al., 2011; ACOG Committee on Obstetric Practice, 2011). In addition, the Nordic Council of Ministers (NORDEN) and the Scientific Advisory Committee on Nutrition (SACN) offer lower dose (400 IU / day) support (Nordic Council of Ministers, 2012; Scientific Advisory Committee on Nutrition, 2016). T. C. On May 2011, the Ministry of Health announced 1200 IU / day vitamin D from the 12th week of pregnancy to the 6th month of postpartum in the 'Gebelere D Vitamine Support Program' report (Republic of Turkey Ministry of Health, 2011). In addition, IOM has been reported to be acceptable for vitamin D, with nontoxic dose of 4000 IU / day (Institute of Medicine, 2011). According to a newly published metaanalysis that examines the preterm

birth risk and newborn outcomes of vitamin supplementation, vitamin D levels < 30 ng /mL have an 11 % increase in the risk of preterm labor. Vitamin D supplementation can reduce the risk of preterm labor and associated perinatal mortality (Amegah et al., 2017).

Because of the different measurement techniques used to measure vitamin D levels, it is difficult to define the threshold value for optimal bone health. For this reason, there is a need for work done with standard reference methods adapted to the whole world that can accurately and reliably measure 25 - OH D levels. Different definitions of deficiency and insufficiency in the literature also makes it difficult to compare the vitamin D deficiency and insufficiency (Ruddersa and Camargo, 2015).

Conclusion

In our study, we observed that vit D deficiency which having maternal effects such as preclampsia, preterm labor, abortus, early osteoporosis and neonatal effects like rickets, tetany, hypocalcemic convulsions, congenital cataracts, and severe shortage, is in a high percentage in our society (95 %). Considering that this high prevalence is related to limited sunlight exposure and dietary factors, we suggest that dietary supplementation and vitamin D supplementation should be appropriate. In addition, the importance of sunbathing and patient education about dietary content can also contribute to treatment.

We concluded that in which ratio vit D treatment decreases perinatal and maternal adverse outcomes is to be evaluated with cross-sectional studies and if the results of that 6 years are positive, it would be improved by more effective methods by taking into consideration the age group, season and geographical region.

Ethics Committee Approval: Ethics committee approval was received for this study from Clinical Research Ethics Committee of Ordu University Medical Faculty.

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