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Original Research

Vitamin D Deficiency in a Cohort of Neapolitan Pregnant Women: Do We Really Live in the City of the Sun?

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Abstract

Background: Insufficient serum 25-hydroxyvitamin D [25(OH)D] levels are a global public health issue, and pregnant women are a significant at-risk group. We aimed to assess maternal serum 25(OH)D concentrations in a cohort of Neapolitan pregnant women and the association with dietary habits, to define which patients are at increased risk of hypovitaminosis and how we can identify them. **Methods**: This was a prospective observational study. We included 103 pregnant women attending a routine third trimester obstetric examination. Information on obstetrical history and socio-demographic characteristics were obtained through interviews and medical records. Vitamin D intake was assessed using a food frequency questionnaire. Serum 25(OH)D concentration was measured by DiaSorin Liaison and the cut-off value for deficiency was set at 20 ng/mL. **Results**: Among the 103 pregnant women recruited, 71 (68.9%) were Vitamin D deficient (mean value 12.6 $\pm$ 0.5 ng/mL). No statistically significant differences were found between the women involved in the study for: maternal age, pre-pregnancy body mass index (BMI), gestational weight gain, and gestational age at investigation. Women with hypovitaminosis reported a significantly lower intake of milk/yoghurt, cheeses/dairy products and fish. Maternal hypovitaminosis D significantly correlated with low birth weight. **Conclusions**: Our study confirms that Vitamin D deficiency is a common finding also in sunny areas. Patients with low level of Vitamin D reported a lower intake of food rich of this micronutrient. An accurate anamnesis can be an easy way to identify pregnant women at risk of hypovitaminosis D for whom screening and supplementation can be suitable.

Keywords: Vitamin D; sun exposure; dietary intake; pregnancy; obstetric outcomes

1. Introduction

Vitamin D deficiency is a widespread health problem and mostly affects children, adolescents and elders, also in well sun exposed countries, especially in the Middle East [1,2]. It is a common finding during pregnancy. Less than 50% of world population presents an adequate Vitamin D status (>20 ng/mL) [3], and Vitamin D deficiency is described in 33% of American and 24% Canadian pregnant women [1,4]. Another recent review including 13 trials from seven countries evidenced a prevalence of Vitamin D deficiency from 39.4% to 76.5%, with the highest prevalence among Chinese (100%), Turkish (95.6%), Iranian (89.4%) and Pakistanian (89.0%) women [5].

Deficiency of Vitamin D seems to be related to poorer outcomes during pregnancy, neonatal and infant development [6].

Maternal Vitamin D serum level is strictly related to fetal and neonatal Vitamin D status [1,2]. Moreover, several studies found that Vitamin D supplementation during pregnancy may reduce the risk of preeclampsia, gestational diabetes, low birthweight and could also decrease the risk of severe postpartum hemorrhage [7].

In Italy, while it has been reported that the incidence of Vitamin D deficiency is high (up to 86%) among women above 70 years old [8], there is few evidence about its incidence among young people. According to the BONTOURNO study, in a cohort of 608 pre-menopausal women, almost one-third of women presented Vitamin D deficiency [9]. However, no recent studies can confirm this data and we do not really know how common is Vitamin D deficiency among our pregnant women.

Currently, in our setting, Vitamin D dosage and supplementation are not routinely recommended during pregnancy, but it has to be decided case by case according to the risk of having hypovitaminosis [10]. However, it has not clearly established how to define such a risk.

Therefore, we decided to introduce a questionnaire regarding dietary habits and sun exposure to verify if we could have relevant information to easily identify patients at high-risk of vitamin deficiency that could benefit from supplementation. Firstly, we assess the incidence of Vitamin D deficiency in a cohort of Neapolitan pregnant women; secondarily, we compared dietary habits between women with normal levels of Vitamin D and those with a deficiency, to define the dietary habits of patients with Vitamin D deficiency.

2. Materials and Methods

This was an observational prospective study. We included pregnant women attending a routine third trimester obstetric examination at the Department of Mother & Child of University Hospital Federico II of Naples, Southern Italy, from January to May 2019. Exclusion criteria were: age <18 years, twin pregnancy, Vitamin D supplementation.

This study was conducted according to the Declaration of Helsinki and all procedures were approved by the local Ethics Committee.

At enrollment, patients were asked to sign a written consent. Moreover, they were invited to answer a specific questionnaire about dietary habits.

The questionnaire was made according to Italian dietary habits. The Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases (SIOMMMS) stated that the main sources of Vitamin D are represented by fish and dairy products [8]. Our questionnaire consisted of four questions: (1) Do you eat fatty fish (salmon, sardine, tuna, mackerel, swordfish, snapper)? (2) Do you drink milk/yoghurt? (3) Do you eat dairy products? (4) Do you eat fruits and vegetables? Moreover, patients were asked to report how often they eat/drink each type of food. We used the same categories reported in the short Vitamin D questionnaire (VDQ) that has been used in previous studies [11]. Compared to VDQ, we included the use of dairy products instead of margarine, because of its uncommon use in Italy and we ask patients to report also about fruits and vegetables.

We did not include mushrooms, since they are not common in our diet and their consumption is seasonal and in general it is limited to autumn.

Moreover, we asked the patient about the frequency of physical activity, since it has been reported that it can affect Vitamin D concentration [12], and the personal perception of sun exposure during the summer period, when the sun exposure should be longest and the production and storage of Vitamin D should be more influenced by sunlight [13].

Data related to general and demographic information, age, gestational age (GA) at investigation, pre-gestational body mass index (BMI), gestational weight gain (GWG), obstetric history, family history of diseases, complications and therapies during pregnancy were also collected and recorded on a dedicated dataset. After delivery, obstetric and neonatal outcomes was assessed from medical records.

For all enrolled patients, a blood sample was collected. We asked all women to respect a 12-h fast before blood collection. Blood was centrifuged for 10 minutes within 0.5–2 h of sampling. Serum was extracted and stored at –80 °C until analysis by liquid chromatography tandem mass spectrometry. The serum concentration of 25-hydroxyvitamin D [25(OH)D] was measured by DiaSorin Liaison and the cut-off values for deficiency were fixed at 20 ng/mL. Values were given as the sum of 25(OH)D3 and 25(OH)D2.

Statistical analysis was performed using the statistical analysis program SPSS 20.0 (Chicago INC, Chicago, IL, USA). Data are presented as mean ± standard deviation for continuous variables, and number (percentage) for categorical variables.

Comparison between groups was performed by the Student's *t* test and the Mann-Whitney test for continuous variables and the Fisher's exact test and the Chi-square test for categorical variables. p value < 0.05 was considered statistically significant.

3. Results

From January to May 2019, 125 pregnant women were eligible for the study, but only 103 women consented to participate. Among them, 71 (68.9%) women presented a deficiency of Vitamin D (<20 ng/mL).

Maternal characteristics of women presenting hypovitaminosis and those with normal Vitamin D levels are summarized in Table 1.

No differences were reported in maternal age, GA at investigation, maternal BMI, GWG, smoking and attitude to physical exercise between the two groups. Based on maternal questionnaires, no significant difference was noticed regarding the intake of fruits and vegetables.

Women with hypovitaminosis D reported a significantly lower intake of milk/yoghurt, cheeses/dairy products and fish: eight patients (25%) with normal levels of Vitamin D and only 7 (9.9%) in the group with hypovitaminosis reported consumption of milk and yoghurt more than once a day ($p < 0.05$); 24 (75%) women with normal Vitamin D level and only 30 (42.3%) in hypovitaminosis group reported an intake of cheese or other dairy products more than once a week ($p < 0.05$), while 18 patients (56.3%) with normal Vitamin D level and 29 (40.9%) with hypovitaminosis consumed fish more than once a week ($p < 0.05$) (Table 2).

About sun exposure, 28 patients with hypovitaminosis (39.4%) and 19 (59.4%) with normal level of Vitamin D reported a sun exposure above 30 minutes per day during the previous summer season ($p = 0.06$).

Regarding obstetric outcomes, no significant difference was found in gestational age at delivery between patients with hypovitaminosis and those with normal Vitamin D levels (38 ± 1.5 weeks *vs.* 39 ± 2 weeks; $p = 0.65$). However, in the hypovitaminosis group the mean birthweight was significantly lower compared to controls (2845 ± 151 grams *vs.* 3049 ± 118 grams; $p < 0.05$). No difference was found for the other considered clinical conditions (preeclampsia, gestational diabetes, preterm birth).

4. Discussion

In our prospective observational study, we found that almost 70% of pregnant women present low levels of Vita-

Table 1. Vitamin D serum level and characteristics of study population.

	Vitamin D deficiency n = 71 (68.9%)	Normal Vitamin D level n = 32 (31.1%)	p value
Vitamin D serum level main value (ng/mL)	12.6 ± 0.5	26.4 ± 5.8	**<0.0001**
Age (years)	32 ± 0.6	32.5 ± 1.1	0.2
BMI (kg/m^2)	26.7 ± 1.5	25.6 ± 1.5	0.6
GWG (kg)	10.9 ± 0.8	10.6 ± 4.5	0.1
GA at investigation (weeks)	30.0 ± 1.5	30.0 ± 2.0	0.8
Smoking (yes)	9 (12.7)	2 (6.3)	0.5
Physical activity†	6 (8.5)	3 (9.4)	1

†Percentage of women reporting physical exercises at least twice per week.

BMI, Body Mass Index; GWG, Gestational Weight Gain; GA, Gestational Age.

Bold face data, p value< 0.0001.

Table 2. Dietary intake in patients with hypovitaminosis and with normal Vitamin D level.

Dietary intake	Vitamin D deficiency n = 71 (68.9%)	Normal Vitamin D level n = 32 (31.1%)	p value
Fish			
>once a week	29 (40.8)	18 (56.3)	**<0.05**
Once a week	19 (26.8)	8 (25)	
<once a week	23 (32.4)	6 (20.7)	
Milk/yoghurt			
>once a day	7 (9.9)	8 (25)	**<0.05**
Once a day	45 (63.4)	18 (56.3)	
<once a day	19 (26.8)	6 (20.7)	
Cheese/dairy products			
>once a week	30 (42.3)	24 (75)	**<0.05**
Once a week	29 (40.8)	6 (18.8)	
<once a week	12 (16.9)	2 (6.2)	
Vegetables			
>once a day	45 (63.4)	22 (68.8)	0.6
Once a day	14 (19.7)	7 (21.9)	
<once a day	12 (16.9)	3 (9.4)	
Fruits			
>once a day	29 (40.8)	14 (43.8)	0.7
Once a day	35 (49.3)	17 (53.1)	
<once a day	7 (9.9)	1 (3.1)	

Bold face data, p value< 0.05.

min D during the third trimester of pregnancy; this is an unexpected high percentage, considering that a previous study reported that the incidence of vitamin D deficiency in fertility period has been estimated to be in 1:3 women in Italy [9].

Despite our study has been conducted in a very sunny area, our percentage is very similar to the one reported in some Northern European countries, like Germany (77%) and in high-risk ethnicities, like South-Asian women, reporting a prevalence of Vitamin D hypovitaminosis that can be up to 96% [7]. Indeed, according to the self-reported perception of sun exposure, even if patients with Vitamin D deficiency reported a lower sun exposure, in all the cohort less than half of women reported a sun exposure above 30 minutes.

Our finding was consistent with the results of a systematic review by Karras *et al*. [14], reporting that, despite a good sun exposure, Vitamin D deficiency seems to be quite high in the Mediterranean region: they reported a prevalence ranging from 22.7% to 90.3%. According to that, apart from sun exposure that was lower in the group with hypovitaminosis D in our population, we should consider other factors, such as dietary habits, to identify patients at risk of deficiency.

Regarding dietary habits, we found that the consumption of milk/yoghurt, cheese, and dairy products significantly differed between the two groups and it could affect Vitamin D serum levels, if we consider that has been stated that the main sources of Vitamin D in the food are represented by fish and dairy products [8].

Several studies reported an association between adverse obstetric outcomes and hypovitaminosis D [15]. In our study, patients with low level of Vitamin D had significantly lower birthweight compared to those with a normal level. However, this data must be confirmed with larger studies and considering other possible actors linked to lower birthweight (i.e., smoke): no definitive conclusion can be drawn on the basis of this result.

Due to the lack of clear evidence about the relationship between Vitamin D and obstetric outcomes, there are no official recommendations about Vitamin D intake: the World Health Organization (WHO) does not indicate it as routine antenatal care [16]. Also, according to our national guidelines, Vitamin D supplementation in pregnancy is not routinely recommended [10].

However, considering the high percentage of hypovitaminosis D in our setting and the long-term effect of this condition during women's life, we cannot ignore that pregnancy could be an important moment to screen for vitamin deficiency; on the contrary, a universal screening to all pregnant women could be difficult to realize.

Vitamin D supplementation has been considered a valid intervention to correct deficiency in a specific population, such as pregnant women [17], but it has been important to stress with our patients that changing the lifestyle is the best way to prevent such a deficit.

Several findings suggest that supplementation around 1000 IU/day may be optimal to obtain a Vitamin D serum level greater than 50 nmol/L (20 ng/mL) [18–21].

This dosage is supposed to increase blood 25-hydroxyvitamin D by 1.2 nmol/L for every mcg (40 IU) of vitamin D3 given orally to individuals with low 25-hydroxyvitamin D levels [22].

To the best of our knowledge, this is the first study reporting the prevalence of hypovitaminosis D among Neapolitan pregnant women. The small sample size represents the main limitation of the study. In future, it will be interesting compare our sample considering different gestational age and different sun exposed population. Moreover, we reported sun exposure based on self-reported personal perception and referring to the previous summer season, while it would be more accurate to use objective methods, such as UV radiations dosimeters [13]. However, our aim was to understand which information directly obtained from the patients could be helpful in identify the risk of Vitamin D deficiency.

5. Conclusions

Despite we conducted this observational study in a sunny area, we demonstrated a high percentage of Vitamin D deficiency among pregnant women during the third trimester and a low sun exposure, based on what emerged from the questionnaires. In a setting where Vitamin D supplementation is recommended only in high-risk subjects but no tools are provided to identify at-risk patients, a good anamnesis addressing nutritional habits and personal sun exposure perception could be an easy way to identify patients at risk of Vitamin D deficiency.

Availability of Data and Materials

All authors are at disposal for any additional data.

Author Contributions

Extraction and drafting of the manuscript—LS, CIA, AC; Analysis of data, manuscript revision—LS, MG, SC, CIA, DM, GP, PF, DT; Design and revision, statistical analysis—LS, MG, SC, DM, GP, PF, DT. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the University of Naples Federico II (prot. n. 80/19).

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] El Koumi MA, Ali YF, Abd El Rahman RN. Impact of maternal vitamin D status during pregnancy on neonatal vitamin D status. The Turkish Journal of Pediatrics. 2013; 55: 371–377.

[2] Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. The American Journal of Clinical Nutrition. 2005; 81: 1060–1064.

[3] van Schoor N, Lips P. Global Overview of Vitamin D Status. Endocrinology and Metabolism Clinics of North America. 2017; 46: 845–870.

[4] Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? The Journal of Steroid Biochemistry and Molecular Biology. 2014; 144: 138–145.

[5] van der Pligt P, Willcox J, Szymlek-Gay EA, Murray E, Worsley A, Daly RM. Associations of Maternal Vitamin D Deficiency with Pregnancy and Neonatal Complications in Developing Countries: A Systematic Review. Nutrients. 2018; 10: 640.

[6] Møller UK, Streym S, Mosekilde L, Heickendorff L, Flyvbjerg A, Frystyk J, *et al*. Changes in calcitropic hormones, bone markers and insulin-like growth factor I (IGF-I) during pregnancy and postpartum: a controlled cohort study. Osteoporosis International. 2013; 24: 1307–1320.

[7] Palacios C, Kostiuk LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. The Cochrane Database of Systematic Reviews. 2019; 7: CD008873.

[8] Adami S, Romagnoli E, Carnevale V, Scillitani A, Giusti A, Rossini M, *et al*. Guidelines on prevention and treatment of vitamin D deficiency. Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases (SIOMMMS). Reumatismo. 2011; 63: 129–147. (In Italian)

[9] Adami S, Bertoldo F, Braga V, Fracassi E, Gatti D, Gandolini G, *et al*. 25-hydroxy vitamin D levels in healthy premenopausal women: association with bone turnover markers and bone mineral density. Bone. 2009; 45: 423–426.

[10] Linee Guida Gravidanza fisiologica, Istituto Superiore di Sanità. 2011. Available at: http://www.salute.gov.it/imgs/C_17_pubblicazioni_1436_allegato.pdf (Accessed: 29 October 2022).

[11] Bärebring L, Amberntsson A, Winkvist A, Augustin H. Validation of Dietary Vitamin D Intake from Two Food Frequency Questionnaires, Using Food Records and the Biomarker 25-Hydroxyvitamin D among Pregnant Women. Nutrients. 2018; 10: 745.

[12] Hauta-Alus HH, Holmlund-Suila EM, Rita HJ, Enlund-Cerullo M, Rosendahl J, Valkama SM, *et al*. Season, dietary factors, and physical activity modify 25-hydroxyvitamin D concentration during pregnancy. European Journal of Nutrition. 2018; 57: 1369–1379.

[13] Webb AR, Kift R, Durkin MT, O'Brien SJ, Vail A, Berry JL, *et al*. The role of sunlight exposure in determining the vitamin D status of the U.K. white adult population. The British Journal of Dermatology. 2010; 163: 1050–1055.

[14] Karras S, Paschou SA, Kandaraki E, Anagnostis P, Annweiler C, Tarlatzis BC, *et al*. Hypovitaminosis D in pregnancy in the Mediterranean region: a systematic review. European Journal of Clinical Nutrition. 2016; 70: 979–986.

[15] Agarwal S, Kovilam O, Agrawal DK. Vitamin D and its impact on maternal-fetal outcomes in pregnancy: A critical review. Critical Reviews in Food Science and Nutrition. 2018; 58: 755–769.

[16] WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience. World Health Organization: Geneva. 2016.

[17] NICE Group. Nice Guidelines. Vitamin D: supplement use in specific populations groups. 2017 Available at: https://www.nice.org.uk/guidance/ph56/resources/vitamin-d-supplement-use-in-specific-population-groups-pdf-1996421765317 (Accessed: 29 October 2022).

[18] Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol [published correction appears in American Journal of Clinical Nutrition. 2003; 78: 1047]. American Journal of Clinical Nutrition. 2003; 77: 204–210.

[19] Hollis BW, Wagner CL. Vitamin D requirements during lactation: high-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. The American Journal of Clinical Nutrition. 2004; 80: 1752S–1758S.

[20] Hollis BW. Vitamin D requirement during pregnancy and lactation. Journal of Bone and Mineral Research. 2007; 22: V39–V44.

[21] Vieth R, Chan PC, MacFarlane GD. Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. The American Journal of Clinical Nutrition. 2001; 73: 288–294.

[22] Dawson-Hughes B, Heaney RP, Holick MF, Lips P, Meunier PJ, Vieth R. Estimates of optimal vitamin D status. Osteoporosis International. 2005; 16: 713–716.