

Original Article

Vitamin D deficiency in young women of childbearing age: the elephant in the room

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Abstract: High prevalence of vitamin D deficiency has been reported from Saudi Arabia. The objective of this study was to assess the vitamin D status among Saudi women of childbearing age and analyze its association with relevant biochemical parameters. We assessed serum 25(OH) vitamin D status in Saudi Arabian pre-pregnant (n=20), pregnant (n=235) and postnatal (n=149) women and analyzed its correlation with various biochemical parameters, including PTH and calcium. Results showed that all the subjects in the pre-pregnant and pregnant groups had less than sufficient 25(OH) vitamin D levels (<75 nmol/L). In the postnatal group only one had sufficient level of 25(OH) vitamin D. In the pregnant group, 80% had severe 25(OH) vitamin D deficiency (<25 nmol/L). The means of 25(OH) vitamin D level in pre-pregnant, pregnant and postnatal women were 20.37, 18.37 and 26.81 nmol/L, respectively. Values of various biochemical parameters in pregnant women, the largest sub-group of subjects, were within normal range. In the whole study population, 25(OH) vitamin D was significantly correlated only to serum phosphorous level (R=0.10, P=0.013). Results of our study confirmed widespread, severe vitamin D deficiency in young Saudi women of childbearing age, who were otherwise normal with respect to various biochemical parameters.

Keywords: 25(OH) vitamin D, perinatal, prenatal, vitamin D deficiency

Introduction

Vitamin D, a fat-soluble hormone acquired through exposure to sunlight and/or diet, has been identified as a precursor that modulates long-term programming of human health [1]. Low vitamin D intakes during perinatal development have traditionally been linked to poor bone development. Furthermore, vitamin D deficiency during the perinatal period is a modifiable risk factor for a range of diseases, including multiple sclerosis, schizophrenia, heart disease, type I diabetes and cancer, among others [2].

Vitamin D deficiency during pregnancy is a worldwide epidemic. Studies have reported a prevalence that ranges from 18-84%, depending on the country of residence and local clothing customs [3-6]. Vitamin D deficiency is alarmingly high among the Saudi population, particularly in women [7-10]. The aim of our

study was to highlight the problems in a cohort of women of child bearing age who had their vitamin D status checked either during pregnancy or in the immediate pre- or post-pregnancy period and correlate them to certain maternal demographic or biochemical variables.

Patients and methods

In this retrospective study, a list of patients who gave birth at the King Khalid University Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia from January to December 2011, were obtained from the Information Technology Unit of the hospital. For the duration of the pregnancy, only 235 pregnant women out of 3483 total deliveries had their 25(OH) vitamin D levels measured. Twenty patients had their vitamin D status checked six months before pregnancy, while 149 had their levels taken postpartum (making a total of 404 women after exclusion criteria were adopted). Vitamin D estimations

Table 1. Stratification of the study cohort

Subject details	(n)	%
Total deliveries for 2011	3482	100
Vitamin D level determined subjects	404	11.60
Pre-pregnant	20/404	4.95
Pregnant	235/404	58.17
Postnatal	149/404	36.88

made during six months before conception or after delivery were assumed to give an indirect estimate of vitamin D status during pregnancy conception.

Clinical and biochemical data were obtained from the medical files of patients whose vitamin D levels were taken during pregnancy. Existence of chronic medical conditions such as diabetes mellitus, hypertension, parathyroid disease, renal and liver diseases, sarcoidosis, osteomalacia, tuberculosis, or any psychiatric illnesses were noted. Subjects who received therapeutic doses of vitamin D at anytime during the pregnancy were excluded from the final list. Other pertinent laboratory results such as patient's bone profile, complete blood count, parathyroid and thyroid tests were also acquired from the hospital's system (normal reference range for our laboratory in index). Other information extracted include the manner of delivery, gestational age, presence of complications to either the mother or the newborn, and the birth weight of the latter along with the measurement of birth length, and head circumference (these are reported elsewhere). This study was ethically approved by the Institutional Review Board of the College of Medicine, King Saud University, Riyadh, Saudi Arabia.

Data analysis was carried out using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). The association between the maternal vitamin D status and maternal age, gestational age, manner of delivery and birth weight of the newborn were analyzed. Chi-square test was used to measure the association between the categorical variables and vitamin D level was categorized into sufficiency, insufficiency, and deficiency as suggested by Dawson-Hughes [11]. All analyses are two-tailed with *P* value <0.05 considered statistically insignificant.

Results

Out of 3482 deliveries for the year 2011, 404 women (11.6%) had their serum 25(OH) vitamin

D checked either pre-pregnancy, during or post natal (within six months period) (**Table 1**). Based on the previously described clinical categories of vitamin D status [12-15], the subjects were classified into four groups as following: deficient (<25 nmol/L), insufficient (25-50 nmol/L); sufficient (50-75 nmol/L) and desirable (>75 nmol/L).

Out of these women (n=404), 25(OH) vitamin D deficiency was seen in 384 women (95%), while 4.7% (19 women) were vitamin insufficient and one subject had normal 25(OH) vitamin D level (**Table 2**). In the pre-pregnant and pregnant groups, all subjects had low 25(OH) vitamin D. In the post-delivery group only one had sufficient 25(OH) vitamin D level. In the pregnant group, 80% had severe 25(OH) vitamin D deficiency (<25 nmol/L).

Table 3 shows the means of 25(OH) vitamin D levels in different groups with the prenatal women having the lowest. None of the pregnant women had a normal vitamin D level. All the means were at or below the severe deficiency limit of 25 nmol/L.

Various biochemical parameters were measured in pregnant women (n=235) and values are shown in **Table 4**. Except for 25(OH) vitamin D, the values of all the biochemical parameters were within normal range. Correlational analysis between 25(OH) vitamin D level and various biochemical parameters indicated a significant association between 25(OH) vitamin D and phosphorous level ($R=0.10$, $P=0.013$). No additional correlations were found. The mean age and the mean parity of mothers were 30.6 (16-48 years) and 3 (1-8), respectively. No significant correlation was found between maternal age and parity versus vitamin D status.

Discussion

Vitamin D status in pregnant women is usually determined by measuring the level of serum 25(OH) vitamin D. Serum 25(OH) vitamin D levels of >75 nmol/L were found to be required for adequacy in non-pregnant adults through association studies between 25(OH) vitamin D levels and intestinal calcium absorption, maximal PTH suppression, bone fracture prevention, and bone turnover. These studies also helped develop a classification of stages for vitamin D status in non-pregnant adults [16, 17], which in pregnant women correlated with maternal and fetal outcomes [18]. Accordingly, levels of less

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Table 2. 25(OH) vitamin D status in all women

Vitamin D status (nmol/L)	Pre-pregnant (n)	Pregnant (n)	Postnatal (n)	Total (n)
Normal (>75)	0	0	1	1
Insufficiency (50-75)	0	7	12	19
Mild deficiency (25-50)	6	40	51	97
Severe deficiency (<25)	14	188	85	287
Total (N)	20	235	149	404

Table 3. Range of 25(OH) vitamin D level in all women

	Pre-pregnant	Pregnant	Postnatal	Overall
Mean (nmol/L)	20.37	18.37	26.81	21.58
Highest (nmol/L)	49.6	71	93.52	93.52
Lowest (nmol/L)	4.7	4	6.34	4

Table 4. Biochemical parameters in pregnant women (n=235)

Biochemical parameter	Mean \pm SE	Normal Range
Age (years)	30.6 \pm 0.4	
Parathyroid Hormone (PTH) (pmol/L)	4.7 \pm 0.4	1.65-6.9
Inorganic phosphorus (PO_4) (mmol/L)	1.2 \pm 0.01	0.87-1.45
Calcium (Ca) (mmol/L)	2.4 \pm 0.1	2.1-2.6
Alkaline Phosphatase (ALP) (U/L)	118.9 \pm 4.4	50-136
25(OH) vitamin D (nmol/L)	18.9 \pm 0.8	>75

than 10 ng/mL (<25 nmol/L) indicated severe vitamin D deficiency that can result in rickets with adverse effects on overall health; concentrations between 10-20 ng/mL (25-50 nmol/L) reflected vitamin D insufficiency was found to affect normal bone metabolism and musculoskeletal health; higher concentrations-those above 32 ng/mL (>80 nmol/L)-were agreed upon as adequate for overall health and disease prevention.

Studies in the past have consistently shown widespread prevalence of severe vitamin D deficiency in pregnant mothers and neonates in Saudi Arabia. A 1984 study involving 119 pregnant Saudi women showed a median 25(OH) vitamin D concentration of 5.7 ng/mL (14.25 nmol/L) and, further, undetectable or extremely low 25(OH) vitamin D in 25% of the subjects; also, vitamin level was even lower in the cord blood with almost 70% of cord blood samples being <4 ng/mL (<10 nmol/L) [7]. In another study in 1984 involving 100 pregnant Saudi women and their asymptomatic neonates, 59 mothers and 70 neonates had

25(OH) vitamin D level below 10 ng/mL (25 nmol/L) [8]. In a more recent screening study, out of 153 near term babies, 88% were vitamin D deficient and 10.5% were insufficient with only 2 babies (1.3%) having sufficient levels of vitamin D in their cord blood [19]. In another cross sectional study on 465 Saudi females of child bearing age (19-40 years), selected from primary health centers, hypovitaminosis was detected in all the subjects [20].

Our current retrospective study of a group of young Saudi women in the childbearing age, with almost 60% of them being pregnant, showed serious vitamin D deficiency with 80% of pregnant women having vitamin D level <25 nmol/L and confirms the results of earlier reports indicating widespread prevalence of severe vitamin D deficiency among women in this region. However, the severe vitamin D deficiency status seen in young Saudi women was not significantly associated with either calcium or parathyroid hormone abnormalities.

High prevalence of vitamin D deficiency among perinatal women of child bearing-age has been reported in other parts of the world too. The Third National Health and Nutrition Examination Survey [NHANES] (1988-1994) found that 4% of white and 42% of black women of childbearing age residing in the United States had serum 25(OH) vitamin D levels less than 10 ng/mL (25 nmol/L), which is consistent with a diagnosis of severe vitamin D deficiency [21]. A 2007 study involving 200 white and 200 black pregnant women showed 10% of white and 46% of black neonates had 25(OH) vitamin D concentrations below 15 ng/mL (37.5 nmol/L), indicating the persistence of widespread vitamin D deficiency even though 90% of women subjects had taken prenatal vitamins [22]. vitamin D deficiency was found to be common in pregnant women (up to 50%) and in breastfed infants (up to 56%) despite the widespread use of prenatal vitamins as the supplements were inadequate to maintain normal vitamin D levels [23, 24].

Results from previous studies mechanistically linked vitamin D deficiency to several pregnan-

cy related issues. Deficiency of vitamin D in pregnant women influenced musculo-skeletal growth, with poor skeletal mineralization in utero and myopathy developing earlier than any biochemical signs of bone disease [25-27], and contributed to higher rates of caesarian births [28]. Pregnant women with serum 25(OH) vitamin D concentrations below 15 ng/mL (37.5 nmol/L) were four times more likely to have a caesarian birth [24]. *In vitro* and animal studies suggested that vitamin D has important roles in glucose and insulin metabolism [21, 29] and gestational diabetes was, indeed, associated with insufficient 25(OH) vitamin D levels compared with the control [30, 31]. Patients with 25(OH) vitamin D levels <15 ng/mL (37.5 nmol/L) had a 5-fold increase in the risk of pre-eclampsia largely due to low calcium levels, perhaps through vitamin D mediation [32].

Taking our small study into consideration along with other studies from the region, we believe that we have a serious epidemic of vitamin D deficiency in women of child bearing age which will not just influence the health status of the women themselves but will have serious consequences on the health of their children and future generations to come. Since vitamin D deficiency can be easily, safely, and cheaply corrected through adequate supplementation, it should be an important strategy to focus on and implement for healthy pregnancy and optimal health of both the mother and the baby.

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Disclosure of conflict of interest

None.

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