

Current Scenario of Vitamin D Status During Pregnancy in North Indian Population

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Abstract

Purpose of the Study The aim of the study was to determine the prevalence and risk factor for vitamin D deficiency in our pregnant population.

Method A total of 418 healthy primigravida with single live pregnancy and sure of dates attending the antenatal clinic between October 2011 and April 2013 were recruited. Women were excluded if they had history of current or

past chronic medical disease. Women were also excluded if they had history of medication with drugs interfering with calcium and vitamin D metabolism.

Results The prevalence of vitamin D deficiency during pregnancy has been found to be 391 (93.5 %). Severe vitamin D deficiency among pregnant patients was 34.44 % (144/418). The levels of serum 25(OH)D and serum calcium were significantly lower in severe deficient group than the adequate group [7.10 ± 1.49 vs. 38.90 ± 4.22 ng/ml ($p = 0.001$) and 7.13 ± 1.41 vs. 9.39 ± 0.88 ng/ml ($p = 0.001$)], respectively. Maternal education, husband education, socioeconomic status, serum calcium, serum phosphorous, and season were significant factors associated with vitamin D deficiency. Significant independent variables for severe vitamin D deficiency were low serum calcium, serum alkaline phosphatase, and serum phosphorus (OR 39.41, 95 % CI 10.30–150.85, $p < 0.01$), (OR 18.03, 95 % CI 3.95–82.44, $p < 0.01$), and (OR 8.40, 95 % CI 2.47–28.61, $p < 0.01$).

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Conclusion Vitamin D deficiency is highly prevalent among pregnant women in Northern India, and these raises concern about the health consequences for the mother and the offspring.

Keywords Pregnancy · Vitamin D · Calcium · Prevalence

Introduction

Vitamin D is a part of the “Calcium-Vitamin D-Parathyroid hormone” endocrine axis [1]. While vitamin D is critical for calcium homeostasis, current studies also highlight role of vitamin D deficiency (VDD) in diseases other than the metabolic bone disorders. The actions of 1,25-dihydroxy-vitamin D [1,25(OH)₂D] are mediated through specific, high affinity vitamin D receptor, which is present in various tissues. It has been estimated that 1 billion people worldwide have VDD or insufficiency [2]. Several modifications of vitamin D metabolism occur during pregnancy. The expression of 1- α hydroxylase is increased in the kidney and placenta, and the concentration of serum 1,25-dihydroxy-vitamin D [1,25(OH)₂D] increases in normal pregnancy from the first to the third trimester. The role of 1,25-dihydroxy-vitamin D during pregnancy to increase intestinal calcium absorption is since long acknowledged [3]. Reports of profound deficiency among pregnant women, those with 25-hydroxy-vitamin D (25(OH)D) concentrations <10 ng/ml (25 nmol/l), are common throughout the world. Approximately 18 % of pregnant women in the UK, 42 % in northern India, 61 % in New Zealand, 89.5 % in Japan, and 60–84 % of pregnant non-Western women in The Hague, Netherlands had serum 25(OH)D concentrations <10 ng/ml (25 nmol/l) [4–8].

Unexpectedly, concerns have been raised that VDD is widespread in tropical countries such as India where majority of its population lives in areas receiving ample sunlight throughout the year. There is widespread prevalence of varying degrees (50–90 %) of VDD with low dietary calcium intake in Indian population according to various studies published earlier [1]. In a population that already has a high prevalence of VDD and poor dietary calcium intake, the problem is likely to worsen during pregnancy because of the active transplacental transport of calcium to the developing fetus. Increasing urbanization results in poor outdoor activity and greater pollution, coupled with skin pigment, may further compound this problem. Furthermore, milk, the primary source of calcium, is an expensive food in India.

A recent study from North-Eastern part of India reported that 41 % of the cases were found to have VDD [9]. Previous studies show varying degree of VDD in different parts of India [9–12]. A recent study suggested that VDD

during pregnancy is associated with multiple adverse health outcomes in mothers [13].

Data regarding the prevalence of vitamin D during pregnancy in India are scanty. At present, there are few research studies which indicate risk factor associated with VDD in Indian pregnant women. Therefore, the present study has been undertaken with the objective to determine the prevalence of VDD in north Indian pregnant population and to identify risk factors for VDD.

Material and Method

Participant

A total of four hundred and eighteen pregnant women were enrolled in the study. All consecutively registered primigravida with uncomplicated pregnancy attending the antenatal clinic of principle investigator at Lok Nayak Hospital, New Delhi were included in the study between October 2011 and April 2013. Gestational ages of the subjects were determined with best obstetric estimates using definite menstrual history and first trimester ultrasonography scan. The experiment was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Institutional Ethics Committee. Written informed consent was taken from the recruited subjects or legally authorized representative if the patient was unable to understand the study protocol. All recruited patients were evaluated on the basis of predesigned and pretested perform with respect to history, clinical examination.

Study Design and Data Collection

In this prospective cohort study, all those women were recruited who were healthy primigravida with single live pregnancy and sure of dates. Women were excluded if they had history of current or past chronic medical disease such as hyperparathyroidism, collagen disease, Cushing’s disease, chronic renal disease, gastrointestinal disease, lung disease, or ovarian tumor. Women were also excluded if they had history of medication with drugs interfering with calcium and vitamin D metabolism like anticonvulsants, corticosteroids, thiazides, thyroxine, and heparin. Serum sample of the eligible primigravida was taken at time of recruitment, centrifuged, and stored at -70°C for assessment of serum 25-hydroxy-vitamin D levels. Serum 25(OH)D level was estimated using a commercially available ELISA kit according to manufacturer’s instruction (DLD Diagnostika GMBH, Germany). The sensitivity of this assay is 1.9 ng/ml, and the total intra assay imprecision CV is 3.3 % at 17 ng/ml. Serum calcium titers were

estimated using a semiautomatic analyzer (MiniTecno; Embiel, Seoul, Korea), and quantification was done using a commercially available ELISA kit according to manufacturer's instruction (Sistemi Intelligenti Elettronici, Rome, Italy). Serum albumin and alkaline phosphatase levels were also measured. Season of sample collection was defined as winter (November, December, January, and February), summer (March, April, May, and June), and spring (July, August, September, and October).

Statistical Analysis

Data were statistically analyzed using the Statistical Package for Social Sciences version 15.0 (SPSS, Chicago, IL, USA). Serum level of VDD was classified as severe VDD (serum 25(OH)D level of <10 ng/ml), vitamin D insufficiency (serum 25(OH)D level of 10–32 ng/ml), and vitamin D adequacy (serum 25(OH)D level of 32–100 ng/ml). Using Kolmogorov–Smirnov Z test, all the variables entered into the main analyses were found to be normally distributed. Anova test was employed to observe significant mean difference between three groups. Post hoc test was employed to see significant mean difference between two variables. The qualitative data between two groups were compared using Chi-square test/Fisher exact test. The correlation between maternal hemoglobin, serum albumin, serum alkaline phosphatase, serum phosphorus, serum calcium, and serum 25-hydroxy-vitamin D was performed using Pearson's correlation. Univariate and multinomial logistic regressions were applied to identify the risk factors for vitamin D. Vitamin D level of 32 ng/ml and above is taken as reference (normals). Socioeconomic factors have been evaluated by modified Kuppaswamy scale [14].

Results

The study population consisted of 418 primigravida attending the antenatal clinic of Lok Nayak Hospital, New Delhi from October 2011 to April 2013. The mean maternal age at recruitment was 23.00 ± 5.85 years. The prevalence of VDD (serum 25(OH)D level <32 ng/ml) during pregnancy has been found to be 93.5 % (391/418). The mean serum 25(OH)D level in severe deficient group was 7.10 ± 1.49 ng/ml, insufficient group 18.35 ± 6.37 ng/ml, and adequate group 38.90 ± 4.22 ng/ml ($p < 0.01$). Severe VDD among pregnant patients was 34.44 % (144/418). Insufficient levels of vitamin D during pregnancy were 59 %, and only 6.45 % had adequate levels of vitamin D. Maternal age has no association with vitamin D levels. Maternal education, husband education, socioeconomic status, and month of sample collection were

found to be significantly associated with vitamin D levels ($p < 0.01$). Increase in maternal education leads to decrease in frequency of severe VDD and increase in frequency of adequate level of vitamin D ($p < 0.01$). Similar trend was observed as increase in husband education reduces severe VDD and was found to be statistically significant ($p < 0.01$). According to modified Kuppaswamy scale, it was observed that as socioeconomic status increases, frequency of severe VDD decreases. Approximately, 25.6 % (37/144) pregnant patients had less severe VDD those who were recruited in month of November to February compared with those were recruited in other months. Only 7 % (2/27) pregnant patients had adequate level of vitamin D recruited in month of July to October (Table 1).

Biochemical profile of recruited primigravida on the basis of maternal serum vitamin D level has been depicted in Table 1. The mean serum level of 25(OH)D, serum calcium, and serum phosphorous was significantly associated with vitamin D levels ($p < 0.001$). The serum alkaline phosphatase was comparable in all the three groups but was significantly associated with vitamin D levels (Table 1). The levels of serum 25(OH)D and serum calcium were significantly lower in severe deficient group than the adequate group [7.10 ± 1.49 vs. 38.90 ± 4.22 ng/ml ($p = 0.001$) and 7.13 ± 1.41 vs. 9.39 ± 0.88 ($p = 0.001$)], respectively.

Maternal vitamin D showed positive correlation with serum phosphorous, calcium, and hemoglobin ($r = 0.472$, $p = 0.000$; $r = 0.504$, $p = 0.000$; and $r = 0.133$, $p = 0.007$), respectively. Distribution of various variables according to vitamin D levels has been depicted in Table 2.

Table 3 shows the result of univariate logistic regression for the association of maternal VDD and predictor variables. Maternal education, husband education, socioeconomic status, serum calcium, serum phosphorous, and season were significant risk factors associated with VDD.

Significant independent variables in univariate analysis were analyzed by multinomial logistic regression. Low serum calcium, serum alkaline phosphatase, and serum phosphorous were independent risk factors for severe VDD (OR 39.41, 95 % CI 10.30–150.85, $p < 0.01$), (OR 18.03, 95 % CI 3.95–82.44, $p < 0.01$), and (OR 8.40, 95 % CI 2.47–28.61, $p < 0.01$). Significant risk factor associated with insufficient level of vitamin D were socioeconomic status, low serum calcium, and low serum alkaline phosphatase (Table 4).

Discussion

Despite of the fact that India is a vast tropical country extending from 8.4°N latitude to 37.6°N latitude where

Table 1 Baseline demographic and biochemical profile of 418 subjects on the basis of maternal serum 25(OH) D level

Demographic characteristics				
Variables	Vitamin D levels			<i>p</i> value
	Severe vitamin D deficiency (<10 ng/ml) <i>N</i> = 144 (34.45 %) [1]	Vitamin D insufficiency (10–32 ng/ml) <i>N</i> = 247 (59 %) [2]	Vitamin D adequacy (32–100 ng/ml) <i>N</i> = 27 (6.45 %) [3]	
Age (years) Mean (SD)	23.10 (1.89)	22.99 (5.45)	22.31 (1.97)	0.631
Maternal education (in number of years) <i>N</i> (%)				
0	48 (33.3 %)	42 (17 %)	4 (14.8 %)	0.0001***
0–10	54 (37.5 %)	97 (39.2 %)	9 (33.3 %)	
10–12	30 (20.8 %)	53 (21.4 %)	4 (14.8 %)	
>12	12 (8.3 %)	55 (15.3 %)	10 (37 %)	
Husband education (in number of years) <i>N</i> (%)				
0	30 (20.8 %)	29 (11.7 %)	2 (7.4 %)	0.0001***
0–10	75 (52 %)	95 (38.4 %)	6 (22.2 %)	
10–12	30 (20.8 %)	63 (25.5 %)	8 (29.6 %)	
>12	9 (6.25 %)	60 (24.2 %)	11 (40.7 %)	
Socio-economic status <i>N</i> (%) [†]				
Lower	76 (52.7 %)	78 (31.5 %)	6 (22.2 %)	0.0001***
Upper lower	63 (43.7 %)	155 (62.7 %)	13 (48.1 %)	
Lower middle	5 (3.47 %)	14 (5.66 %)	8 (29.6 %)	
Upper middle	0	0	0	
Months of blood sample collection <i>N</i> (%)				
March–June	66 (45.8 %)	86 (34.8 %)	17 (62.9 %)	0.008**
July–October	41 (28.4 %)	80 (32.3 %)	2 (7.4 %)	
November–February	37 (25.6 %)	81 (32.7 %)	8 (29.6 %)	
Biochemical characteristics mean (SD)				
Hemoglobin (g/dl)	10.59 (0.61)	10.68 (0.76)	10.85 (1.36)	0.214
Serum calcium levels (mg/dl)	7.13 (1.41)	8.63 (1.26)	9.39 (0.88)	0.001*
Serum albumin levels (gm %)	2.69 (0.59)	2.71 (0.71)	2.48 (0.63)	0.254
Serum alkaline phosphatase(IU/l)	152.62 (86.36)	142.07 (84.65)	198.56 (85.92)	0.004*
Serum phosphorus (mmol/l)	2.27 (0.52)	3.05 (0.75)	3.34 (0.62)	0.001*

Normal values of maternal hemoglobin, serum calcium, albumin, phosphorus, and alkaline phosphatase are 10–12 g/dl, 8.5–10.5 mg/dl, 3.5–5 gm %, 2.5–4.5 mmol/l, and 125–250 IU/l, respectively

* *p* value < 0.05 significant, ** *p* value < 0.01 significant, *** *p* value < 0.0001 significant

[†] Modified Kuppusswamy scale

ample of sunlight is available throughout the year, nearly 42 % of the pregnant women in northern India were deficient of 25(OH)D concentrations <10 ng/ml [5]. In the present study, the prevalence of VDD during pregnancy has been found to be 93.5 % (391/418) which is a matter of great concern. Mostly, pregnant women 59 % (247/418) had insufficient levels of vitamin D which reflects that they may develop severe deficiency of vitamin D if not treated.

Maternal age has no association with vitamin D levels. Few prevalence studies reported that VDD is high in Europe, and pregnant women are at high risk of developing VDD [8, 15] whereas it is relatively less common in USA and Canada as milk is usually fortified with vitamin D and use of vitamin supplements is common [16]. Previous studies from southern and northern part of India had reported that 61 and 96.3 % of the pregnant women had VDD,

Table 2 Variables according to vitamin D levels

Variables	Vitamin D levels			Total
	<10 ng/ml	10–31.99 ng/ml	≥32 ng/ml	
Maternal education (number of years)				
0	48 (33.3 %)	42 (17 %)	4 (14.8 %)	94
0–12	84 (58.3 %)	150 (60.72 %)	13 (48.1 %)	247
>12	12 (83.3 %)	55 (22.26 %)	10 (37 %)	77
Husband education (number of years)				
0	30 (20.8 %)	29 (11.7 %)	2 (7.40 %)	61
0–12	105 (72.9 %)	158 (63.96 %)	14 (51.9 %)	271
>12	9 (6.25 %)	60 (24.29 %)	1 (47.4 %)	80
Socioeconomic status[†]				
Lower	76 (52.7 %)	78 (31.5 %)	6 (22.22 %)	160
Upper lower	63 (43.7 %)	155 (62.7 %)	13 (48.1 %)	231
Lower middle	5 (3.47 %)	14 (5.66 %)	8 (29.6 %)	27
Upper middle	0	0	0	0
Serum calcium (mg/dl)				
<8.5	125 (86.8 %)	91 (36.84 %)	4 (14.81 %)	220
8.5–10.5	15 (10.41 %)	143 (57.89 %)	19 (70.3 %)	177
>10.5	4 (2.77 %)	13 (5.26 %)	4 (14.81 %)	21
Serum albumin (gm %)				
<3.5	129 (89.58 %)	214 (86.63 %)	25 (92.59 %)	368
3.5–5	15 (10.41 %)	33 (13.36 %)	2 (7.40 %)	50
Hemoglobin (g/dl)				
<10	17 (11.80 %)	31 (12.55 %)	6 (22.22 %)	54
10 & Above	127 (88.19 %)	216 (87.44 %)	21 (77.77 %)	364
Serum alkaline phosphatase (IU/L)				
<125	58 (40.27 %)	101 (40.89 %)	3 (11.11 %)	162
125–250	65 (45.13 %)	117 (47.36 %)	16 (59.25 %)	198
>250	21 (14.58 %)	29 (11.74 %)	8 (29.62 %)	58
Serum phosphorous (mmol/l)				
<2.5	110 (76.38 %)	55 (22.26 %)	5 (18.51 %)	170
2.5–4.5	34 (23.61 %)	192 (77.73 %)	22 (18.48 %)	248
Season				
Spring	41 (28.4 %)	80 (32.3 %)	2 (7.4 %)	123
Summer	66 (45.8 %)	86 (34.8 %)	17 (62.9 %)	169
Winter	37 (25.6 %)	81 (32.7 %)	8 (29.6 %)	126

[†] Modified Kuppaswamy scale

respectively [10, 11]. Serum 25(OH) levels were significantly lower in winter in the second and third trimester [11]. Recently, Dasgupta et al. from North-Eastern part of India reported that 42 % of pregnant women were found to have VDD and 14 % of them had insufficient vitamin D levels which are quite less compared with present study where 93.5 % of pregnant women had VDD and 59 % had insufficient vitamin D levels [9]. Variation in deficiency of vitamin D levels during pregnancy has been observed from different parts of the country. One earlier study done by Sachan et al. observed that 84 % of pregnant women were deficient of vitamin D taking the cut-off of 22.5 ng/ml and

serum mean 25(OH) level of 14 ± 9.3 ng/ml which is comparable with mean serum 25(OH) level of 15.41 ± 8.97 ng/ml in the present study population [5]. Recently, a study by Fariba et al. 2013 demonstrated that vitamin D insufficiency is associated with an increased risk of gestational diabetes, pre-eclampsia, and small for gestational age infants. Pregnant women with low 25(OH)D levels had an increased risk of bacterial vaginosis and lower birth weight infants, but they did not deliver by cesarean section [13]. Research studies showed adverse outcomes of VDD such as neonatal rickets, neonates (wheezing), and in children (low bone mineral density,

Table 3 Factors for vitamin D deficiency based on univariate analysis

Variables	<i>p</i> value	Vitamin D levels			
		Severe vitamin D deficiency versus vitamin D adequacy (<10 vs. \geq 32 ng/ml)		Vitamin D insufficiency versus vitamin D adequacy (10–31.99 vs. \geq 32 ng/ml)	
		OR	95 % CI	OR	95 % CI
Maternal education (number of years)					
0	<0.001**	10	2.67–37.47	1.99	0.59–6.51
0–12		5.39	1.94–14.97	2.1	0.87–5.06
>12		1	–	1	–
Husband education (number of years)					
0	<0.001**	18.33	3.41–98.44	2.66	0.55–12.78
0–12		9.17	3.23–26.03	2.07	0.89–4.81
>12		1	–	1	–
Socioeconomic status[†]					
Lower	<0.001**	20.26	5.03–81.58	7.43	2.23–24.71
Upper lower		7.75	2.18–27.52	6.81	2.42–19.21
Lower middle		1	–	1	–
Upper middle		–	–	–	–
Serum calcium (mg/dl)					
<8.5	<0.001**	39.58	11.88–131.94	3.02	1.0–9.17
8.5–10.5		1.27	0.27–5.92	0.43	0.13–1.46
>10.5		1	–	1	–
Serum phosphorous (mmol/l)					
<2.5	<0.001**	14.29	5.01–40.45	1.26	0.46–3.48
2.5–4.5		1	–	1	–
Season					
Spring	0.01*	4.43	0.88–22.22	3.95	0.81–19.18
Summer		0.84	0.33–2.13	0.5	0.20–1.22
Winter		1	–	1	–

OR odds ratio, CI confidence interval

* *p* value < 0.05 significant, ** *p* value < 0.01 significant

[†] Modified Kuppuswamy scale

type-1 diabetes, and eczema) [17, 18]. However, there is so far no conclusive evidence about the causality of these relationships. Skin complexion, poor sun exposure, vegetarian food habits, and lack of vitamin D food fortification program in the country explain the high prevalence of VDD in India despite its sunny climate. Multiple factors explain VDD especially during pregnancy as with modernization, the number of hours spent indoor has increased thereby preventing adequate sun exposure. This is particularly true in the urban Indians. Changing food fads and food habits contribute to low dietary calcium and vitamin D intake. Cultural and traditional habits prevalent in certain religions like “Burqa” and the “pardah” system in Muslims have been well known. Moreover, repeated and unplanned, unspaced pregnancies in dietary deficient patients can aggravate VDD in the mother and the fetus.

The education level is one of the most important demographic factors associated with socioeconomic status which in turn is important determinant of a host of social and environmental exposures responsible for poor vitamin D status in pregnant women. Moreover, poor economic status has led to VDD which may be due to hike in milk prices. Nutrition is closely linked with education and socioeconomic status. The present study showed that education level and socioeconomic status were the factors associated with poor vitamin D status. Illiterate women are more severely deficient 33.3 % in vitamin D compared to the educated women 8.3 %. A better educational level correlates with better living conditions and thus may indirectly improve the quality of the diet during pregnancy. Variation in prevalence of VDD during pregnancy has been observed in research

Table 4 Multinomial logistic regression analysis to identify risk factor for vitamin D deficiency

Variables	Vitamin D levels					
	Severe vitamin D deficiency versus vitamin D adequacy (<10 vs. \geq 32 ng/ml)			Vitamin D insufficiency versus vitamin D adequacy (10–31.99 vs. \geq 32 ng/ml)		
	<i>p</i> value	OR	95 % CI	<i>p</i> value	OR	95 % CI
Socioeconomic status [†]						
Lower	0.21	4.72	0.42–53.27	0.01*	14.67	2.13–101.19
Upper lower	0.47	2.14	0.27–16.88	0.01*	7.99	1.74–36.69
Lower middle	–	1.00	–	1.00	–	–
Season						
Spring	0.09	4.74	0.79–28.56	0.21	2.94	0.55–15.84
Summer	0.93	0.95	0.29–3.14	0.10	0.41	0.14–1.19
Winter	–	1.00	–	1.00	–	–
Serum calcium (mg/dl)						
<8.5	0.00***	39.41	10.30–150.85	0.04*	3.44	1.04–11.45
8.5–10.5	–	1.00	–	0.41	0.51	0.11–2.47
>10.5	0.78	0.76	0.10–5.54	1.00	–	–
Serum alkaline phosphatase (IU/l)						
<125	0.00***	18.03	3.95–82.44	0.00***	8.70	2.13–35.54
125–250	–	1.00	–	0.12	0.41	0.14–1.26
>250	0.51	0.64	0.17–2.39	1.00	–	–
Serum phosphorous (mmol/l)						
<2.5	0.00***	8.40	2.47–28.61	0.66	0.77	0.24–2.43
2.5–4.5	–	1.00	–	1.00	–	–

Normal values of maternal serum calcium, phosphorus, and alkaline phosphatase are 8.5–10.5 mg/dl; 2.5–4.5 mmol/l; and 125–250 IU/l, respectively

OR odds ratio, CI confidence interval

p value < 0.05 significant, *** *p* value < 0.0001 significant

[†] Modified Kuppuswamy scale

studies from various parts of India which may be due to difference in ethnicity, food habits, and geographical location.

However, data associated with risk factors of VDD during pregnancy are really scanty. Therefore, this study is of vital importance because it explains vitamin D status which is a menacing factor during pregnancy. VDD is highly prevalent among pregnant women in Northern India, and these raises concern about the health consequences for the mother and the offspring. Low serum calcium, serum alkaline phosphate, serum phosphorus, and socioeconomic status are major risk factors associated with VDD in our study population. Pregnant women who have insufficient vitamin D levels may become severely deficient in near future.

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Compliance with ethical requirements and Conflict of interest All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments. Authors declare that they have no conflict of interest.

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