

Correlation between maternal and newborn's Vitamin D level and the factors affecting it

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Abstract

Background: Vitamin D deficiency is highly prevalent in India that too among mothers and as a result newborn baby is prone to develop its deficiency and complications.

Aim: To study the correlation between maternal and newborn's Vitamin D level and to study the variables affecting them.

Materials & method: This prospective observational study was conducted at the Department of Paediatrics, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior (M.P). 97 full term newborns and their mothers were recruited for the study. Maternal and cord blood sample were collected to assess their Vitamin D level. Data was recorded on a pre-designed proforma.

Results: High prevalence of Vitamin D deficiency was found among mothers(85.6%) and their newborns (46.4%) and their levels correlated significantly with each other($p=0.01, r=0.745$). Majority of the mothers had low total sun exposure score during pregnancy (65%). The mothers with medium sun exposure had higher adequate levels of Vitamin D than those who had low sun exposure. Maternal sun exposure

significantly correlated with their newborns Vitamin D level ($p=0.009$). Newborns of the mother who didn't take Calcium and Vitamin D supplements during pregnancy had significantly inadequate Vitamin D levels ($p=0.04$).

Conclusion: High prevalence of Vitamin D deficiency was found among mothers and their newborns. Maternal sun exposure had significant impact on newborn's Vitamin D level.

Keyword: Vitamin D level, Mother, Newborn, Sun Exposure.

Introduction

Vitamin D deficiency is a worldwide problem currently affecting nearly one billion people in the whole world. Vitamin D deficiency among pregnant women ranges from 25% to as high as 84% and in newborns from 11-93% worldwide [2]. In India Vitamin D deficiency among pregnant mothers is highly prevalent and ranges from 76-98%[7].

Vitamin D is fat soluble vitamin and is an important part of Calcium-Vitamin D-Parathyroid hormone endocrine axis. It is important for bone mineralization, muscle contraction, cellular function, nervous system

activities, hormone secretion, cell proliferation and differentiation and immune function. 90% of it is synthesized in body through the direct effect of sunlight (UV-B radiations) on skin hence the level of Vitamin D are affected by sun exposure, time of the day during sun exposure(ideally between 10AM TO 3PM), skin pigmentation, season of exposure, latitude, cloud cover, etc.[16]. Remaining 10% of Vitamin D is obtained through dietary sources (via dairy products, egg yolk, fatty fish and fish oil). During fetal life baby gets Vitamin D from its mother and most of it is stored in baby during last trimester. In previous studies it was found that obese (Body Mass Index(BMI) $\geq 25\text{kg/m}^2$) mothers had lower vitamin D level as it is stored in body fat stores making it less bio available[9]. Infants born to mothers with vitamin D deficiency are at high risk of developing its deficiency and its complications like fetal hypovitaminosis D, neonatal rickets and tetany, low birth weight and small for gestational age (SGA) newborns, infantile rickets, higher prevalence of lower respiratory tract infections secondary to rickets, poor fetal growth and altered neonatal development that may persist into later life[1]. Also there are higher chances of developing infections, diabetes mellitus (due to development of insulin resistance), autism, dental problems, asthma and atopy in later life.

Hence this study was conducted to know the prevalence of Vitamin D deficiency among mothers and their newborn's in the Gwalior region of central India and to study the variables affecting them.

Materials & Method

Present study is a prospective observational study conducted at the Department of Paediatrics, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior between December 2018 to June 2020 after getting

approval from the institute approval committee (IEC protocol no. 106/IEC/GRMC/2018). 97 full term pregnant women and their babies (appropriate for gestational age) were included in the study.

Mothers who didn't give consent, having current or past chronic medical disease such as hyperparathyroidism, collagen disease, cushing disease, chronic renal disease, gastrointestinal disease, lung disease, ovarian tumor and having history of medication with drugs interfering with calcium or vitamin D metabolism like anticonvulsant, corticosteroids, thiazides, thyroxin, heparin were excluded from the study. Preterm and IUGR(intrauterine growth retardation) newborns, twins, sick newborn, newborns with gross congenital malformation were also excluded.

Cord blood and maternal blood sample were collected in non-EDTA vial and immediately transported on ice to the laboratory. Sample were centrifuged and stored at -70°C for assessment of 25(OH) Vitamin D level. Chemiluminiscent immunoassay (CLIA) [LIASION 25(OH) Vitamin D TOTAL assay, DiaSorin] was done to assess its level. Sensitivity of CLIA is $< 4\text{ng/ml}$ and analytical range is 4 - 150 ng/ml. Maternal Vitamin D level was categorized as $< 10\text{ng/ml}$ -deficient, 10-32ng/ml- insufficient and $> 32\text{ng/ml}$ - sufficient for mothers as per ACOG(American College of Obstetric and Gynaecology)[15] guidelines and for newborns as $< 12\text{ng/ml}$ -deficient, 12-20ng/ml-insufficient and $> 20\text{ng/ml}$ -sufficient as per IAP(Indian academy of Paediatric) guidelines[16].

Data was collected on proforma regarding demographic variables of mother, maternal characteristics (age, parity, dietary habits, occupation), anthropometric variables of mother (weight, height and body mass index) and newborn (birth weight, length, head

circumference and anterior fontanelle size), calcium and vitamin D supplementation during pregnancy and sun exposure. Sun exposure scores were recorded on the basis of Hanwell, Vieth, et al[11] criteria[Table 1]. Data was statistically analyzed using the SPSS (statistical package for social sciences, Chicago,IL,USA) software version 16.0 and MS EXCEL. The Chi-square test was used to compare the qualitative data. Pearson coefficient was used to find the correlation between maternal and newborn's Vitamin D level. p value <0.05 was considered significant.

Table 1: Daily sun exposure score

Time of exposure	
<5mins.	Score 0
5-30mins.	Score 1
>30mins.	Score 2
Skin exposed to sun	
Face and hands uncovered	Score 1
Arms uncovered	Score 2
Legs uncovered	Score 3
Bathing suit	Score 4
Total sun exposure	
Score 0-2	Low exposure
Score 3-5	Medium exposure
Score 6-8	Good exposure

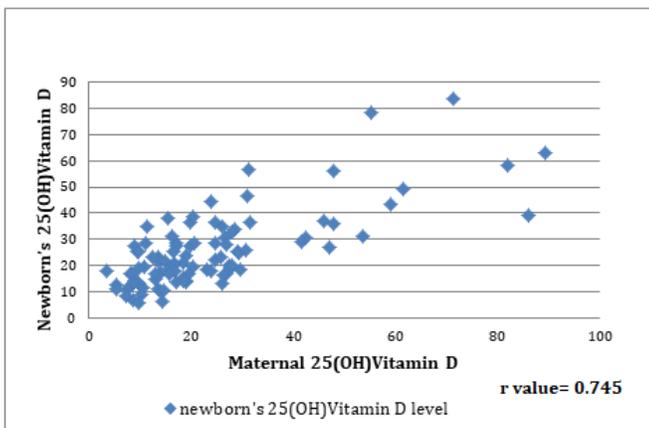
Results

In this study Vitamin D level was found to be inadequate in 85.6% mothers. 18.5% mothers were severely deficient(<10ng/ml), 67.1% had insufficient levels (10-32ng/ml) whereas only 14.4% mothers had sufficient levels (>32-100ng/ml). Among newborns 46.4% had inadequate levels. 11.4% newborns had severe deficiency(<12ng/ml), 35% had insufficiency(12-20ng/ml) while 53.6% newborns had

adequate levels(>20ng/ml). So high prevalence of Vitamin D deficiency was found among both mothers and their newborns. Also significant correlation was found between their Vitamin D levels (p=0.01, r=0.745)[Figure 1]. Cord blood alkaline phosphatase (ALP) level of majority of the newborns (88.6%) was in the normal range(150-420IU/L)[17] and no significant correlation was found with newborn's Vitamin D level (p=0.057, r = -0.194). It wasn't found to be increased in newborns with deficient level of 25(OH) Vitamin D.

Majority of the mothers (65%) had low daily sun exposure score (0-2) during pregnancy while 34% had medium exposure (scores 3-5) and only 1% had good exposure (score 6-8). Mothers with low sun exposure had comparatively more deficient Vitamin D level (22.2%) than those who had medium sun exposure (12.2%). Also newborns of the mother with medium sun exposure had significantly more adequate level of Vitamin D than those newborns whose mother had medium sun exposure(p=0.001). Vitamin D level of mother was significantly affected by the season of sample collection with least deficient and most adequate level found during summer season (p=0.01). Most of the mothers who didn't take Calcium and Vitamin D₃ supplements during pregnancy had inadequate Vitamin D level but it wasn't statistically significant but among their newborns statistically significantly inadequate levels were found (p=0.04).

Figure 1: Linear regression curve showing correlation of Maternal and Newborn's 25(OH) Vitamin D level



Weight and height of mother individually had no significant impact on their and their newborn's Vitamin D level but all the mothers with Body Mass Index (BMI) <18.5kg/m²(underweight) and ≥25kg/m² (overweight) and their newborns had significantly insufficient levels (p<0.05). All the mothers with BMI within normal range (18.5-24.9kg/m²) and their newborns had adequate levels. Mothers within the younger age group (20-30yrs) had

significantly deficient level of Vitamin D than the mothers in the age group of 30-40yrs (p<0.05). Residence (rural/ urban), socio- economic status(p=0.7), religion(p=0.7), parity(p=0.47), educational status(p=0.49), dietary habits(p=0.9) and skin tone of mother (p=0.5) had no significant impact on Vitamin D level of mother and their newborn. Among newborn's male -female sex ratio was 0.8:1. Nearly 60% newborns with length between 50-53cm had adequate levels whereas the newborns with length between 46-49cm only 30% had adequate levels and their length significantly correlated with their Vitamin D level(p=0.008).Newborn's birth weight (83.5% had weight between 2500-3000gms), head circumference (62% had HC between 32-34cm), anterior fontanalle size (76% had AF size between 2.5-4.5cm) and gender had no significant correlation with their Vitamin D level.

Table 2: Relation of Maternal Variables with their 25(OH) Vitamin D level

Sn.	Variables	Severe Vit D deficiency (<10ng/ml)	Vit D insufficiency (10-32ng/ml)	Vit D adequacy (32-100 ng /ml)	CI	p value
		n=18(18.5%)	n=65(67.1%)	n=14(14.4%)		
1	Age(yrs) ▪20-30 ▪30-40	16 (18%) 02 (25%)	62 (69.6%) 03 (37.5%)	11 (12.4%) 03 (37.5%)	-	0.00001
2	Maternal weight (kg) ▪40-55 ▪55-70	17 (18.7%) 01 (16.6%)	60 (65.9%) 05 (83.4%)	14 (15.4%) 00	47.8, 49.37	0.75
3	Height(cm) ▪145-150 ▪151-155 ▪>156	11 (17.8%) 07 (20.5%) 00	42 (67.7%) 22 (64.7%) 01 (100%)	09 (14.5%) 05 (14.8%) 00	149.3, 150.26	0.92
4	Body mass index(kg/m ²)					

	▪<18.5	00	03 (100%)	00	21.39,2	0 .000
	▪18.5-24.9	18 (19.4%)	61 (65.6%)	14 (15%)	2.02	01
	▪≥25	00	01 (100%)	00		
5	Type of skin					
	▪Light	08 (25%)	21 (65.6%)	03 (9.4%)	-	0.55
	▪Medium	06 (12.6%)	34 (70.8%)	08 (16.6%)		
	▪Dark	04 (23.6%)	10 (58.8%)	03 (17.6%)		
6	Season					
	▪Spring	08 (17%)	17 (70.2%)	01 (12.8%)	1.99,	0.015
	▪Summer	04 (15.4%)	16 (69.2%)	09 (15.4%)	2.33	
	▪Winter	06 (21.6%)	32 (62.2%)	04 (16.2%)		
7	Maternal Calcium and Vitamin D supplementation during pregnancy					
	▪No	11 (29.7%)	20 (54%)	06 (16.3%)	-	0.059
	▪Yes	07 (11.6%)	45 (75%)	08 (13.4%)		
	▪Started at-					
	-1st trimester	00	21 (100%)	00		
	-2nd trimester	06 (20.7%)	18 (62%)	05 (17.3%)		0.58
	-3rd trimester	01 (10%)	06 (60%)	03 (30%)		
	▪Duration of intake					
	-<1month	00	01 (100%)	00		
	-1-3months	02 (15.4%)	09 (69.2%)	02 (15.4%)		0.36
	-4-6months	03 (11.6%)	21 (80.7%)	02 (7.7%)		
	->6months	02 (10%)	14 (70%)	04 (20%)		

CI - Confidence interval

Table 3: Correlation of Newborn's variables with their 25(OH)Vitamin D level

Sn.	Variables	Severe Vit D deficiency (<12ng/ml)	Vit D insufficiency (12-20ng/ml)	Vit D adequacy (>20ng/ml)	CI	p value
		n=11(11.4%)	n=34(35%)	n=52(53.6%)		
1	Birth weight(gms)					
	▪2500-3000	10 (12.4%)	24 (29.6%)	47 (58%)	.06,	0.056

	<ul style="list-style-type: none"> ▪3000-3500 ▪3500-4000 	01 (8.4%) 00	07 (58.3%) 03 (75%)	04 (33.3%) 01 (25%)	10.6	
2	Length(cm) <ul style="list-style-type: none"> ▪46-49 ▪50-53 	00 11 (13.6%)	11 (68.7%) 23 (28.4%)	05 (31.3%) 47 (58%)	50.07,50.4	0.008
3	Head circumference(cm) <ul style="list-style-type: none"> ▪32-34cm ▪35-37cm 	09 (14.6%) 02 (5.7%)	17 (27.4%) 17 (48.6%)	36 (58%) 16 (45.7%)	31, 43.7	0.08
4	Anterior fontanelle size(cm) <ul style="list-style-type: none"> ▪<2.5cm ▪2.5-4.5cm ▪>4.5cm 	02 (6.3%) 06 (10.7%) 03 (33.3%)	14 (43.7%) 16 (28.6%) 04 (44.4%)	16 (50%) 34 (60.7%) 02 (22.3%)	2.96, 3.36	0.07
5	Cord blood ALP level (U/L) <ul style="list-style-type: none"> ▪<150 ▪150-420 ▪>420 	00 11 (12.8%) 00	04 (36.4%) 30 (34.8%) 00	07 (63.6%) 45 (52.4%) 00	255.8,299. 2	0.81
7	BMI of mother (kg/m ²) <ul style="list-style-type: none"> ▪<18.5 ▪18.5-24.9 ▪≥25 	00 11 (11.8%) 00	03 (100%) 30 (32.2%) 01 (100%)	00 52 (56%) 00	21.39,22.0 2	0.00001
8	Maternal Calcium and Vitamin D supplementation during pregnancy <ul style="list-style-type: none"> ▪No ▪Yes ▪Started at- <ul style="list-style-type: none"> -1st trimester -2nd trimester -3rd trimester ▪Duration of intake 	08 (21.6%) 03 (5%) 01 (48%) 02 (6.9%) 00	11 (29.8%) 23 (38.3%) 05 (23.8%) 15 (51.7%) 03 (30%)	18 (48.6%) 34 (56.7%) 15 (71.4%) 12 (41.4%) 07 (70%)	-	0.04 0.1

-<1month	00	00	01 (100%)		0.18
-1-3months	00	04 (30.7%)	09 (69.3%)		
-4-6months	01 (3.4%)	14 (46.6%)	15 (50%)		
->6months	02 (12.5%)	05 (31.3%)	09 (56.2%)		

CI - Confidence interval, BMI- Body Mass Index

Table 4: Effect of sun exposure of mother on Maternal and Newborn's Vitamin D level

Daily sun exposure of mother	Maternal Severe Vit D deficiency (<10ng/ml) n=18(18.5%)	Maternal Vit D insufficiency (10-32ng/ml) n=65(67.1%)	Maternal Vit D adequacy (32-100ng/ml) n=14(14.4%)	CI	p value
▪Time of exposure					
-Score 0	07 (36.8%)	09 (47.4%)	03 (15.8%)	1.03,	0.11
-Score 1	05 (12.7%)	31 (75.6%)	05 (12.2%)	1.33	
-Score 2	06 (16.2%)	25 (67.6%)	06 (16.2%)		
▪Skin exposed to sun					
-Score 1	10 (29.4%)	21 (61.8%)	03 (8.8%)	1.58,	0.11
-Score 2	08 (13.3%)	41 (68.4%)	11 (18.3%)	1.79	
-Score 3	00	03 (100%)	00		
-Score 4	00	00	00		
▪Total Score					
-Score 0-2	14 (22.2%)	40 (63.5%)	09 (14.3%)	1.82,	0.48
-Score 3-5	04 (12.2%)	24 (72.7%)	05 (15.1%)	2.42	
-Score 6-8	00	01 (100%)	00		
Daily sun exposure of mother	Newborn's Severe Vit D deficiency (<12ng/ml) n=11(11.4%)	Newborn's Vit D insufficiency (12-20ng/ml) n=34(35%)	Newborn's Vit D adequacy (>20ng/ml) n=52(53.6%)	CI	p value
▪Time of exposure					
-Score 0	02 (10.6%)	07 (36.8%)	10 (52.6%)	1.03,	0.26
-Score 1	04 (9.7%)	19 (46.4%)	18 (43.9%)	1.33	
-Score 2	05 (13.6%)	08 (21.6%)	24 (64.8%)		
▪Skin exposed to sun					
-Score 1					
-Score 2	04 (11.7%)	20 (58.8%)	10 (29.5%)	1.58,	0.001

-Score 3	07 (11.6%)	14 (23.4%)	39 (65%)	1.79	
-Score 4	00	00	03 (100%)		
	00	00	00		
▪ Total Score					
-Score 0-2	08 (12.6%)	28 (43.7%)	28 (43.7%)	1.82,	0.009
-Score 3-5	03 (9%)	06 (18.3%)	24 (72.7%)	2.42	
-Score 6-8	00	01 (100%)	00		

Discussion

In present study high prevalence of Vitamin D deficiency was found among both mothers(85.6%) and their newborns (46.4%) in the Gwalior region of Central India. This is the first landmark study of this region. Similarly the studies done in different parts of India in past showed high prevalence of Vitamin D deficiency in mothers and their newborns. Minhaz Husain et al[2](north India) found deficient levels in 47% mothers and 45% of their newborns. Paulraj et al[4] (south India) found 62.97% mother and 63% of their newborns with deficient levels and strong positive correlation ($r=0.898$, $p<0.05$) between their levels was found. So it shows that Vitamin D status of mother needs to be improved which will eventually improve the Vitamin D status of newborn.

In spite of the availability of ample of sunlight majority of the mothers had overall low sun exposure score. Sun exposure of mother significantly affected newborns Vitamin D level($p=0.009$). No significant correlation between sun exposure of mother and their Vitamin D level was found by Maria et al[19] (studied 225 mothers, Brazil)($p=0.52$) and Busadee et al[20] (recruited 147 pregnant women, Thailand)($p=0.62$) but Dipti Sarma et al[7] (250 mother-newborn pairs, Assam) and Dipali et al[10] (100 mother-newborn pairs, Patna)found that maternal Vitamin D level was

significantly adequate in mothers with higher sun exposure($p=0.0001$ and $p=0.003$ respectively). Daily sun exposure of pregnant mothers needs to be increased to improve Vitamin D levels in their newborns. Mothers with face, hands, arms and legs exposed to sun for 5-30mins or mothers with face, hands and arms(not legs) exposed for >30mins daily had more adequate levels in the present study. So pregnant women should be exposed to sunlight daily for at least 30mins. between 10am to 3pm[16]. Season of sample collection significantly affected maternal Vitamin D level with most adequate levels found during summer and most deficient level found during winters($p=0.01$). Similarly Busadee et al[20] found higher proportion of pregnant women to be deficient during winter season ($p=<0.01$). Mothers with BMI $\leq 18\text{kg/m}^2$ and $\geq 25\text{kg/m}^2$ had insufficient Vitamin D levels. Similarly Mamta et al[12] found 95% of the obese women in their study to be severely deficient which was statistically significant ($p=0.002$). Lisa, Janet et al[8] found pre pregnancy obese mothers to be having deficient levels of Vitamin D level. So nutritional status of mother needs to be regulated during pregnancy. Body Mass Index(BMI) of mother at the first antenatal visit or if possible pre pregnancy BMI should be documented and not merely the weight of mother. Thereafter mother should be advised to gain weight according to their BMI as per the recommended guidelines.

The mothers who didn't take Calcium and Vitamin D₃ supplements during pregnancy had comparatively more deficient levels than those mothers who took supplements. Though the values weren't statistically significant ($p=0.059$) their newborns had significantly deficient levels ($p=0.04$) So it indirectly suggests that all the pregnant mothers should receive Calcium and Vitamin D₃ supplements. Arif et al[21] found that pregnant women who didn't take supplements during pregnancy had 4.5 times increased risk of developing Vitamin D deficiency during pregnancy.

Among newborn's anthropometric variables length of the newborn significantly correlated with their Vitamin D levels and newborns with longer lengths were found to have more adequate levels ($p=0.008$). Paulraj et al[4] found that newborns with deficient levels of Vitamin D had shorter length. Morley et al [14] found that low maternal Vitamin D was associated with reduced intrauterine long bone growth. Birth weight($p=0.056$), head circumference($p=0.08$) and anterior fontanelle size($p=0.07$) had no significant correlation with newborn's Vitamin D level.

Most of the newborns (88.6%) had cord blood ALP level within normal range(150-420U/L). ALP level is supposed to increase in Vitamin D deficient states but none of the newborn with Vitamin D deficiency had elevated cord blood ALP level. It may be because in case of Vitamin D deficiency in newborns metabolic bone disorders may take time to develop and hence cord blood alkaline phosphatase levels weren't elevated. Similar results were found by Minhaz Husain et al[2] hence ALP seems to be less sensitive in detecting of Vitamin D deficiency among newborns. In contrast O G Brooke et al[6] found inverse relation between newborn's Vitamin D level and cord blood ALP level

i.e. newborns with deficient levels of Vitamin D were found to have high ALP level.

Conclusion

This highly prevalent Vitamin D deficiency among both mothers and their newborns needs to be addressed urgently. As highly significant correlation between their levels was found so if the Vitamin D status of mother is improved it will eventually improve the Vitamin D status of their newborn. Sun exposure of mother significantly affected their newborn's Vitamin D level. As majority of the mothers had low sun exposure during pregnancy there is need to increase it and for this training for sun exposure of pregnant mothers should be included in the curriculum of ASHA(Accredited social health activist) and AWW(Anganwadi worker) workers. Also the newborns of mothers who didn't take Calcium and Vitamin D supplements during pregnancy had significantly deficient Vitamin D levels hence all the mothers should take supplements during pregnancy and to ensure this the Maternal and Child Protection (MCP) Card should have column for dose and duration of Calcium and Vitamin D supplements taken pre and post conception.

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