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Original article

Maternal Vitamin D Levels in Gestation - An Observational Cross Sectional Study in the Rural Population of South India

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Abstract

Background:Vitamin D* called the sunshine vitamin is essential throughout life. Pregnancy is an altered physiological state in women, which requires proper nourishment. During gestation, this vitamin also plays an important role in development of the fetus. ***Objective:***To observe the serum vitamin D (25diohydroxycholicalciferol) levels and serum calcium levels in the maternal blood during the three trimesters. ***Design:*** Observational Cross sectional study. ***Study population:*** Rural Mothers from Kancheepuram District, Tamil Nadu South India. We used 50 antenatal blood samples as experimental group and 15 as control group. The age group included 20-40 years. Blood samples were collected from 50 antenatal mothers between 20 – 40 years age group, from Obstetrics and Gynecology OPD for their routine antenatal check-ups, after getting duly signed informed consent. Control group had 15 women in the same age group not pregnant. ***Results:*** The results were tabulated. The mean value of 25dihydroxy vitamin D was observed very low than normal levels in all the three trimesters. The mean value of serum vitamin D in first trimester was 50.87 ng/ml, mean value of serum vitamin D in second trimester was 54.05.ng/ml, and mean third trimester vitamin D was 61.24ng/ml which was well below the optimum level of 100ng/ml. ***Conclusion:*** The vitamin D deficiency with normal level maintenance of serum calcium shows the compensatory mechanism that involves the normal calcium level maintence with resorption of bones by the osteoclastic actions to correct the deficit. If the deficiency is left untreated it may lead to faster osteoporosis in the mother.

***25 dihydroxycholicalciferol**

Keywords: ***Maternal, Vitamin D, First trimester, Second trimester, Third trimester, Serum Calcium***

Introduction

80% of the vitamin is synthesized from the sunlight sources and remaining 20% from dietary sources (Kamal AS shoumer A, 2015).Vitamin D is a vitamin with primary source from the sunlight. Being a fat soluble vitamin with cholesterol structure vitamin D is produced from the 7-hydroxycholesterol (subcutaneous fat) on exposure to sunlight. Vitamin D is therefore not a real vitamin. Safe sunlight exposure or consumption of food stuffs artificially supplemented with vitamin D is necessary (Kamal AS 2015, ChihChien Sung 2012) 7 Hydroxycholesterol is stored in the liver and activated whenever demand arises. The fetus depends on the maternal supply of vitamin D, calcium, and phosphorus, which is transmitted across the placenta. In fact, maternal and cord blood 25-hydroxyvitamin D (25[OH] D) are highly correlated in terms of supporting the importance of this vitamin for fetal development (ChihChien Sung 2012). Vitamin D deficiency has been reported as a common problem worldwide. Vitamin D deficiency [defined as 25(OH)D< 30 n mol/L according to the Institute of Medicine (National Academy of Sciences, Washington, D.C., USA)] or inadequacy [25(OH)D of 30–49.9 n mol/L], but the RDA for tropical countries has not been determined. RDA of this vitamin differs based on the sunlight exposure, climatic changes (Xiao J-P, Zang J,2015). Deficiency during gestation is more acute. The vitamin deficiency not only affects the mother but also the foetus. The study focuses on the vitamin D levels in various trimesters of pregnancy. The compensatory mechanism involved in maintaining the serum calcium levels normal despite there is deficiency of vitamin D.

Materials and methods

Vitamin D levels (serum 25 dihydroxycholicalciferol) were estimated from venous blood samples of 15 antenatal women of first, second , third trimester each and in 15 non pregnant women. 60 venous blood samples got from Obstertics and Gynaecology Outpatient department of Ponniayah Ramajayam Institute of Medical Sciences, Kancheepuram were used for the study. The blood samples were collected after getting ethical clearance and institutional review board permission from the institution (PRIMS/IEC-certi-002/16.02.2018) The mothers involved in the study were informed about the study and written consent was got from the participants.The blood collected for routine procedures was used for the assessment of the vitamin D levels.

The participants were dark pigmented, with considerable outdoor activities. Tamil Nadu in India has tropical climatic conditions with sufficient sunlight exposure. The samples were collected from January – May. Life style, food habits were accessed with questionnaires.The participants were not on supplementation for nutrients except iron and folic acid. Most of the patients were unaware of their vitamin D status. All the participants predominantly had rice based diet. The BMI was observed to be on the higher side

Exclusion criteria

Mothers with chronic infections, diabetes, hypertension, epileptic (seizures), multiple gestations were not included in the study.

Study Type: Observational Cross Sectional Study

Sample Size: 60 samples

Method

Under aseptic conditions 5ml of venous blood from antenatal mothers were taken during their routine checkup. The blood collected was centrifuged and serum was separated using REMI 250-300 RPM/per minute. The sample was centrifuged for 3 minutes. The serum was utilized for estimation of vitamin D. The vitamin D estimation was done in Vimta labs pvt limited Chennai.

The estimation was done using Chemiluminescence (CLIA) method

Observations

First Trimester

The value of serum 25 OH Cholicaliciferol in venous blood samples was observed to be lower than 30nmol/L(12ng/ml) in most of the peripheral blood samples. The mean of 25 dihydroxycholicalciferol level and serum calcium was calculated. The mean vitamin D level was insufficient in the first trimester, gradually increased in second trimester and in the third trimester. The serum calcium levels were found to be normal in all the trimesters while the vitamin D (25 hydroxy vitamin D) was recorded insufficient. Vitamin D insufficiency was not affecting the serum calcium levels in the patients. (Table 1)(Anne Marie Uwitoze et al 2018, BrittevanWeert 2015 et al, Souberbielle JC 2010 et al)

In first trimester the mean serum vitamin D was 50.86ng/ml.

Second Trimester

The mean value recorded was 54.05ng/ml the values were slightly higher in second trimester when compared to the first trimester. The values recorded were still lower than the optimal 25 dihydroxyvitamin D values recommended as dietary allowance. (Table 2)

Third Trimester

The mean value of third trimester serum 25 dihydroxy vitamin D is 64ng/ml. This has progressively increased from second trimester to third trimester. There is gradual increase in the 25 dihydroxyvitamin D in the third trimester. While the serum calcium levels were maintained normal. Third trimester has reported a gradual increase in the serum vitamin D levels when compared to first and second trimester.(Table 3)

Control Samples

The mean vitamin D levels in control sample were 56.85ng/ml. The control sample was taken from non-pregnant women from second to fifth decade of life. (Table 4)

Table 1: Tabulation of serum calcium and vitamin D values estimated by Chemiluminescence (CLIA) 25 dihydroxy vitamin D has been discussed in terms of ng/ml

[2.5 nmol/L 25(OH)D = 1 ng/mL25(OH)D]. In first, second and third trimester

SI Units: < 50 nmol/L - Deficient 50 - < 75 nmol/L - Insufficient 75 - 250 nmol/L - Sufficient > 250 nmol/L - Upper Safety Limit

Pt.id*	Age	Serum Calcium	Vitamin D	Gestation weeks	Levels in SI units interpretation
1	24/F	7mg/dl	56.25ng/ml	9 weeks 2 days	Insufficient
2	21.f	6.5mg/dl	59.5ng/ml	15 weeks	Insufficient
3	28/f	10mg/dl	52ng/ml	12 weeks	Insufficient
4	28/F	8.2mg/dl	44.25ng/ml	11 weeks 4 days	Deficient
5	24/F	7mg/dl	34.75ng/ml	12 weeks 4 days	Deficient
6.	25/F	7.8mg/dl	55.5ng/ml	10 weeks	Insufficient
7	25/f	8.9mg/dl	51ng/ml	7 weeks	Insufficient
8	22/F	8.3mg/dl	65.75ng/ml	11 weeks	Insufficient
9	22/F	9.4mg/dl	54ng/ml	9 weeks 5 days	Insufficient
10	23/F	9.2mg/dl	36ng/ml	8 weeks 2 days	Deficient
11	39/F	8.6mg/dl	40ng/ml	12 weeks 6 days	deficient
12	27/F	9.2mg/dl	46ng/ml	7 weeks 3 days	deficient
13	22/F	8.5mg/dl	62ng/ml	8 weeks	insufficient
14	22/F	8.8mg/dl	42ng/ml	9 weeks	deficient
15	27/F	9.1mg/dl	64ng/ml	11 weeks	insufficient

Mean serum vitamin D: 50.87ng/ml
First Trimester: Deficient –40% of the first trimester mothers
Insufficient -60% of the first trimester mothers

Table 2: Serum vitamin d and calcium observed in second trimester tabulated.
SI Units: < 50 nmol/L - Deficient 50 - < 75 nmol/L - Insufficient 75 - 250 nmol/L - Sufficient > 250 nmol/L - Upper Safety Limit

	SECOND TRIMESTER				
Pt.id	**Age**	**Gestation in weeks**	**Serum calcium**	**Vitamin D**	**Levels in SI units interpretation**
1	23/F	22 weeks	9.7mg/dl	55ng/ml	Insufficient
2	24/F	24 weeks	9.9mg/dl	65ng/ml	insufficient
3	24/f	23 weeks	9.8mg/dl	56ng/ml	insufficient
4	26/f	24 weeks	8mg/dl	49.75ng/ml	deficient
5	23/f	28 weeks 4 days	9.8mg/dl	54.25ng/ml	insufficient
6	27/f	18 weeks 3 days	9mg/dl	51ng/ml	insufficient
7	27/f	27 weeks	9.8mg/dl	68 ng/ml	insufficient
8	27/f	19 weeks	8.3mg/dl	31 ng/ml	deficient
9	20/f	20 weeks 5 days	8.6mg/dl	42ng/ml	deficient
10	24/f	17 weeks	9.3mg/dl	62ng/ml	insufficient
11	29/f	16 weeks	9.8mg/dl	81.1ng/ml	sufficient
12	28/F	14 days	9.5mg/dl	44.25ng/ml	deficient
13	24/F	16 weeks 4 days	8.4mg/dl	34.75ng/ml	deficient
14	25/F	17 weeks 2 days	8.1mg/dl	51ng/ml	insufficient
15	22/F	20 weeks	9.5mg/dl	65.75ng/ml	insufficient

Mean serum vitamin D in second trimester 54.05 ng/ml
Deficient – 33.3.% of the second trimester mothers
Insufficient – 60% of the second trimester mothers
Sufficient – 6.7% of the second trimester mothers

Table 3: Serum vitamin D and serum calcium observed in third trimester tabulated
SI Units: < 50 nmol/L - Deficient 50 - < 75 nmol/L - Insufficient 75 - 250 nmol/L - Sufficient > 250 nmol/L - Upper Safety Limit

	THIRD TRIMESTER				
Pt.id	Age/sex	Gestation in weeks	calcium	Vitamin D	Levels in SI units interpretation
1	28/F	35weeks 3 days	8.9mg/dl	15.25ng/ml	Deficient
2	20/f	32 weeks	9mg/dl	59.9ng/ml	Insufficient
3	28/f	29 weeks 6 days	7.8mg/dl	29ng/ml	deficient
4	22/F	31 weeks 3 weeks	10.4mg/dl	42ng/ml	deficient
5	27/F	30 weeks 3 days	11mg/dl	64ng/ml	insufficient
6	20/F	34 weeks	8.7mg/dl	72ng/ml	insufficient
7	26/F	34 weeks	8.2mg/dl	63.25ng/ml	insufficient
8	21/F	30 weeks	7.3mg/dl	86.5ng/ml	sufficient
9	26/F	34 weeks	9.4mg/dl	56.25ng/ml	insufficient
10	20/F	33 weeks	10.5mg/dl	72.75ng/ml	Insuffcient
11	39/F	34 weeks 6 day	11.2mg/dl	101.25ng/ml	sufficient
12	22/F	33 weeks 4 days	9.5mg	43.5ng/ml	Deficient
13	24/F	35 weeks	9.3mg/dl	55ng/ml	insufficient
14	26/F	32weeks 4 days	8.2mg/dl	78ng/ml	sufficient
15	28/F	34weeks	9.4mg/dl	80ng/ml	sufficient

Mean serum vitamin D in third trimester: 61.24ng/ml
Deficient -27%
Insufficient – 46%
Sufficient – 27%

Table 4: Vitamin D tabulation in control group –Women of the same age group as experimental group but not pregnant
SI Units: < 50 nmol/L - Deficient 50 - < 75 nmol/L - Insufficient 75 - 250 nmol/L - Sufficient > 250 nmol/L - Upper Safety Limit

Pt.id	**Age**	**Serum calcium**	**Vitamin D**	**Levels in SI units interpretation**
1	27/f	9.8mg/dl	45.45nmol/L	deficient
2	35/f	9.3mg/dl	58.78nmol/L	insuffcient

3	42/f	8.5mg/dl	68.45nmol/L	insufficient
4	33/f	8.8mg/dl	54.93nmol/L	insufficient
5	48/f	10.3mg/dl	89.7nmol/L	Sufficient
6	18/f	9.6mg/dl	70.2nmol/L	insufficient
7	36/f	8.1mg/dl	60.78nmol/L	insufficient
8	40/f	10.3mg/dl	45nmol/L	deficient
9	32/f	11.4mh/dl	68nmol/L	insufficient
10	37/f	12.1mg/dl	76nmol/L	sufficient
11	26/F	11.8mg/dl	62nmol/L	insufficient
12	23/F	8.4mg/dl	56nmol/L	insufficient
13	27/f	9.2mg/dl	55nmol/L	insufficient
14	31/f	11.3mg/dl	42nmol/L	deficient
15	22/f	11.7 mg/dl	44nmol/L	deficient

Mean Serum Vitamin D levels: 59.75nmol/L

Control group:

26 % deficient

60% insufficient

13.3% sufficient

Discussion

Vitamin D deficiency is commonly observed in 5-50% of pregnant women (Megan L. Mulligan, BA et al2010). The study brings to light the vitamin D status of women in early reproductive age group during various trimesters of gestation in and around Kanchipuram district. The mean maternal age group was 26 years. The study mainly enlightens on the early reproductive age group participants belonging to rural population of Kancheepuram district, India. The patients who were in middle and low socio economic status were included.

The samples were collected between the months of January – May 2017, when it was summer at Tamil Nadu.

The study was conducted as a public health awareness programme for rural pregnant women. Random sample selection was done.

The serum 25 hydroxyvitamin D levels were low in 80% of the population first trimester and third trimester. There is a sharp decrease in the 25 (OH) D levels. This is due to the increased utilisation of vitamin D in maintaining calcium homeostasis and involving itself in development of bones (Elvira Larque, Eva Moralo2018). This may lead to development of reduced bone density in women at early ages. While during second trimester an optimum level of 50ng/l was maintained as an average.

The overall median value was 65nmol/L, while the first second and third trimester average was 55, 60 and 67nmol/L has been recorded in the studies conducted in western countries like UK. (Lawlor DA, Wills AK2013)

First Trimester

According to Sera Ates et al the first trimester serum vitamin D levels were observed to be less than 10ng/ml in 45% of the singleton pregnancies in reproductive age group. (Ates S, Sevket O, et al 2016)

The vitamin D levels were also observed to be between 15-50ng/ml. Deficiencies during the developmental period remains crucial. Deficiency of vitamin D has been associated with preterm births. According to Bodnar et al 2007 and Baker et al 2010 , vitamin D deficiency in first trimester has been associated with preeclampsia. Adverse health outcomes such as preeclampsia, low birth weight, neonatal hypocalcemia, poor postnatal growth, bone fragility, and increased incidence of autoimmune diseases have been linked to low vitamin D levels during pregnancy and infancy.(Megan L. Mulligan, BA et al 2010)According to Li N et al (2017)25 (OH) deficiencyhas also been associatedwith recurrent miscarriages at fetal maternal interface (Li N,Wu HM et al 2017).

Li N et al also states that the decidua tissues collected during the abortion procedure had 25 (OH) D deficiency, IL- 17, TGF beta, IL- 23 was estimated to be deficient in recurrent spontaneous abortion cases. (Li N,Wu HM et al 2017).

According to Specker B in 2004 High maternal levels of 1,25(OD)2D is essential to increase intestinal calcium absorption during pregnancy and to support calcium for maternal and foetal metabolism

Second Trimester

This study reports mean vitamin D level of 55ng/ml was observed in south Indian rural pregnant women during second trimester.According to Xiao J-P et al in 2015 the mean serum vitamin D levels among Chinese pregnant women in second trimester was 35ng/ml.

The mean value in Chinese pregnant women in second trimester remains at the deficient limit and it has been recorded low due to the seasonal variations and dress code etc. In comparison the median serum vitamin D in Indian pregnant women population is recorded more than the Chinese population due to the tropical climatic conditions.

Third Trimester

Significant changes occur in maternal vitamin D and calcium metabolism during pregnancy to provide calcium needed for fetal bone mineral accretion. The calcium is made available to the developing fetus from the maternal serum levels. The study reports a median value of 61ng/ml in the third trimester pregnant women.

According to Thomas D et al in 2011 the mean serum vitamin D values were less 48nmol/L (19.2ng/ml). The longitudinal assessment of the serum vitamin D levels indicate that the serum vitamin D levels were very low in first trimester and it progressively increased in second trimester and the third trimester reports the peak of the recorded values, though values reported were within deficient range.

According to Bonny Specker approximately 25-30 g of calcium are transferred to the foetus for skeletal development, most of which is transferred during the last trimester.(Bonny Specker 2004) It has been estimated that 250mcg/d calcium is sent to the foetus during third trimester (Widdowson EM 1981). The requirement for serum calcium levels increases in the third trimester. The normal level is maintained by increased intestinal absorption, reabsorption and bone demineralization. Mothers with acute vitamin D deficiency have normal calcium levels by the compensatory mechanism of the body. In order to maintain normal serum calcium levels bone osteoclastic activity increases leading to osteoporosis in earlier ages in women (Bonny specker et al 2004)

The compensatory mechanism can lead to secondary hyperparathyroidism in mothers due to increase in parathromone.

The results of the longitudinal study by Y Agudelo-Zapata et al.in 2018 reports the lowest median serum vitamin D levels reported in first trimester , increased in second trimester and in third trimester it graduallyincreased based on the limits in gestational demand(Augdelo Zapata at al)

On comparing the control group women with experimental group the mean 25OHD levels in non-pregnant women were 31.9 ng/mL and 34.9 ng/mL during follicular and luteal phase, respectively ($P < 0.01$). Mean serum 25OHD levels in healthy pregnant women were 26.5, 30.1 and 31.9 ng/mL, at first, second and third trimester, respectively ($P < 0.001$).(Agudelo Zapata Y et al) Women are to educated about the importance of vitamin D supplementation and its association with infertility, polycystic ovary syndrome, obstetrical complications(N li,HM Wu et al 2017)

Community based studies conducted earlier have shown significant deficiency in the vitamin D levels in all age groups. (Table 5)

Inference

Early detection of vitamin D deficiency can prevent risk factors in pregnancy. New studies are warranted on this subject to elucidate the relationship of maternal vitamin D deficiency with skeletal, non-skeletal, autoimmune, cardiovascular disorders, diabetes and certain types of foetal imprinting (Souberbielle JC et al 2010)

Further monitoring of calcium and vitamin D levels in gestation along with iron and folic acid supplements to be given to the mother.Health education on intake of calcium and vitamin D to be given to the rural mothers. First trimester deficiency is often associated with miscarriages hence supplements to be started when the gestation is planned.

Table 5: Community-based studies on prevalence of Vitamin D deficiency in India (cited from Vitamin D deficiency in India by Aprna et al) [21, 22-38]

S.No	Author, year of publication	Site of study	Sample size	Study participants	Prevalence (%)
1	Suryanarayana et al[22] 2018	Hyderabad, Urban	298	≥60 yearsTotal MenWomen	56.3 57.2 54.2
2	Kapil et al[23] 2017	Shimla, himachal Pradesh	626	Children (6-18 years)	93
3	Chowdhury et al [24]2017	Delhi	960	6-30 months	34.5
4	Srimani et al [25] 2017	West Bengal	222	Rural postmenopausal women (45-70 years)	51
5	Misra et al[26] 2017	Ballabargh	381	Rural Women (20-60) years	90.8
6	Rattan et al [27] 2016	Cuttack ,Odisha	3056	30-65 years	84.9
7	Gunjaliya et al [28], 2015	Ahmadabad, Gujarat	444	No specific age group	93.3
8	Bachhel et al [29] 2015	Punjab	150	17-68 years	90
9	Tandon et al,[30] 2014	Jammu and Kashmir	312	Postmenopausal women	53.4
10	Agarwal and Sharma [31]2013	Varanasi	200	Adults ≥50 years	58
11	Marwa et al 2011 [32]	Delhi	1346	Urban Adults≥ 50	91.2
12	Harinarayan et al [38]2011	Tripuati	55	Reproductive female age 20-35	76.3
13	Sahu et al 2009 [33]	Barabanki	139	Rural Pregnant	74
14	Paul et al 2008 [34]	Tirupati	150	Semi urban postmenopausal women	50
15	Puri et al 2008 [35]	Delhi	404	Urban Female adeloscent	90.8
16	Goswami et al 2008 [36]	Agota village, Delhi	57	Rural adults	68.5
17	Vupputuri et al 2006 [37]	Delhi	105	Urban Adults	94
18	Harinarayan 2005 [38]	Tripuati	164	Rural postmenopaural women	82

Conflict of Interest

No Conflict of Interest

Sources of Support

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Abbreviations

mmol/L (milli moles per litre)

Vitamin D – 25 hydroxycholicalciferol

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