



VITAMIN D LEVELS IN EARLY PREGNANCY & PREGNANCY OUTCOMES

Gynaecology

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ABSTRACT

Aims and objectives - To find out the correlation of serum Vitamin D levels in early pregnancy and pregnancy outcomes (i.e. development of preeclampsia, birth weight, apgar score and NICU admissions etc.).

Material methods - This is a hospital based observational study done in Department of Obstetrics & SMS Medical College, Jaipur from March 2015 to Oct 2016 on 800 pregnant women attending the Antenatal clinic between 13-20 weeks gestation. Serum Vitamin D levels were assessed, all women were followed till delivery and three days after delivery.

Results - Serum 25(OH)D concentrations in early pregnancy were lower in women who subsequently developed preeclampsia as compared to women who did not developed preeclampsia [mean, 13.58 ± 7.61 ng/ml, vs. 17.14 ± 6.91 ng/ml], Mean birth weight of newborns where the mothers was Vitamin D deficient came out to be 2.205 ± 0.44 kg, for insufficient mothers mean birth weight was 2.59 ± 0.407 kg while the mean birth weight was 2.83 ± 0.49 kg in newborns of Vitamin D sufficient mothers. When APGAR score of neonate at 5 minute ≥ 7 , mean maternal Vitamin D was 17.31 ± 6.99 ng/ml whereas when APGAR score of neonate at 5 minute was < 7 , mean maternal Vitamin D was 13.48 ± 6.99 ng/ml. Mean maternal vitamin D level was 17.27 ± 6.903 ng/ml in newborns who did not require NICU admission, whereas it was 13.87 ± 7.22 ng/ml in those who required NICU admission.

Conclusion - Thus we conclude that Low serum Vitamin D levels in early pregnancy is associated with increased incidence of Preeclampsia low birth weight, low apgar score and increased NICU admissions.

KEYWORDS:

Vitamin D, preeclampsia, low birth weight, apgar score, NICU admissions.

Introduction

Hypertensive disorders represent the most common medical disorder of pregnancy affecting between 7-15% of all the gestations.¹

The national high blood pressure education programme (2000) working group on high blood pressure in pregnancy defined preeclampsia as BP $\geq 140/90$ mm hg 6 hours apart on two separate occasions with proteinuria greater than 0.3 gm/dL in a 24 hours urine collection or greater than 1 gm/l or +1 on urine dipstick examination after 20 weeks of gestation.² Vitamin D is a hormone rather than a vitamin. Vitamin D was involved in many aspect of human life such as bone metabolism, cell functioning, and reproduction. Vitamin D is involved in implantation and placental development and displays anti proliferative and immunomodulatory actions. Low serum 25(OH)D levels have been related to adverse obstetric and neonatal outcomes such as preterm birth, low birth weight, low APGAR score, increased NICU admissions, hypertensive disorder in pregnancy and gestational diabetes mellitus.

The pathogenesis of preeclampsia involves a number of biological processes that may be directly or indirectly affected by vitamin D.^{3,4,5,6}

The active form of vitamin D, 1,25-dihydroxyvitamin D₃, has been shown to regulate the transcription and function of genes associated with placental invasion, normal implantation and angiogenesis.^{4,7} Furthermore abnormal implantation has been proposed to be mediated by an appropriate immune response between mother and baby. The immunomodulatory properties of 1, 25-dihydroxy vitamin D₃ may be relevant in this regard.^{5,8}

Also proteinuria of preeclampsia is thought to be mediated by renal

vascular endothelial growth factor. 1, 25-dihydroxy vitamin D₃ has been shown to regulate angiogenesis process through direct effects on VEGF genes transcription.³

Aim & Objectives

The aim of our study was to evaluate Vitamin D levels in early pregnancy and to determine the correlation of serum Vitamin D levels with pregnancy outcomes i.e. development of preeclampsia, Low birth weight, low APGAR score and NICU admissions.

Material & Methods

This prospective Hospital based study was conducted in Department of Obstetrics & Gynecology, SMS Medical College, Jaipur from March 2015 to October 2016.

800 pregnant Women with gestational age between 13-24 weeks, singleton pregnancy and age up to 35 years, attending the antenatal clinic were included in study. Women >35 year, with multifetal pregnancy, history of chronic hypertension, Diabetes mellitus, Liver, cardiac or renal disease, collagen disorder, molar pregnancy or any other major illness were excluded from study. All selected women underwent a blood test to assess their serum level of 25(OH) Vitamin D. Reference value of maternal serum 25(OH) vitamin D level - Deficiency < 20 ng/ml; Insufficiency 20-30 ng/ml; Sufficiency > 30 ng/ml.

All selected women followed till delivery and development of preeclampsia was noted.

Women were considered in mild preeclampsia if SBP was between 140-160 mmHg and DBP between 90-110 mmHg and in severe

preeclampsia if SBP > 160 mmHg or DBP > 110 mmHg. Follow up was done for perinatal outcomes.

Assessment of serum 25(OH)D was done by Chemiluminiscent Immune Assay method in department of biochemistry SMS medical college Jaipur.

Table no.1 mean vitamin D levels and development of preeclampsia

Vitamin D Levels (ng/ml)	With Preeclampsia	Without Preeclampsia	95% CI	p-value
Mean±SD	13.58 ± 7.61	17.14 ± 6.91	1.54-5.37	0.001 (Sig)

Table no.2 Relation of Maternal Vitamin D Levels and Mean Birth Weight of Newborn

Vitamin D Levels (ng/ml)	Birth Weight (in kg) (Mean ± SD)	p-value	Confidence Interval
Deficient (<20)	2.205 ± 0.44	0.001 (Sig)	2.61-2.55
Insufficient (20-30)	2.59 ± 0.407		
Sufficient (>30)	2.83 ± 0.49		

Table no.3 Maternal Vitamin D Levels and APGAR Score at 5 Minutes

	Vitamin D (ng/ml) Mean ± SD	p-value	95% CI
APGAR Score at 5 min <7	13.48 ± 6.99	0.001 (Sig)	17.35 - 16.38
APGAR Score at 5 min >7	17.31 ± 6.91		

Table no. 4 Maternal Vitamin D Levels and NICU Admissions

	Vitamin D (ng/ml) Mean ± SD	p-value	95% CI
NICU Admissions	13.87 ± 7.22	0.001 (Sig)	4.94 -1.85
No NICU Admissions	17.27 ± 6.903		

Results

Out of 800 women of study population 61(7.6%) developed PE. All women of study population was non smoker and housewives. Mean gestational age of blood collection was 14 weeks. There was no significant difference between mothers who developed PE and mothers who did not developed PE in terms of age, literacy, religion, socioeconomic status, residence, pre pregnancy BMI, gravidity status of women, p value > 0.05. Women with PE had higher proportion of caesarean delivery as compared to women without PE, p value < 0.05(Sig).

Out of 800 women of study population 483 (60.37%) had Vitamin D deficiency, 289 (36.13) had Vitamin D insufficiency. Only 28 (3.5%) women in this study had Vitamin D sufficiency. This shows that in India there is widespread Vitamin D deficiency. Among the women who developed PE, 72.13% shows vitamin D deficiency in early gestation.

Table no.1 Showed that mean serum vitamin D concentration was significantly lower in women who later developed PE than in women who did not developed PE [13.58±7.61 vs.17.14±6.91, 95% confidence interval 1.54-5.37; p value 0.001(Sig)].

Table no. 2 shows that mean birth weight of newborns was decreased when vitamin D level decreases (p value <0.001). Mean birth weight of newborns where the mothers was Vitamin D deficient came out to be 2.205 ± 0.44 kg, for insufficient mothers mean birth weight was 2.59 ± 0.407 kg while the mean birth weight was 2.83 ± 0.49 kg in newborns of Vitamin D sufficient mothers.

Table no. 3 The above table shows that when APGAR score of neonate at 5 minute ≥ 7, mean maternal Vitamin D was 17.31 ± 6.99 ng/ml whereas when APGAR score of neonate at 5 minute was < 7, mean maternal Vitamin D was 13.48 ± 6.99 ng/ml. This difference was statistically significant (p-value=0.001).

Table no.4 Shows that mean maternal vitamin D level was 17.27 ±

6.903 ng/ml in newborns who did not require NICU admission, whereas it was 13.87 ± 7.22 ng/ml in those who required NICU admission.

This was because newborn with low maternal Vitamin D levels were at increased risk of low birth weight, IUGR, neonatal hypocalcaemia, poor postnatal growth, hyperbilirubinemia, increase in the risk of respiratory tract infection and early onset neonatal sepsis.

DISCUSSION-

Vitamin D deficiency

Harinarayan CV et al⁹ in their study observed that there is widespread prevalence of varying degrees (50-90%) of Vitamin D deficiency in Indian population.

Bassir M et al¹⁰ in their study in Iranian mothers and their neonates, observed that 80% of the women had Vitamin D < 25nmol/L.

Our study revealed that prevalence of vitamin D deficiency and in sufficiency in pregnant women was 60.37% and 36.13% respectively. Only 3.5% women had sufficient vitamin D levels.

Preeclampsia-

Bodnar LM et al¹¹, in their study concluded that in early pregnancy Vitamin D deficiency was more common among women who later developed PE as compared to women who did not developed PE. Early pregnancy maternal Vitamin D deficiency < 37.5 nmol/l was associated with 5 fold increase in the odds of PE.

Baker AM et al¹² observed that midgestation (15-20 weeks) maternal 25(OH)D concentration was lower in women who subsequently developed PE than women who did not [Median (interquartile range), 75 (47-107) nmol/l vs. 98 (66-113) nmol/l; p-value = 0.001]

Achkar M et al¹³ in a study reported that women who develop PE had a significantly lower Vitamin D concentration at a mean gestational age of 14 weeks compared with women in control (mean ± SD - 47 17.7 vs 52.3 17.2 nmol/l). Singal R et al¹⁴ also reported significantly lower mean vitamin D levels in cases of PE as compared to controls (9.7 ± 4.95 ng/ml and 14.8 ± 4.95 ng/ml respectively).

In our study findings revealed that maternal Vitamin D deficiency in early pregnancy is significantly associated with elevated risk of PE. Mean vitamin D at 14 weeks of gestation was significantly lower in women who later developed PE.

Low Birth Weight-

Aghajafari F et al¹⁵ observed that women with low Vitamin D levels were associated with increased risk of SGA infants (odds ratio 1.85, 95% confidence interval 1.52-2.26).

Dave et al¹⁶ observed that 80% of LBW newborn were born to Vitamin D deficient women.

Halhali A et al¹⁷ observed that mean birth weight was 3.185 ± 0.312 kg when mean maternal Vitamin D levels was 63 ± 13 nmol/l and 2.093 ± 0.366 nmol/l when mean Vitamin D level was 47 ± 10 nmol/l.

In our study mean birth weight was also lower in newborns of vitamin D deficient mother than vitamin D sufficient mother(2.205±0.44 vs.2.83±0.49 kg).

APGAR score at 5 minute-

Reichetzeder C et al¹⁸ studied that Maternal Vitamin D deficiency was independently associated with low APGAR score.

Lindqvist PG et al¹⁹ studied that APGAR score of newborns was low in mothers with Vitamin D levels < 50 nmol/l as compare to mothers with Vitamin D > 50 nmol/l.

In our study mean maternal vitamin D levels were lower in women who gave birth to newborns with low APGAR score at 5 minute.

NICU admissions-

Cetinkaya M et al²⁰ Maternal and neonatal Vitamin D (22.2/8.6 ng/ml, respectively) was significantly lower in newborn with Early onset neonatal sepsis as compared with controls (36.2/19 ng/ml respectively).

Marshall I et al²¹ observed that there was an increased use of phototherapy in infants born to mother with vitamin D deficiency as compared to those with vitamin D sufficiency.

In our study neonates those admitted to NICU, mean maternal vitamin D levels were lower when compared to mothers of neonates who were not admitted to NICU.

Conclusion

To conclude serum Vitamin D levels has significant association with development of preeclampsia and with adverse pregnancy outcomes. It can be used as a prognostic tool for assessing the development of preeclampsia and low birth weight. So it can be suggested that maternal Vitamin D level should be assessed in early pregnancy and all the deficient women should be given Vitamin D supplementation in appropriate doses.

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