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RESEARCH ARTICLE

PREVALENCE OF VITAMIN D DEFICIENCY AND ITS OUTCOME IN PREGNANCY AT TERTIARY CENTRE

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Abstract

Introduction: Vitamin D is most essential during pregnancy and is necessary to neonates calcium homeostatis, bone maturation, mineralization and brain development. The aim of study is to evaluate the serum vitamin D3 level in pregnancy and follow up of cases for maternal and fetal outcome. **Method:**104 pregnant women were enrolled in the study in Netaji Subhash Chandra Bose Medical College from June 2013 to Oct 2014. Maternal blood sample were taken from first or second trimester of pregnancy(first visit). The serum was assayed for 25(OH)D(Vitamin D3) by fully automated chemiluminescent immune assay. **Results**: The prevalence of vitamin D deficiency in pregnancy was 72.1%. incidence of vitamin D deficiency was more in age group 25.04±4.10 years(mean age). In term of maternal outcome , prevalence of vitamin D deficiency more in preeclamptic women and bacterial vaginosis patient. Vitamin D deficient women had low birth weight babies. **Conclusion:** In view of mortality scenario referred cases who came in large number in our institute were pregnancy induced hypertension. It is worthwhile to find the cause of pregnancy induced hypertension. This study was undertaken to found correlation between pregnancy induced hypertension, bacterial vaginosis, low birth weight babies and suppressed immunity with hypovitaminosis.

Keywords:- bacterial vaginosis , chemiluminescent immune assay, preconceptional screening , 25(OH)vitaminD .

INTRODUCTION

It is interesting that during pregnancy alone and at no other time during the lifecycle there is an uncoupling of vitamin D metabolism from calcium such that by the end of the first trimester, 1,25$(OH)_2$D levels are more than double what they are during the nonpregnant state without concurrent changes in serum calcium concentrations [1]. It is not surprising, then that during pregnancy PTH as a marker of vitamin D status is a less reliable predictor than in nonpregnant adults [2].

Vitamin D deficiency during pregnancy is common throughout the world. There is a strong relationship between maternal and fetal (cord blood) circulating 25(OH)D levels[3] such

that maternal vitamin D deficiency is mirrored by neonatal vitamin D status. Its play a role in fetal skeletal development, tooth enamel formation, and general fetal growth and development. Mannion et al.[4], reported that every additional 40 IU of maternal vitamin D intake, there was an associated 11-g increase in birth weight. Marya *et al*(5) from Rohtak, reported higher body weight, crown heel length, head circumference and mid arm circumference in mothers who received two doses of 60,000 IU of vitamin D3 during third trimester pregnancy compared to those who did not receive vitamin D3[5].

Vitamin D act as a modulator of the immune system encompasses the adaptive immune system as well. $1,25(OH)_2D$ not only has the ability to affect processes within macrophages and monocytes, but also in T and B lymphocytes as well. By binding to the VDR on T cells, $1,25(OH)_2D$ acts to: (1) inhibit the proliferation of uncommitted TH (helper) cells and (2) promote the proliferation of immunosuppressive regulatory T cells, or Treg S, with notable accumulation of these cells at sites of inflammation [6]. It appears that $1,25(OH)_2D$ suppresses certain B cell functions such as proliferation and immunoglobulin production and retards the differentiation of B-lymphocyte precursors to mature plasma cells in vitro. These in vitro findings help to explain the significant association between vitamin D deficiency and autoimmune diseases, such as systemic lupus erythematosus, multiple sclerosis , rheumatoid arthritis , diabetes-both types 1 and 2, and certain cancers, such as colon breast and prostate. Additionally, the role of vitamin D in immune function intensifies the need to establish vitamin D sufficiency during pregnancy.

Pathophysiological changes are suggested to be secondary to abnormal endothelial function which accompanies generalized increase in the inflammatory activation that constitutes normal pregnancy by Redman et al., 1999[7]. 1–25-dihydroxyvitamin D3, the active form of vitamin D has been shown to control the transcription and function of genes connected to placental invasion, normal implantation and angiogenesis by Evans et al., 2004; Daftary and Taylor, 2006[8]. Vascular structure, and function as well as vascular compliance, elasticity and intima media thickness are all better off in women optimally supplemented with vitamin D [9].

Adequate maternal vitamin D levels are also important for fetal and child health. Vitamin D-deficiency in mothers have significantly increased risk of infantile rickets due to inadequate maternal-fetal transfer of 25-hydroxyvitamin D.[10] Lower maternal vitamin D status was associated with lower bone mineral concentration and impaired glucose homeostasis in newborn infants, craniotabes,[11] that is one of the earliest signs of vitamin D deficiency, in a case study with neonatal seizures of a hypocalcemic infant and with impaired skeletal development in utero.[12] Vitamin D deficiency during pregnancy is also associated with risks of health problems later in childhood, including improper bone development at 9 yrs of age, asthma, dental cavities, schizophrenia, and type I diabetes.

MATERIAL AND METHOD:

This prospective study included antenatal women of 1st and 2nd trimester of pregnancy attended the department of obstetrics and gynaecology NSCB Medical College and Hospital, Jabalpur during a period of June 2013 to Oct 2014. Study was conducted after obtaining clearance from ethical committee. Pregnant women coming to the out patient department were briefed about the study and their verbal consent taken to get enrolled in the study. Antenatal counseling, detailed history and examination was done. Antenatal counseling included ,discussion about their diet, significance of vitamin D and other nutritional deficiencies. Women were followed up and outcome of the pregnancy studied.

Apart from routine obstetrical investigation, serum vitamin D3 level estimation was done by fully automated chemiluminescent immune assay.[13]

Reference range

	Vit D3 Level	
	ng/ml	**nmol/l**
Vitamin D deficiency	<20	<50
Vitamin D insufficiency	21-29	51 – 74
Vitamin D sufficiency	>30	75 – 80
Vitamin D intoxication	>150	>375

1 nmol/l = 0.4 ng/ml

Vitamin D deficiency further divided: mild - 10-20ng/ml
moderate - 5-10ng/ml
severe - <5ng/ml

Results: The present study was undertaken to determine the serum 25(OH)vitamin D i.e. vitamin D3 level in 104 pregnant women, age range of 18-40years with first and second trimester of pregnancy . A total of 104 pregnant women were enrolled and out of these 75cases (72.1%) were found with vitamin D3 deficiency , the prevalence of vitamin D3 deficiency was 72.1% or 721.15 per thousand women reported to OPD of N.S.C.B. MCH Jabalpur.

Mean age of vitamin D3 deficiency group i.e. <30 was 25.04±4.10 years.

Preeclamptic cases in our study were 10.6% and all of them were vitamin D3 deficient and insufficient. The normotensive cases were 89.4%, had deficiency of vitamin D in 68.8%. This correlation between vitamin D3 deficiency and development of preeclampsia was statistically significant($p<0.05$).

In our study only 2.9% cases developed gestational diabetes mellitus and all of them were vitamin D 3 deficient. Therefore correlation between diabetes and vitamin D deficiency could not be established because of small number of gestational diabetes cases. (These cases were screened for gestational diabetes mellitus by 75g glucose and venous blood sample was taken 2hrs after glucose administration).

In present study majority (51%) of cases delivered vaginally and out of this **75.5%** were vitamin D3 deficient, 48.1% of cases delivered by cesarean section and out of this **68%** were vitamin D3 deficient.

In present study 8.7% of cases were develop vaginal infection although number of cases were less but all were vitamin D3 deficient. (Table-1) (Fishers Exact : 1-tailed P Value : 0.0457132) Which indicates that a significant association between positive vaginal infection and low vitamin D_3levels.

In term of outcome of pregnancy majority 95.2% cases delivered term babies and out of this 70.7% cases were vitamin D3 deficient and insufficient, 3.8% cases were delivered preterm baby and 1% cases aborted spontaneously and all of them were vitamin D3 deficient.

When the relation of vitamin D3 level of mother was correlated with birth weight it was found that, 21.2% of cases had birth weight of <2.5kg out of this 72.7% were deficient and 27.3% were vitamin D3 insufficient. Majority 58.7% of cases had birth weight of >2.5kg and out of this 39.5%, 24.7%, 58.7% were deficient ,insufficient and sufficient respectively. (Table-2) As the birth weight is directly proportion to serum vitamin D3 level. This correlation between vitamin D3 deficiency and birth weight of babies was statistically significant($p<0.002$).

In our study correlation between vitamin D deficiency and apgar score was not statistically significant($p>0.05$).

In our study 31.1% cases had babies with respiratory infection and out of this 75% cases were vitamin D3 deficient. Majority 68.9% cases had no respiratory disorder and out of this 70.4% cases were vitamin D3 deficient. This correlation between vitamin D3 deficiency in mother and development of respiratory infection in newborn was statistically not significant ($p>0.05$).(Table-2)

Table-1Vitamin D Level and maternal outcome

Outcome	Deficient (<20ng/dl)	Insufficient (20-30ng/dl)	Sufficient (>30ng/dl)	
Preeclampsia	9 81.8%	2 18.2%	0 0%	11/104 10.6%
Gestational diabetes mellitus	2 66.7%	1 33.3%	0 0%	3/104 2.9%
Cesarean section	24 48%	10 20%	16 32%	50/104 48.1%
Vaginal delivery	30 56.6%	10 18.9%	13 24.5%	53/104 51%
Vaginal Infection	6 66.7%	3 33.3%	0 0%	9/104 8.7%

Table-2Vitamin D Level and fetal outcome

	Deficient (<20ng/dl)	Insufficient (20-30ng/dl)	Sufficient (>30ng/dl)	
Spontaneous abortion	1 100%	0 0%	0 0%	1/104 1%
Preterm	3 75%	1 25%	0 0%	4/104 3.8%
Term	47 47.5%	23 23.2%	29 29.3%	99/104 95.2%
Birth Weight < 2.5	16 72.7%	6 27.3%	0 0%	22/104 21.2%
Birth Weight > 2.5	32 39.5%	20 24.7%	29 35.8%	61/104 58.7%
Respiratory tract infection present	22 68.8%	2 6.2%	8 25%	32/104 30.8%
Respiratory tract infection absent	28 39.4%	22 31%	21 29.6	72/104 69.2%

DISCUSSION:

Prevalence of vitamin D3 deficiency during pregnancy has a wide geographic variation. Reports of profound deficiency among pregnant women, those with 25(OH)D concentrations <10 ng/mL (25 nmol/L) are common throughout the world: 18% of pregnant women studied in the UK, 25%

in the UAE, 80% in Iran, 42% in northern India [14], 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). Study conducted by Meddab et al 2004 in Tunisia population found that the accumulated prevalence of hypovitaminosis D was 47.6%, increasing with age(P<0.001).[15]

In present study the prevalence of vitamin D3 deficiency was 72.1% or 721.15 per thousand women. Preeclamptic cases in our study were 10.6% and all of them were vitamin D3 deficient. The normotensive cases were 89.4%, had deficiency of vitamin D in 68.8%.(Table-1) This correlation between vitamin D3 deficiency and development of preeclampsia was Statistically significant($p<0.05$).

Baker et al,2010[16] found a possible association of midgestation vitamin D deficiency and the risk of severe preeclampsia in 51 cases out of an overall cohort of 3992 pregnant women, they documented that women who developed preeclampsia had lower midgestation maternal 25OHD concentrations relative to control women.

In 2011, Robinson et al examined the association of vitamin D levels and small-for–gestational-age (SGA) in 56 patients with early-onset severe preeclampsia (EOSPE), and found that 25(OH)D levels were lower in women with GDM are at high risk for gestational or delivery problems and developing diabetes after the delivery.[17]

In our study number of cases of gestational diabetes mellitus were less so association between vitamin D deficiency and gestational diabetes mellitus statistically not significant ($p>0.05$).

Vitamin D regulates insulin secretion by pancreatic β-cells and thereby affects circulating glucose levels.[18] Vitamin D deficiency during early pregnancy significantly increases the risk for gestational diabetes in later pregnancy. Deficiency of vitamin D was shown to be associated with fetal brain growth deficiency and type 1 diabetes in children.

In our study majority (51%) of cases delivered vaginally and out of this **75.5%** were vitamin D3 deficient and insufficient , 48.1%% of cases delivered by cesarean section and out of this **68%** were vitamin D3 deficient and insufficient. (Table-1) This association was not statistically significant.($p>0.05$). Most of the cases of primary cesarean section are taken for section generally, hence it is difficult to find association with vitamin D deficiency and incidence of cesarean section.

Cesarean sections became established, in part, to manage this condition: "… malformed pelvises often prohibited normal delivery. As a result the rate of cesarean section went up markedly." Poor muscular performance[19] is an established symptom of vitamin D deficiency. The term rachitic pelvis has fallen into disuse, but an association has been noted between cesarean birth and a narrow pelvis.

In our study 8.7% of cases were develop vaginal infection although number of cases were less but all were vitamin D3 deficient and insufficient. (Table-1) (Fishers Exact : 1-tailed P Value : 0.0457132) Which indicates that a significant association between positive vaginal infection and low Vit. D_3levels.

L.M. Bodnar et al 2009 also found that maternal vitaminD deficiency is associated with bacterial vaginosis in first trimester of pregnancy and they found that approximately 41% of women had bacterial vaginosis and 52% had a serum 25(OH)D concentration <37.5 nmol/L. The

mean unadjusted serum 25(OH)D concentration was lower among bacterial vaginosis cases (29.5 nmol/L; 95% CI: 27.1, 32.0) compared with women with normal vaginal flora (40.1 nmol/L; 95% CI: 37.0, 43.5; $P < 0.001$). Bacterial vaginosis prevalence decreased as vitamin D status improved ($P < 0.001$). Approximately 57% of the women with a serum 25(OH)D concentration <20 nmol/L had BV compared with 23% of women with a serum 25(OH)D concentration >80 nmol/L.[20].

In our study majority 95.2% cases delivered term babies and out of this 70.7% cases were vitamin D3 deficient and insufficient , 3.8% cases were delivered preterm baby and 1% cases aborted spontaneously and all of them were vitamin D3 deficient. (Table-2)However this correlation was statistically not significant.($p \geq 0.05$) As the study population were small strong inference could not be drawn in favour of preterm labour in vitamin D deficient pregnant women.

When the relation of vitamin D3 level of mother was correlated with birth weight it was found that, 21.2% of cases had birth weight of <2.5kg out of this 72.7% were deficient and 27.3% were vitamin D3 insufficient. Majority 58.7% of cases had birth weight of >2.5kg and out of this 39.5%, 24.7%, 58.7% were deficient ,insufficient and sufficient respectively. (Table-2) As the birth weight is directly proportion to serum vitamin D3 level. This correlation between vitamin D3 deficiency and birth weight of babies was statistically significant($p<0.002$).

Mannion *et al* have shown that each additional microgram of vitamin D, was associated with an 11 g increase in birth weight.[4]

In our study correlation between vitamin D deficiency and apgar score at 1 minute and at 5 minute was not statistically significant($p>0.05$).

In our study 30.8% cases had babies with respiratory disorder and out of this 75% cases were vitamin D3 deficient and insufficient. Majority 69.2% cases had no respiratory disorder and out of this 70.4% cases were vitamin D3 deficient and insufficient. (Table-2) This correlation between vitamin D3 deficiency in mother and development of respiratory infection in newborn was statistically not significant ($p>0.05$).

Several studies conclude, that a significant number of women with vitamin D3 deficiency overlooked by risk-based screening, the association of rising incidence of vitamin D deficiency with adverse pregnancy outcome like preeclampsia, cesarean section rate, bacterial vaginosis, low birth weight, preterm delivery and a demonstrated improvement in outcomes with treatment, it would seem prudent to offer screening by checking serum vitamin D3 level to all women to identify the deficient women and treat them for better outcome of pregnancy.

CONCLUSION:

In view of the high prevalence of low vitamin D status in pregnancy worldwide. Looking into the prevalence of deficiency of vitamin D deficiency in population, it is proposed that all women desirous of pregnancy should be subjected to preconceptional screening of vitamin D and if not so then earliest in first trimester or first visit to antenatal clinic.The currently recommended supplementation amount of vitamin D is not sufficient to maintain a value of vitamin D above 30 ng/ml, during pregnancy. Studies are underway to establish the recommended daily doses of vitamin D in pregnant women. The need of hour is a meticulous well planned study catering large number of pregnant population would be required to validate the result of the study.

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