Research Paper Medical Science

A Study Of Vitamin D Deficiency, Its Supplementation And Effect On Fetomaternal Outcome During Pregnancy.

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ABSTRACT

Aim: The present has been conducted to study vitamin D deficiency, its supplementation and effect on fetomaternal outcome during pregnancy. Method: The present study was conducted on 200 pregnant women attending department at Upper India Sugar Exchange Maternity Hospital, Department of obstetrics and Gynaecology, G.S.V.M Medical College, Kanpur during the period of april 2013-15. Vitamin D measured on first visit and supplementation of vitamin D 2000IU/day accordingly. Patients were followed till delivery for antenatal and neonatal outcome. Result: Vitamin D supplementation had significant reduction in incidence of pre-eclampsia, fetal growth restriction, gestational diabetes mellitus, preterm birth, caesarean section, neonatal hypocalcemia, NICU admissions. Vitamin D supplementation had significant 3.2 times reduction in incidence of pre eclampsia(p=0.0025), 3 times reduction in FGR(p=0.0052) and gestational diabetes(p=0.0317). Cesarean section rate and NICU admissions were significantly reduced in women who were supplemented with vitamin D. Conclusion:Vitamin D supplementation is associated with improved maternal and fetal outcome during pregnancy.

KEYWORDS vitamin D deficiency, improved fetomaternal outcome, supplementation.

INTRODUCTION:-

At no other time during the life cycle is Vitamin D status more important than during pregnancy as mother is the sole source of vitamin D substrate for her developing fetus. While vitamin D status during pregnancy varies around the globe as a function of maternal sunlight exposure, degree of skin pigmentation, latitude, lifestyle, BMI and the intake of oral vitamin D supplements(5).

The term vitamin D is in fact a misnomer. Whereas true vitamins are ingested only through exogenous supplementation, vitamin D may be produced endogenously and moves to other areas in the body to exert its action. Vitamin D is therefore a hormone, not a vitamin. There are two forms of vitamin D. Vitamin D2 (ergocalceferol) is derived from the ultraviolet irradiation of plant ergosterol, and vitamin D3 (cholecalciferol). Vitamin D3 is produced from 7-dehydrocholesterol in skin exposed to ultraviolet B radiation(Holick ,2006). Vitamin D is hydroxylated in the liver and becomes 25(OH)D, or calcidiol, the primary circulating form of vitamin D. 25(OH)D may be converted 1,25(OH) D2 (calcitriol), the active form of vitamin D, by 1α-hydroxylase(-CYP27B1) in the kidneys and other organs. The production of 1,25(OH)D2 in the kidney is regulated by plasma parathyroid hormone levels as well as calcium and phosphorus levels (Holick 2007). 1,25(OH)D2 is broken down into its inactive metabolite by 24-hydroxylase. Negative feedback aids in regulating 1,25(OH)D2 levels as 1,25(OH)D2 inhibits renal 1α-hydroxylase and stimulates 24-hydroxylase, and this maintains circulating levels within a limited range (Aranow 2011).

More than 80% of vitamin D requirement is derived from cutaneous synthesis(Holick 2007). It can also be ingested through supplementation or through vitamin D rich foods, including oily fish such as salmon, mackerel and sardines, some fish oils such as cod liver oil, egg yolk, and vitamin D-enriched foods(milk, infant formula,cereal, orange juice, yogurt and margarine)(Holick 2006). Supplements are usually required to reach the minimum recommended daily intake of vitamin D especially during the winter months (Holick 2006).

Vitamin D metabolism is greatly altered during pregnancy, and pregnancy itself is the primary driver for these extraordinary circulating 1,25(OH)D levels. The dramatic rise in maternal circulating of 1,25(OH)D level following conception is remarkable for many reasons:by 12 weeks of gestation, maternal circulating 1,25(OH)D is already triple those of nonpregnant female. Going forward through gestation 1,25(OH)D continues to rise as a function of substrate 25(OH)D availability. This substrate dependence of 1,25(OH)D on 25(OH)D for optimal production is never observed in normal human physiology driven by classic calcium hemeostasis.(6).

Although vitamin D is active form vitamin D, it is not good indicator of vitamin D status(Papandreou, Malindretos et al. 2010). Serum or plasma 25(OH)D has a half-life of two-three weeks and is the major circulating form of vitamin D (Holick, Binkley et al.2011). 25(OH)D is therefore the most appropriate biochemical marker of vitamin D status(Papandreou, Malindretos et al, 2010).

There is no age-specific reference ranges for serum vitamin D status. The endocrine society definitions of vitamin D sufficiency, insufficiency and deficiency are(Holick, Binkley et al.2011) which is 25(OH)D levels >30ng/ml, 20-30ng/ml, <20ng/ml respectively.

Vtamin D deficiency during pregnancy is rampant throughout the world.Maternal effect postulated to be due to the defi-

ciency are: Eclampsia, insulin resistence, increased risk of gestational diabetes mellitus. Fetal effects are plenty some being short term and others may become apparent in later life. Vitamin D supplementation during pregnancy has been suggested to safely improve pregnancy and infant outcomes.

AIMS AND OBJECTIVES:-
To study Vitamin D deficiency, its supplementation and effect on fetomaternal outcome during pregnancy.

MATERIALS AND METHODS:-
The present study is randomised control study conducted on 200 patients in early second trimester of pregnancy attending department of Upper India Sugar Exchange Maternity Hospital, Dept of Obs and Gynaecology.,G.S.V.M Medical College, Kanpur, over a period of 2 years (April 2013-15). The subjects were randomly allocated and were classified in two groups.

Study groups A(cases):women who received vitamin D supplementation (2,000IU/d) along with conventional antenatal care.

B(controls):women who received conventional antenatal care only and no vitamin D supplementation.

Criteria for inclusion:
Pregnant women attending antenatal clinic at UISEMH

Patient who have agreed to participate in the study and ready to receive vitamin D.

Criteria for exclusion:
Patient with chronic hypertension, hypercalcemia or family history of parathyroid disorders.

Patients having liver or kidney disease, active tuberculosis, sarcoidosis, lymphoma and other granulomatous disease.

Patients on drugs known to affect vitamin D metabolism.

Study protocol:
vitamin D-25(OH) was measured in first visit in ng/ml, study group A received vitamin D 2000IU/day in 2nd and 3rd trimester. Both groups received tab ferrous sulphate, calcium and folic acid.

On first visit: All enrolled patients were subjected to detailed history and examination

They were subjected to thorough investigations. Vitamin D-25-hydroxy in ng/ml (chemiluminescence micro particle immunoassay) was measured in first visit. In study group A,women with vitamin D-25(OH) >30ng/ml were given 400IU day and required no further testing or follow up whereas women with vitamin D-25(OH) <30ng/ml recommended vitamin D 2000 IU/day.

In study group B, vitamin D supplementation not done.

During follow up:
Blood pressure, weight charting, Hb and urine albumin were measured in every visit.

Phosphorus and calcium concentrations were repeated at term. All patients were followed till delivery. Fetal outcome was reported in terms of birth weight, Sr. Cal level.

RESULTS:
Total 200 patients were included in the study age ranged from 20-35yrs, majority of them were in age range of 25-29years. Out of 200 patients, 65% were hindu and 35% were muslims. Majority of patients were of low socioeconomic status(59%) and only 9% were of high socioeconomic status. 122 subjects were primigravidae(63 in case group and 59 in control group(Table 1). 60% of patients had first visit to antenatal clinic at 24-28weeks and 13.5% visited at 28-32 weeks of gestation. (Table 2).

In our study 76.5% (153/200) of subjects were vitamin D deficient of which 79 were in case group and 74 in control group. (Table 3).

Out of 200 subjects 30 subjects had pre-eclampsia, 9% had fetal growth restriction, 10% had Gestational Diabetes Mellitus, 19.5% had preterm delivery. In mode of delivery cesarean section was performed in 94 subjects out of 200(Table 4).

In neonatal outcome, out of 200 neonate 13(6.5%) developed neonatal hypocalcemia and 39(19.5%) had NICU admissions(mainly because of respiratory infection).(Table 5).

DISCUSSION:
In our study 76.5% subjects were vitamin deficient. Lee et al (2007) reported that 50% of mothers and 65% of newborn infants were severely vitamin D deficient. Holick MF (2007) reported that 1 billion people worldwide have vitamin D deficiency or insufficiency. Sachan A (2005) reported that pregnant women in India have been shown to have upto 84% prevalence of vitamin D deficiency which correlated significantly with serum 25(OH)D status of their newborn.

Pre eclampsia: Grant, W. B. (2010) studied that low vitamin D may explain the link between preeclampsia and cardiovascular disease. Grant, W.B. (2009) studied the role of vitamin D in upregulating VEGF and reducing the risk of preeclampsia. In our study there was significant reduction (p=0.0025) in incidence of preeclampsia(>3times).

Fetal growth restriction: in our study cases had 5 times reduced incidence of fetal growth restriction in accordance with James M Robert (2005). According to him the active form of vitamin D has been shown to regulate the transcription and function of genes associated with placental invasion, normal implantation and angiogenesis.

Impaired glucose tolerance in pregnancy: Diabetes during pregnancy affects about 5% of all pregnant women, is increasing in incidence. Sooy K et al (1999) described that vitamin D may directly or indirectly modulate pancreatic β cell function. Dr. Cuilin Zhang (2008) and colleagues found women with low 25(OH)D were almost 3 times more likely to develop diabetes during pregnancy. In accordance with above our study shows 3 times reduction(p=0.0317) in subjects who were supplemented with vitamin D.

Low birth weight: in a study from Holland, women with vitamin D deficiency had a 2.4 fold increased risk of having an SGA baby. Australian researchers found that mean birth weight was 200g lower(p<0.001) in babies of vitamin D deficient mothers. In our study there was 2 fold risk of low birth weight in deficient women.

Other complications: Dr. Anne Merewood et al (2003) and her colleagues found that there was an inverse association with having a cesarean section and serum 25(OH)D levels. In the present study 47% subjects had caesarean section as mode of delivery(p=0.0158).

Vitamin D deficiency is also associated with bacterial vaginosis in pregnant women.

Neonatal hypocalcemia and morbidity: in an Australian study, hypovitaminosis D was found in 15% of pregnant women and 11% of neonate. Vitamin D deficiency is a major cause of hypocalcaemic seizures in neonates and infants. In our study neonatal hypocalcemia was present in 6.5% of neonates(p=0.0184). In our study NICU admissions were significantly (p=0.0313) reduced(2 times) with maternal vitamin D supplementation. Karatekin G et al (2009) studied the association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection.

Table 1. Socio Demographic profile of subjects

S.NO	Cases	Controls
Age(yrs)		
20-24	23	30
25-29	62	59
30-34	13	9
>35	2	2
Religion		
Hindu	68	62
Muslim	32	38
Socioeconomic status		
Low	58	60
Middle	32	32
High	10	8
Gravidity		
G1	63	59
G2	27	26
G3	10	15

Table 2. Distribution according to time of first visit to antenatal clinic

Time of first visit	Cases	Controls
20-24 weeks	27	28
24-28 weeks	62	58
28-32 weeks	13	

Table 3. Distribution according to level of vitamin D-25(OH) at first visit

Vitamin D(ng/ml)	Cases	Controls
30-40	21	26
20-<30	20	32
10-20	46	38
<10	13	

Table 4. Maternal outcome vs. Group

Maternal outcome in present pregnancy	Cases	Controls	P value
1)Pre-eclampsia	7/100	23/100	P=0.0025
2)Fetal growth restriction	3/100	15/100	P=0.0052
3)Gestational Diabetes Mellitus	5/100	15/100	P=0.0317
4)low birth weight			
5)Caesarean section	13/100	26/100	P=0.0313
	38/100	56/100	P=0.0158

Table 5. Neonatal outcome vs. Group

Neonatal outcome in present pregnancy	Cases	Controls	P value
Neonatal hypocalcemia	2/100	11/100	P=0.0184
NICU admissions	13/100	26/100	P=0.0313
Prematurity	13/100	26/100	P=0.0313

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