EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 7
283-290
Year: 2017

VITAMIN D DEFICIENCY: ITS IMPACT ON MATERNAL AND FETAL OUTCOME

Dr. Neelu Rajput*

Rewa, Madhya Pradesh, India

***Corresponding Author: Dr. Neelu Rajput**
Rewa, Madhya Pradesh, India

Article Received on 24/04/2017 **Article Revised on 15/05/2017** **Article Accepted on 06/06/2017**

ABSTRACT

Background: Vitamin D insufficiency is associated with an increased risk of preeclampsia,gestational diabetes, preterm and small for gestational age infants.[1] Vitamin D has direct effect on pathogenesis of preeclampsia such as trophoblastic invasion and immunomodulation.[2] Low level of Vitamin D is associated with increased risk of GDM,vitamin D regulates glucose metabolism through influencing insulin sensitivity.Vitamin D increases risk of preterm delivery due to increased colonization by bacterial vaginosis species.[3,4] **Material and Method:** This randomized case control study was conducted on 300 women, admitted in Gandhi Memorial Hospital, associated Shyam Shah Medical College, Rewa(M.P.) from 1st August 2015 to 31st July 2016. Comparison was made between control and study groups and data were analysed.Results were expressed using Chi square test and P value. **Result:** Total cases of PIH,GDM,Preterm and SGA were 43,13,34 and 28.In study group, out of 150 cases,66% of women have maternal complications.Vitamin D deficiency was associated with maximum number of PIH cases(24.7%), followed by Preterm (20%), SGA(14%) and GDM(7.3%).Among PIH cases, maximum have deficiency (39.5%).Out of 13 GDM cases, most of them have deficiency(38.4%).Out of 34 Preterm cases, maximum have insufficiency(38.2%) of vitamin D.Incidence of stillbirth and early neonatal death was more in study group(4.6%,3.3%) than control group(2%,1.3%). **Conclusion:** The study results suggest that vitamin D deficiency in pregnancy is associated with elevated risk for Preeclampsia, GDM, Preterm birth and Small for gestational age baby. Vitamin D supplementation in early pregnancy may be a simple way to reduce the risk of these adverse pregnancy outcome.

KEYWORDS: Pregnancy induced hypertension,gestational diabetes mellitus,small for gestational age,vitamin D.

MATERIAL AND METHODS

This randomized case control study was conducted on 300 women, admitted in Gandhi Medical Hospital, associated Shyam Shah Medical College, Rewa(M.P.) for a period of oneyear from 1 August 2015 to 31 July 2016. Antenatal women were enrolled in the study on the basis of following

Inclusion criteria

1.Women beyond 28 weeks of gestation
2.Primigravida women
3.Singleton Pregnancy

Exclusion criteria

1.Before 28 weeks of gestation
2.Multigravida women
3.Multiple pregnancy
4.Chronic hypertensive women
5.Known diabetic women
6.Smokers
7.Alcoholics

Out of all women who attended OPD, 700 women were fulfilled the inclusion criteria's. Out of 700 women, 520 women given consent for inclusion in study and they all were subjected to 25 hydroxy vitamin D test. Among them, 238 women were having low vitamin D level and 282 were having normal vitamin D level. Out of 238 women, 150 women were selected by randomization and were included in study group. Out of 282 women,150 women were selected by randomization and were included in control group.A detailed history was taken.

General examination and obstetrical examination was done.Routine antenatal tests and special tests when needed were done in all.

Classification of clinical categories of Vitamin D Level

a. Severe deficiency (<25 nmol/L)
b. Deficiency (25 to <50 nmol/L)
c. Insufficiency (50 to <75nmol/L)
d. Sufficiency (>75 nmol/L)

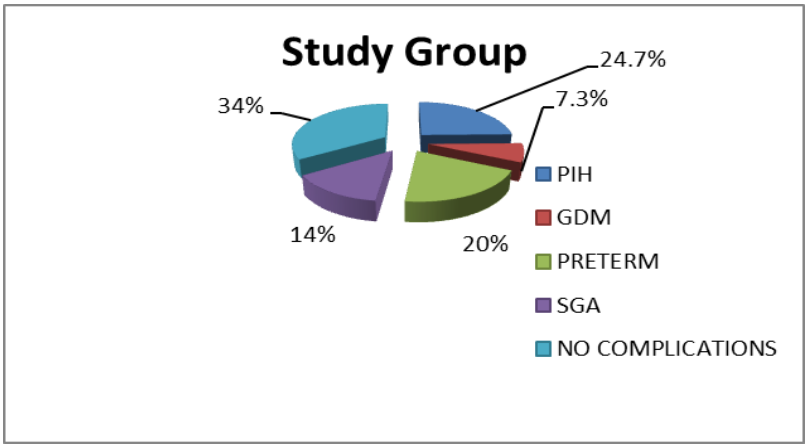
Comparison was made between control and study groups and data were analysed.Resultwere expressed using Chi square test and P value. P value of <0.05 was considered as significant.

RESULTS

Table 1.distribution of cases according to maternal complications in study and control group

CASES	STUDY/LOW VIT D GROUP		CONTROL/NORMAL VIT D GROUP		TOTAL
	No.	%	No.	%	No.
PIH	37	24.7	6	4	43
GDM	11	7.3	2	1.3	13
PRETERM	30	20	4	2.7	34
SGA	21	14	7	4.7	28
No Complications	51	34	131	87.3	182
TOTAL	150	100	150	100	300

X^2=90.627 p=<0.0001 significant



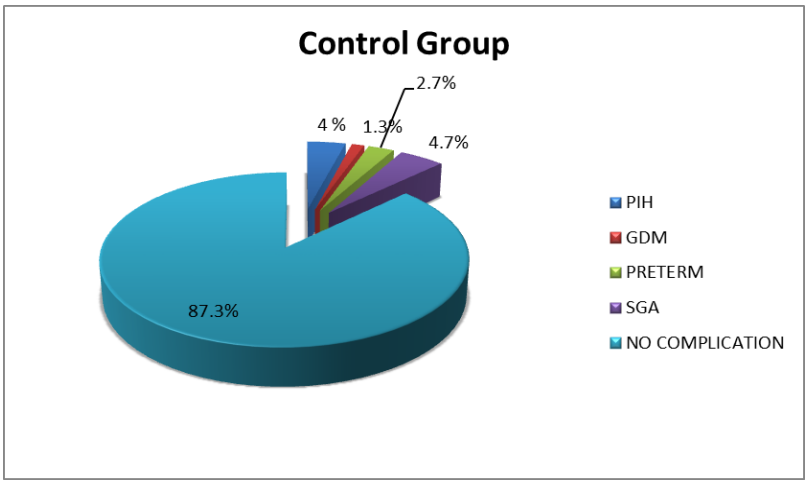
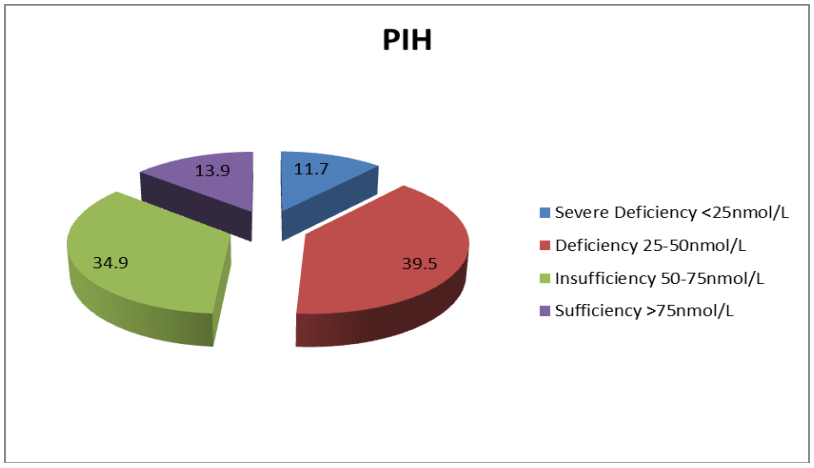
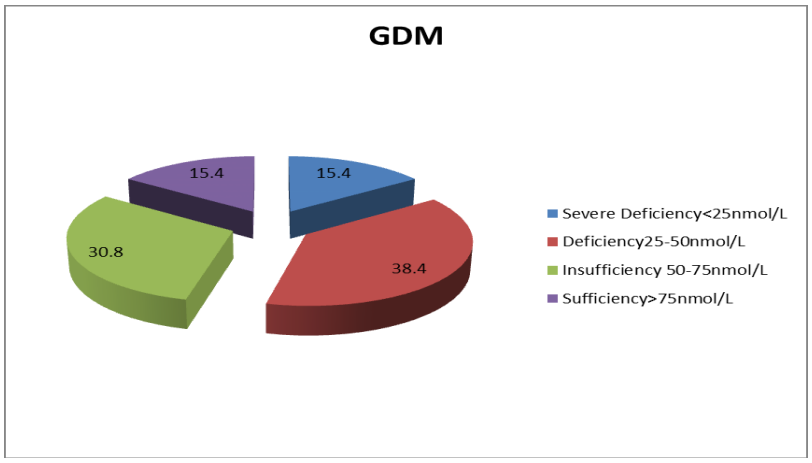


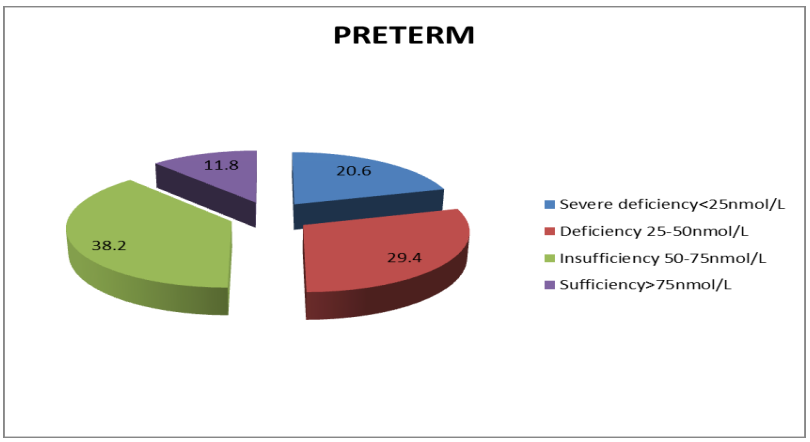
Table 2.distribution of cases according to serum level of vitamin D

Maternal Compli--cation	Serum level of vitamin D							
	Total cases	Severe Deficiency <25 nmol/L		Deficiency 25-50 nmol/L		Insufficiency 50-75 nmol/L		Sufficiency >75 nmol/L	
PIH	43	5	11.7%	17	39.5%	15	34.9%	6	13.9%
GDM	13	2	15.4%	5	38.4%	4	30.8%	2	15.4%
Preterm	34	7	20.6%	10	29.4%	13	38.2%	4	11.8%
SGA	28	5	17.8%	8	28.6%	8	28.6%	7	25%
No compli- -cation	182	6	3.4%	22	12.1%	23	12.6%	131	71.9%
Total	300	25	8.3%	62	20.7%	63	21%	150	50%

X^2=95.522 p=<0.0001 significant


PIH
11.7
39.5
34.9
13.9
Severe Deficiency <25nmol/L
Deficiency 25-50nmol/L
Insufficiency 50-75nmol/L
Sufficiency >75nmol/L


GDM
15.4
38.4
30.8
15.4
Severe Deficiency<25nmol/L
Deficiency25-50nmol/L
Insufficiency 50-75nmol/L
Sufficiency>75nmol/L


PRETERM
20.6
29.4
38.2
11.8
Severe deficiency<25nmol/L
Deficiency 25-50nmol/L
Insufficiency 50-75nmol/L
Sufficiency>75nmol/L

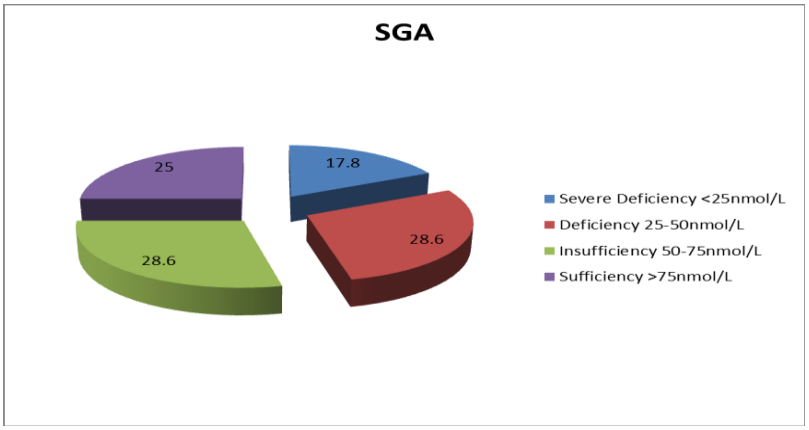

SGA
17.8
28.6
28.6
25
Severe Deficiency <25nmol/L
Deficiency 25-50nmol/L
Insufficiency 50-75nmol/L
Sufficiency >75nmol/L

Table 3.distribution of cases according to perinatal outcome

Perinatal Outcome	Study/low vit D Group(n=150)		Control/normal vitDGroup(n=150)	
	No.	%	No.	%
Alive	136	90.7	145	96.7
Fresh SB	5	3.3	2	1.3
Macerated SB	2	1.3	1	0.7
Early NND	5	3.3	2	1.3
Congenital malf.	2	1.3	0	-
Total	150	100	150	100

X^2=5.193 p=0.2681notsignificant

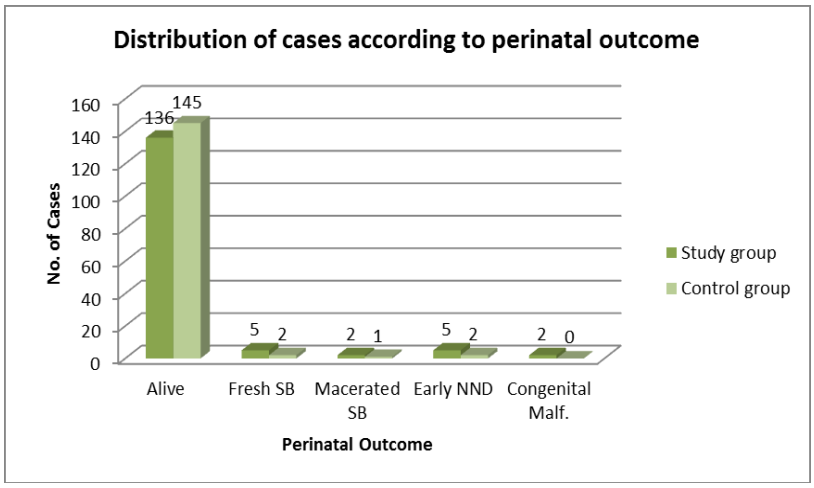


Table 4.distribution of cases according to baby weight

Baby weight(kg)	Study/low vit D Group(n=150)		Control/normal vitDGroup(n=150)	
	No.	%	No.	%
<2	18	12	5	3.33
2 - <2.5	36	24	7	4.67
2.5-<3	54	36	104	69.33
3-<3.5	26	17.33	27	18
3.5-<4	11	7.33	7	4.67
≥4	5	3.33	0	0
Total	150	100	150	100

X^2=48.637 p=<0.0001 significant

Distribution of cases according to baby weight

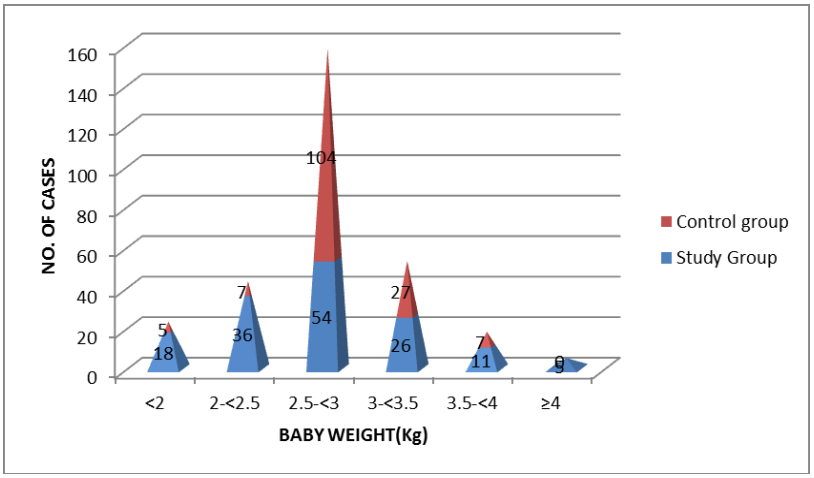
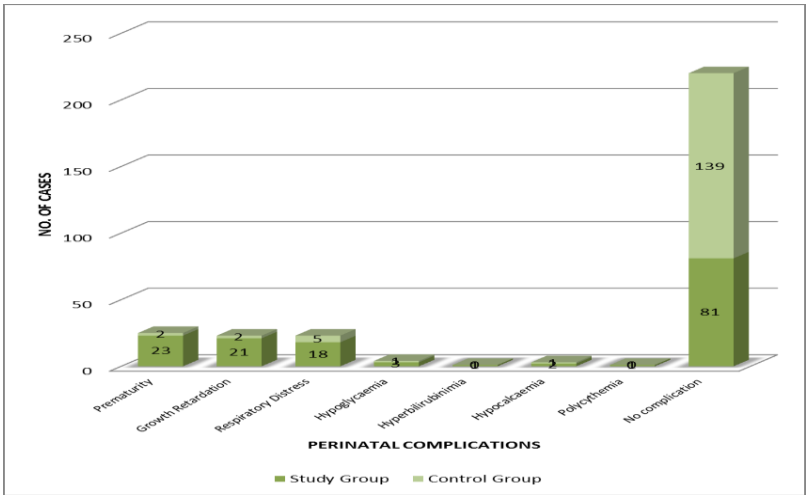


Table 5.distribution of cases according to Perinatal complications

Perinatal complications	Study/low vit D Group(n=150)		Control/normal vit D Group(n=150)	
	No.	%	No.	%
Prematurity	23	15.3	2	1.3
Growth Retardation	21	14	2	1.3
Respiratory Distress	18	12	5	3.3
Hypoglycemia	3	2	1	0.7
Hyperbilirubinimia	1	0.7	0	0
Hypocalcaemia	2	1.3	1	0.7
Polycythemia	1	0.7	0	0
No complication	81	54	139	92.7
Total	150	100	150	100

X^2=59.308 p=<0.0001 significant

Distribution of cases according to Perinatal complications



DISCUSSION

Table 1

- In the present study, total cases of PIH, GDM, Preterm and SGA were 43, 13, 34 and 28 including both the groups.

- In study group, out of 150 cases of study group, 66% of women have maternal complications. Vitamin D deficiency was associated with maximum number of PIH cases (24.7%), followed by Preterm (20%), SGA (14%) and GDM (7.3%).

- Out of 43 cases of PIH, 86.05% of women have low vitamin D and 13.95% of women have normal vitamin D.

Tabesh et al (2013)[5] in their systematic review and metaanalysis of eight observational studies found a significant relationship between vitamin D deficiency and increased risk of preeclampsia.

Hypponen et al (2014)[6] found that low maternal serum 25(OH)D levels lead to an increased risk of preeclampsia.

- Out of 13 cases of GDM, 84.6% of women have low vitamin D and 15.4% of women have normal vitamin D.

Burris et al(2012)[7] in a study on 2128 participants found that low vitamin D level in women associated with increased risk of GDM.

Parlea et al (2012)[8] in their study on 116 women with gestational diabetes and 219 control subjects ,observed that women with gestational diabetes had significantly lower serum 25-hydroxyvitamin D compared with control subjects.

- Above studies have result similar to our study.3

- Among all Preterm cases, 88.2% of women have low vitamin D and 11.8% of women have normal vitamin D.

In a study on 93 women,Shibata et al.(2011)[9] found that lower levels of vitamin D among pregnant women are associated with premature delivery.

- Among all SGA cases, 75% of women have low vitamin D and 25% of women have normal vitamin D.

Burris HH et al (2012)[10] they studied on 1067 white and 236 black mother-infant pairs and found that the odds of SGA were higher with maternal 25(OH)D levels

less than 25 versus 25 nmol/L or greater (adjusted odds ratio, 3.17; 95% confidence interval, 1.16-8.63).

Gernard et al (2014)[11] in their study on 1851 women found that 25(OH)D concentrations of 50-74 nmol/L and ≥75 nmol/L compared to <30 nmol/L were associated with 43% and 54% reductions in risk of SGA and 8.4 and 10.7fewer cases of SGA per 100 births, respectively.

- In the study group, 34% cases have no maternal complication.
- The results were found to be statistically significant.
- From the above table, we can conclude that vitamin D deficiency is associated significantly with maternal complications.

Bener et al (2013)[12] in a study, over 24 weeks of gestation among 1,873 pregnant women found a significant association between vitamin D deficiency in pregnancy and the elevated risk for preeclampsia, GDM.

Wei SQ el al (2014)[13] in their study, they observed that low vitamin D status is associated with adverse pregnancy outcomes like Preeclampsia, GDM, Preterm and small for gestational age.

In their systematic review and metaanalysis on 24 observational studies, Shu-Qin Wei et al (2013)[14] found that vitamin D level less than 50nmol/L associated with an increased risk of Preeclampsia, GDM, Preterm and SGA.

- The results of present study were similar to above studies.

Table 2

- Out of 300 cases, 150 cases were vitamin D sufficient, 21% cases were vitamin D insufficient, deficiency was seen in 20.7% cases and severe deficiency was seen in 8.3%cases.

- Among maternal complications, insufficiency found to be maximum among PIH cases (37.5%), deficiency found to be maximum among PIH cases (42.5%) and severe deficiency found to be maximum among Preterm cases (36.8%).

Pregnancy induced hypertension

- Out of 43 cases of PIH, deficiency seen in 39.5% cases, insufficiency seen in 34.9% cases, severe deficiency seen in 11.7% cases and sufficiency seen in 13.9% cases.

- Severe deficiency was seen in eclampsia and severe preeclampsia cases while mild cases of PIH have either insufficiency ornormal vitamin D level.

Bodnar et al (2014)[15] in a study on 717 patients found that maternal vitamin D deficiency might be a risk factor for severe preeclampsia but not for its mild subtypes.

Robinson et al (2010)[16] in their study revealed that Early-onset severe preeclampsia (EOSPE) subjects had reduced total 25-OH-D levels in comparison to healthy controls.

Gestational diabetes Mellitus

- Among GDM women, deficiency seen in 38.4% cases, insufficiency seen in 30.8% cases, severe deficiency seen in 15.4% cases and sufficiency seen in 15.4% cases.

- Severe deficiency was mainly seen in uncontrolled cases of GDM who were on insulin therapy.

Maghbooli et al (2009)[17] in their study on 741 women, concluded that among 29 % of participants with 25(OH)D levels <15 nmol/L, the prevalence of GDM was significantly higher compared to women with 25(OH)D levels ≥ 35 nmol/L. In the present study 15.4% patients had vitamin D level <25nmol/L,38.4% patients had Vitamin D level between 25-50nmol/L and 30.8% patients had Vitamin D level between 50-75nmol/L.

Zuhur et al (2013)[18] in their study on 234 women, states that an increased risk of GDM was present only in subgroup with severe 25 (OH)D deficiency (<12.5 nmol/L).

In a nested case-control study on 4225 women, Baker et al (2012)[19] found that maternal vitamin D deficiency was more among GDM women than non GDM women.

PRETERM BIRTH

- Among women with preterm labour, insufficiency was seen in 38.2% cases, deficiency seen in 29.4% cases, severe deficiency seen in 20.6% cases and sufficiency was seen in 11.8% cases.

In a study on 487 pregnant women, Wagneret al. (2015)[20] reported that pregnant women with serum concentrations of vitamin D less than 20 ng/mL had3.81 times the odds of a preterm birth compared to those with serum concentrations of vitamin D greater than 40 ng/mL.

Bodnaret al (2015)[21] in a study found that women with serum 25(OH)D concentrations ≥40 ng/mL (*n* = 233) had a 57% lower risk of preterm birth compared to those with concentrations ≤20 ng/mL

Lu-Lu Qin et al (2016)[22] conducted metaanalysis of 10 observational studies on 10,098 women and found that pregnant women with vitamin D deficiency (maternal serum 25 (OH) D levels < 20 ng/mL) experienced a significantly increased risk of PTB (odds ratio (OR) = 1.29, 95% confidence intervals(CI): 1.16, 1.45) with low heterogeneity (I2 = 25%, p = 0.21).

Small for gestational age

- Out of 28 cases of SGA, insufficiency seen in 28.6% cases, deficiency seen in 28.6% cases, severe deficiency seen in 17.8% cases and sufficiency seen in 25% cases.

- Severe deficiency seen in IUGR cases with severe oligohydramnios.

- Among uncomplicated cases, 71.9% cases have vitamin D sufficiency followed by vitamin D insufficiency in 12.6% cases, vitamin D deficiency seen in 12.1% cases and severe vitamin D deficiency seen in 3.4% cases.

- The result was found to be statistically significant.

- Finally, we can conclude that severity of complications increases with decrease in serum level of vitamin D.

Table 3

- In the present study, maximum number of babies were born alive in study(90.7%) and control group(96.7%).Perinatal outcome was poor in study group(9.3%) as compared to control group(3.3%).In study group,3.3%, 1.3%, 3.3% and 1.3% women had fresh stillbirths, IUDs, early neonatal deaths and congenitally malformed babies respectively. In control group only 1.3%, 0.7% and 1.3% women had fresh stillbirths, IUDs, early neonatal deaths respectively.

Because of increased chances of maternal complications in vitamin D deficient cases, perinatal outcome becomes poor.

Table 4

- In the present study, maximum number of babies had birth weight between 2.5-<3Kg in study group (36%) and control group (69.33%).

- In study group, 12%cases had birth weight below 2 Kg compared to 3.33% cases in control group. This difference is due to maximum IUGR cases had birth weight below 2Kg and some severe Preeclampsia cases and Preterm cases also had birth weight below 2Kg.

- In study group, 24% cases and in control group, 4.67% cases had birth weight between 2-<2.5Kg.

- In study group, 17.33% cases and in control group, 18% cases had birth weight between 3-<3.5Kg.
- In study group,5 cases(3.3%) had birth weight more than 4Kg.All the 5 macrosomic babies were born by mothers with GDM(5 out of 11,i.e.45%).

- Hunter et al (1993)[23] in his study, reported 45% incidence of macrosomia in pregnant diabetic women. A study by Nathanson et al (1950)[24] also showed 40% incidence of macrosomia, result comparable to present study.

Table 5

- In the present study, it was observed that newborns of study group had more neonatal complications than newborns of control group. Prematurity (15.3%)was the commonest perinatal complication in study group followed by growth retardation(14%)and respiratory distress(12%). Hypoglycaemia, hyperbilirubinimia, hypocalcaemia and polycythemia was seen in 2%, 0.7%, 1.3% and 0.7%cases.In control group,1.3%,1.3%,3.3%,0.7%,0.7% had prematurity, growth retardation, respiratory distress, hypoglycaemia and hypocalcaemia.

- At the time of registration, total cases of SGA were 28, out of them, 23 have intrauterine growth restricted baby and 5 cases have normal weight baby after treatment.

- As per study by Godwin et al (1999)[25], the newborns of women with gestational diabetes were seven times more likely to have hypoglycaemia, nine times more likely to have respiratory distress and three times more likely to have hyperbilirubinimia.

- Michael S Krameret al (1990)[26] in a study on 8719 infants found that with progressive severity of IUGR, there was significant(all P <.001) linear trends for increasing risks of fetal distress, neonatal hypoglycaemia, hypocalcaemia and polycythemia.

- Resnik et al (2002)[27] in a study found that intrauterine growth restriction increases the risk of perinatal morbidity and mortality.

CONCLUSION

The vitamin D-deficiency epidemic during pregnancy is caused by a lack of adequate sunlight exposure needed to synthesize vitamin D_3 in skin, coupled with overall intakes that are too low to meet the increased demand of pregnancy.The study results suggest that low levels of 25(OH) D may be a modifiable risk factor in pregnancy and maternal vitamin D deficiency in pregnancy is significantly associated with elevated risk for Preeclampsia, GDM, Preterm birth and Small for gestational age baby. Vitamin D supplementation in early pregnancy may be a simple way to reduce the risk of these adverse pregnancy outcome and health-care providers should at least encourage pregnant women for vitamin D intake.In our region, considering the high incidence of vitamin D deficiency, vitamin D supplementation should be strongly recommended to all pregnant females from the early weeks of pregnancy.

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