

Assessment of maternal vitamin D status in gestational diabetes mellitus

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Abstract

Introduction: Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Recently it has been discovered that vitamin D plays a major role in glucose homeostasis. Studies have also reported that vitamin D deficiency may increase the risk of GDM.

Aim: To assess the maternal vitamin D status in women with GDM and to compare the levels of vitamin D in women with GDM and normal pregnancy.

Materials and Method: A total of 100 pregnant women during 24 to 28 weeks of pregnancy between the age group of 20 to 35 years and BMI of 18.5 to 29.99 kg/m² were selected. Fifty women diagnosed having GDM by 75 gm OGTT with the blood sugar levels of ≥ 140 mg/dl after 2 hours of oral glucose according to WHO criteria were taken as GDM group and 50 women with normal OGTT values as control group. The total Serum 25(OH)D levels were estimated by fully automated chemi luminescence immunoassay. The results were analyzed by chi square test and Student's 't' test. A p value of <0.05 is considered significant.

Results: The mean vitamin D level was significantly decreased in women with GDM (11.78 ± 7.86 ng/ml) compared to normal pregnancy (31.48 ± 5.01 ng/ml) with p value <0.0001 and is found to be significant.

Conclusion: Vitamin D levels were found to be lower in women with GDM as compared to women with normal pregnancy. As the vitamin D level decreases, the blood sugar level increases in women with GDM.

Keywords: Gestational Diabetes Mellitus, Vitamin D, Oral Glucose Tolerance Test, Chemi luminescence Immunoassay

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Introduction

"Pregnancy is a physiological process that invites a woman to yield to the unseen power behind all life where soul and spirit are stretched". But, pregnancy has its own risks. We know, diabetes mellitus is a rapidly growing metabolic disarray in modern era, mainly due to insulin resistance, referred as diabetes.⁽¹⁾ Gestational Diabetes Mellitus (GDM) is one of the commonly encountered medical problem, in pregnancy.^(1,2) Women with GDM, have an increased possibility of acquiring diabetes later on. So, identification of GDM is a major health concern. Pregnancy is a diabetogenic state, as insulin requirements during pregnancy are increased.⁽³⁾ As the pregnancy advances, insulin resistance increases, as the placental hormones like human placental lactogen, prolactin and cortisol, which has anti-insulin effect also increases.^(3,4) GDM appears usually after 24 weeks of pregnancy.⁽⁴⁾

Vitamin D has been well recognized for its beneficial effect on bone health. Recent discovery is that, receptors for vitamin D are identified in many body tissues like beta cells of pancreas, muscle, and placenta.⁽⁵⁾ Multiple tissues in our body like placenta, breast, lung, colon, prostate, bone, parathyroid, pancreas, immune system express vitamin D receptors.⁽⁵⁾ Vitamin D deficiency (VDD) is pandemic throughout the world, it not only has its influence on skeletal tissues but also influences the non-skeletal tissues. Vitamin D deficiency during pregnancy has a special importance as it has a chance to affect both the mother and fetus.⁽⁶⁾ During pregnancy, vitamin D deficiency is linked to adverse effects on mother like

preeclampsia, obesity, GDM, bacterial vaginosis, and increased rates of cesarean delivery.^(6,7) The active metabolite of vitamin D, 1,25-dihydroxy vitamin D is found to regulate the secretion of beta cells by complexing to the vitamin D receptors present in the beta cell and also helps in maintaining the equilibrium between the intracellular and extracellular calcium stores.⁽⁵⁾ Vitamin D enhances insulin sensitivity by inducing the expression of insulin receptors and influencing beta cell function.^(8,9)

Epidemiological reports have revealed that women with Vitamin D deficiency during pregnancy, have a higher risk of GDM. As vitamin D deficiency is more common nowadays, it created an interest in me to assess the maternal vitamin D levels in women with GDM attending Coimbatore Medical college Hospital, Coimbatore and also to find any relationship between deficiency of vitamin D and GDM. This study may be an eye opener for the treating physicians to substitute vitamin D along with calcium during pregnancy, to prevent GDM due to Vitamin D deficiency. The body's vitamin D status is assessed by estimating the serum 25-hydroxyvitamin D levels (25(OH)D).⁽¹⁰⁾

Aims and Objectives

- To assess the maternal vitamin D status in women with GDM
- To compare the levels of vitamin D in women with GDM and normal pregnancy
- To find correlation between blood sugar levels and vitamin D levels in GDM.

Materials and Method

This is a Cross Sectional study. The study was performed in the department of Physiology along with the department of Obstetrics and Gynaecology, Coimbatore Medical College and Hospital, Coimbatore. A total of 100 pregnant women between 20 - 35 years of age and Body Mass Index (BMI) of 18.5 – 29.9 Kg/m² were selected for the study. Fifty women diagnosed having GDM by 75gm OGTT with blood sugar levels of ≥ 140 mg/dl after 2 hours of oral glucose were considered as GDM group. The control group comprised of fifty women with normal glucose levels after 75 gm OGTT.

Inclusion criteria:

- Fifty women diagnosed having GDM who were age as well as BMI matched taken as GDM group
- Fifty normal pregnant women who were also age as well as BMI matched – control group
- Both primigravida and multigravida were included.
- Pregnant women having antenatal records with height and weight recorded at first booking visit (around 6-8 weeks of pregnancy) were included.
- Pregnant women were selected for estimation of serum 25(OH)D concentrations during 24 to 28 weeks of gestation.

Exclusion criteria:

- Pre-gestational diabetes
- Hypertension
- Twin pregnancy
- Obese women (BMI >30Kg/m²)
- Women with other systemic diseases like hypothyroidism, autoimmune diseases, liver and renal diseases.
- H/o drug intake like steroids and anti-epileptic drugs

Materials used for the study:

- Proforma - To obtain a detailed history and clinical examination findings.
- Fetoscope - to determine the fetal heart sound
- Auto analyser – for analysis of blood sugar level.
- Immuno analyser - to measure total 25(OH)D levels

After obtaining clearance from the institutional ethical committee, the cases and controls were selected.

The cases and controls were explained about the procedure in detail and informed written consent was obtained. The study protocol consists of:

History Taking And Clinical Examination: Detailed history was elicited from the cases and controls to rule out signs and symptoms of pre-gestational diabetes, cardiovascular diseases, liver and kidney diseases and any intake of drugs. The last menstrual period (LMP) was noted and weeks of pregnancy was calculated using Naegele's rule (add 7 days to the first day of LMP and count back three months). General examination was done. Obstetric examination was done to confirm the weeks of pregnancy. The height as well as weight recorded during the first visit of pregnancy (6-8 weeks of gestation) were obtained from the antenatal records and BMI was calculated. BMI was calculated by using Quetelet's index. (BMI = Weight in Kilogram / Height in squaremeters). The subjects were selected with a BMI between 18.5 to 29.99 kg/m² which included women with normal BMI (18.5 to 24.99) and overweight (25 to 29.99) according to WHO criteria. The obese women (BMI >30) were not included in the study.

Blood Investigations

75 gm OGTT – WHO criteria: This is a 75 gm, 2 hour OGTT.⁽¹⁾ This investigation was done to standardize the diagnosis of GDM. A cut-off value for diagnosing GDM is a plasma glucose level of ≥ 140 mg% after 2 hours oral glucose according to WHO criteria. The test was done irrespective of the last meal. The test was done at 24 to 26 weeks of pregnancy. In the antenatal clinic, the pregnant women were given a 75 gram glucose load orally. Then a blood sample was collected from a peripheral vein after 2 hrs and the estimation of plasma glucose was done using Glucose Oxidase-Peroxidase (GOD - POD) technique.

Measurement of total Serum 25(OH)D Levels: With strict aseptic precautions, the blood sample was collected from the antecubital vein. The serum was separated by centrifuging the blood to 3000 rpm for 5 minutes. The serum was used to estimate total 25(OH)D level. This was done by fully automated Chemiluminescence assay. (ADVIA centaur immune assay technique).



Statistical Tools: Data analysis was done using Epidemiological Information Package (EPI 2010) in the computer, given by the Centre for Disease Control at Atlanta. Employing the above software, calculations of the mean, the range, the frequencies, percentages, standard deviations(SD), chisquare and 'p' values were done. Student's 't' test was employed to analyse the significance of difference between the quantitative variables (25(OH)D and OGTT). A significant association is considered only when the 'p' value is less than 0.05. Microsoft Power point was employed to prepare graphs.

Results

Table 1: OGTT values between GDM and control group

Parameter	OGTT (mg/dl)	
	GDM Group	Control Group
Range	144 – 273	84 – 136
Mean	183.1	113.1
S.D.	30.3	14.1
'p'	< 0.0001 Significant	

Oral Glucose Tolerance test shows a significant difference in both the groups. The mean blood sugar level in GDM group was 183 ± 30.3 mg/dl and in control group was 113.1 ± 14.1 mg/dl. The p value was found significant ($p < 0.0001$).

Table 2: Vitamin D Levels between GDM Group and control group

Vitamin D status 25(OH)D(ng/ml)	GDM Group		Control group	
	Number	%	Number	%
Severe deficiency (< 5)	7	14	-	-
Moderate deficiency (5.1 – 10)	23	46		
Mild deficiency (10.1 - 20)	12	24	2	4
Insufficiency (20.1 – 30)	5	10	12	24
Sufficient levels (> 30)	3	6	36	72
Total	50	100	50	100
25(OH) D (ng/ml)				
Range	4.56 – 32.26		17.42 – 44.42	
Mean	11.78		31.48	
SD	7.86		5.01	
'p'	< 0.0001 Significant			

Women in the GDM group showed significantly lower concentrations of vitamin D levels compared to women with normal pregnancy.

Table 3: Vitamin D Status and OGTT in GDM Group

Vitamin D Status (ng/ml)	OGTT values	
	Mean	S.D.
Severely deficient (< 5)	195.9	31.2
Moderate deficient (5.1 – 10)	194.3	31.4
Mild deficient (10.1 - 20)	175.4	20.2
Insufficient (20.1 – 30)	150.4	4.4
'p' Value	0.0042 Significant	

This infers that severe VDD was found in women with higher blood sugar level.

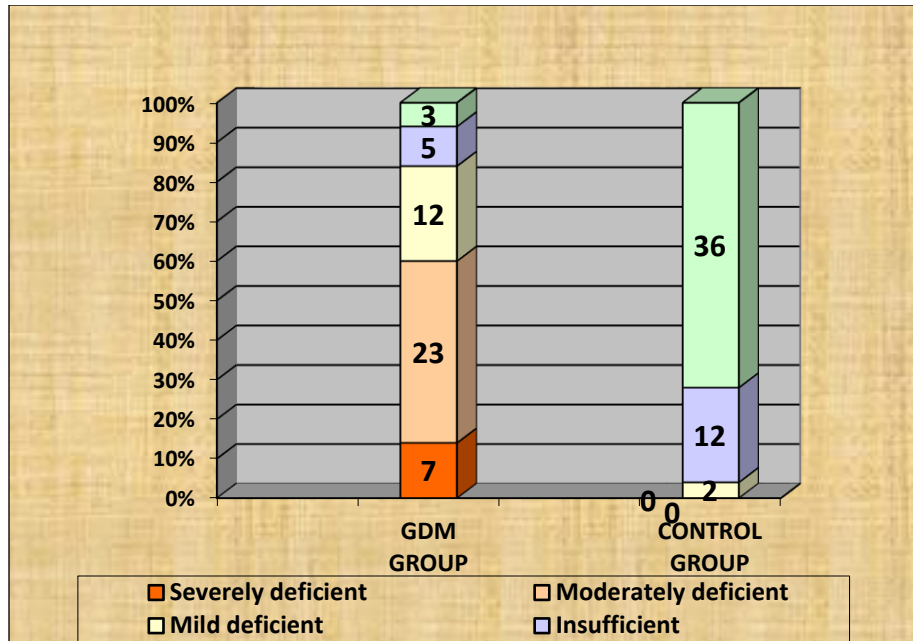


Fig. 1: Vitamin D Status in GDM Group and Control Group

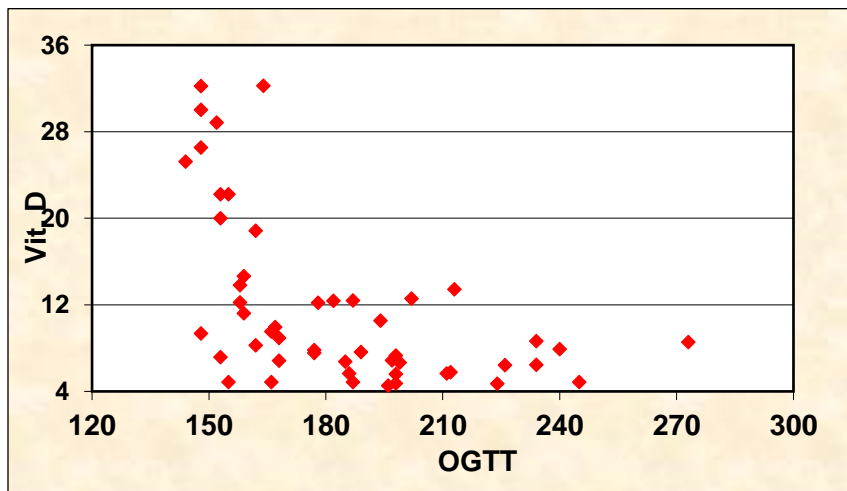


Fig. 2: Correlation between OGTT and Vitamin D

Correlation coefficient between OGTT values and 25(OH)D is found - 0.5455 (negative correlation). This shows that, as the vitamin D level decreases, the blood sugar level increases in women with GDM.

Discussion

Pregnancy is a diabetogenic state since insulin requirements during pregnancy are increased.⁽³⁾ The most important reason why pregnancy increases the diabetic tendency of asymptomatic women is the progressive increase in insulin resistance.⁽¹²⁾ During the second half of pregnancy, there is increased synthesis of placental hormones which are responsible for insulin resistance as well as diabetogenic tendency.⁽¹³⁾ Many studies emphasize the need of vitamin D in regulating glucose metabolism. Recent evidence suggest that

vitamin D is essential for the release of insulin directly and indirectly.⁽⁵⁾

In the present study, 50 women with GDM were taken as GDM group and 50 women with normal pregnancy who were age and BMI matched, as control group. The study was done between 24 to 28 weeks of pregnancy, as the diabetogenic tendency is maximum after second trimester of pregnancy due to the peaking of placental hormones which is done similar to the studies by Soheilykhah et al,⁽¹⁴⁾ Maghbooli et al.⁽¹⁵⁾ The current study inferred that the mean 25(OH)D concentration was statistically lower in GDM group as compared to controls. The mean 25(OH)D concentration in the GDM group was 11.78 ± 7.86 ng/ml and in control group was 31.48 ± 5.01 ng/ml. These findings were consistent with the results of Soheilykhah et al,⁽¹⁴⁾ Maghbooli Z et al.⁽¹⁵⁾

In current study, 84% of women with GDM showed VDD, in which 14% of women in GDM group were severely vitamin D deficient (<5ng/ml), 46 % of women with GDM reported moderate deficiency (5.1 to 20ng/ml), 24% of GDM women showed mild deficiency (10.1 to 20ng/ml), 10% showed insufficiency (20.1 -30 ng/ml) and 6% had normal vitamin D levels (>30ng/ml). Women with normal OGTT showed 4% VDD, 24% had insufficiency and 72% had normal levels of vitamin D. These findings were consistent with results of Soheilykhah et al.⁽¹⁴⁾ It is inferred that 25(OH)D levels were inversely associated with the blood glucose levels. These findings were consistent with the results of Soheilykhah et al,⁽¹⁴⁾ Madhu Jain et al.⁽¹⁶⁾

The probable mechanisms by which it influences glucose homeostasis and its deficiency leads to risk of GDM are: Vitamin D acts by modulating pancreatic β - cell action as well as secretion of insulin by binding to Vitamin D Receptors(VDR) present on beta cells and thereby regulating the extracellular as well as intracellular calcium pools.⁽¹⁷⁾ Vitamin D acts directly on beta-cells to induce secretion of insulin by increasing calcium levels intracellularly through voltage sensitive calcium channels. Facilitates the stimulation of endopeptidases in the beta cells which are also calcium dependant and thereby helps to convert proinsulin to insulin.⁽¹⁸⁾ Vitamin D is important for maintaining the extracellular calcium so that to ensure intracellular calcium influx normally through the cell membranes.⁽¹⁸⁾ This action helps in mediating depolarization induced release of insulin. Vitamin D helps in recruitment of GLUT-4 to cell surface that improves glucose uptake.⁽¹⁹⁾ Vitamin D enhances the expression of calbindin which protects β -cells from cytokine stimulated cell death.⁽⁵⁾ It acts a potent immune modulator which down regulates the transcription of pro-inflammatory mediators like interleukins which are responsible for autoimmune beta cell damage.⁽⁵⁾

Limitations

Large sample size and follow up studies would be of great value. Further, studies with vitamin D substitution in women with GDM would strongly help in revealing the influence of vitamin D in glucose homeostasis.

Conclusion

From the current study, it is found that vitamin D levels were found to be lower and deficient in women with GDM compared to women with normal pregnancy. This study throws light on the relationship between the vitamin D deficiency and GDM. Vitamin D deficiency is considered as a preventable and modifiable risk factor for GDM. As GDM has adverse health impacts on the mother and the fetus, screening for Vitamin D deficiency in pregnancy is essential.

Supplementation of vitamin D, encouraging outdoor activities and exercise which increases exposure to sunlight, may play a pivotal role in decreasing the incidence of GDM and diabetes mellitus in future.

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