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Research Article

Correlation of Vitamin D Levels and Gestational Diabetes Mellitus in Antenatal Women

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Abstract

Background: Gestational Diabetes Mellitus (GDM) is considered as an early marker of glucose intolerance, associated with both insulin resistance and impaired insulin secretion. GDM also leads to substantial fetal morbidity and mortality. Multiple reports have demonstrated birth anomalies, growth restriction, obesity and macrosomia in the offspring of diabetic women. Vitamin D deficiency is also commonly observed during pregnancy. It is well documented that Vitamin D plays a role in improving insulin sensitivity and glucose tolerance. However, it is still unclear whether vitamin D deficiency induces GDM or whether supplementing vitamin D to deficient pregnant woman can prevent GDM and its adverse outcomes.

Aims: This study was carried out to elicit relationship between vitamin D deficiency and GDM in antinatal women.

Materials and Methods: In this observational cross-sectional study, 214 subjects were enrolled from the out - patients attending obstetrics services. A pregnant women undergoing clinical examination is given a 75 g oral glucose load between 24- 28 weeks of gestation, irrespective of her fasting or non-fasting state and time of last meal. GDM is diagnosed if 2 hour plasma glucose is ≥ 140 by GOD- POD (glucose oxidase- peroxidase) method. Their serum vitamin D levels are also assessed at the same time. Sample size and study subjects was calculated by:

$N= (Z\alpha/2 +Z\beta)*PQ*2/d^2$

All the data was compiled in a Microsoft Excel Sheet for various variables of interest which was presented in the form of graphs and tables appropriately. Pearson's chi-square test was applied to find out the association between independent categorical data.

Results: In the present study we observed that 68 (31.4%) women were having GDM, deranged GCT was seen in another 73 women (34.11%). All 68 women with GDM belonged to the age group of 21-35 years and only one women out of 73 with deranged GCT was less than 20 years of age. We observed that majority of women were having sufficient levels of vitamin D (41.1%), 55(25.7%) had vitamin D deficiency and 71 (33.2%) had insufficient levels of vitamin D.

Conclusion: This study shows a weak correlation between GDM and Vitamin-D deficiency.

Keywords: 25-hydroxy-vitamin-D; Pregnancy; Gestational Diabetes Mellitus

Abbreviation

GCT: Glucose Tolerance Test; GDM: Gestational Diabetes Mellitus; DGCT: Deranged Glucose Tolerance Test

Introduction

Gestational Diabetes Mellitus (GDM) is one of those markers of glucose impairment which is associated with both defective insulin secretion and insulin resistance [1]. The prevalence of gestational diabetes mellitus (GDM) is increasing globally. Well-established risk factors for GDM include advanced maternal age, obesity or maternal overweight status, prior history of GDM, family history of type-2 diabetes mellitus [2,3]. However, it is not clear whether vitamin D status is associated with the risk of GDM. Accumulating evidence links vitamin D deficiency with abnormal glucose metabolism and epidemiological studies have shown that women who develop GDM are more likely to be vitamin D deficient [4]. Observational studies revealed correlation between low vitamin D levels and preeclampsia or GDM [5]. Vitamin D deficiency in pregnancy was related to the incidence of GDM and serum 25(OH)D was significantly lower in women with GDM than in those with normal glucose tolerance [6-10]. Whether this association is causal, however remains unclear [11]. Women diagnosed to have GDM are at increased risk of diabetes in future, predominantly type 2 DM.

Aims and Objectives

This study has been carried out to elicit any relationship between vitamin-D deficiency and GDM considering high risk of women with GDM of type-2 diabetes mellitus in future.

Materials and Methods

This observational cross-sectional study was conducted in the department of Obstetrics and Gynaecology, Asian Institute of Medi-

cal Sciences, Faridabad, Haryana. 214 subjects were enrolled from among the out – patients at obstetrics services.

Exclusion criteria: Diagnosed case of:

- Type 1 diabetes mellitus
- Type 2 diabetes mellitus
- Chronic hypertension
- Multiple pregnancy
- Cardiac disease
- Tested positive for HbsAg, VDRL or HIV
- Conceived with ART

After undergoing preliminary clinical examination glucose challenge test with 75 g oral glucose load is done between 24- 28 weeks of gestation, irrespective of her fasting or non-fasting state and time of last meal. GDM is diagnosed if 2 hour post 75 gram oral glucose value of plasma sugar level is ≥ 140 by GOD- POD (glucose oxidase- peroxidase) method. Their serum vitamin D levels are also assessed by electro chemiluminescence binding immunoassay technique.

Categorization of vitamin-D status:

Category	SERUM 25- OH VITAMIN D
Vitamin d deficient	<= 20 ng/mL
Vitamin d insufficient	20-30 ng/mL
Vitamin d sufficient	>30 ng/mL

Table a

DIPSI guidelines for diagnosis of GDM

Criteria	In pregnancy	Outside pregnancy
2 hr >= 200 mg/Dl	Diabetes	Diabetes
2 hr >= 140 mg/dL	Gestational diabetes mellius	Impaired glucose tolerance
2 hr >= 120 mg/dL	Deranged glucose challenge test	

Statistics

N= Sample Size

$Z_{\alpha/2}$= Z value at 10% alpha (type-I) error (1.64)

Z_{β}= Z value at 20% beta (type-II) error (0.84) (Power of study 80%)

P= $(p_1+p_2)/2$

Q=1-P

Observation and Results

Table 1: Distribution of Vitamin D Values in our study group.

Vitamin D results (ng/ml)	Frequency	Percent	Prevalence
Deficient (≤20)	55	25.7	25.70
Insufficient (21–30)	71	33.2	33.18
Sufficient (>30)	88	41.1	41.12
Total	214	100.0	

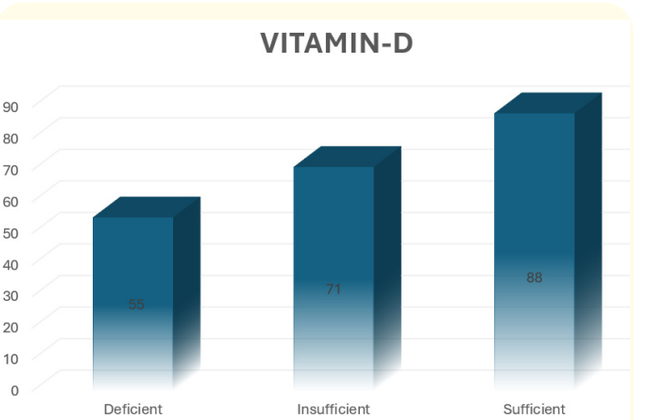

Figure 1

Table 2: GCT results (DIPSI).

Sugar levels after 75gm glucose challenge (mg/dl)	Frequency	Percent	Prevalence
Normal (<120)	73	34.11	34.11
DGCT (≥120)	73	34.11	34.11
GDM (≥140)	68	31.78	31.78
Total	214	100.0	

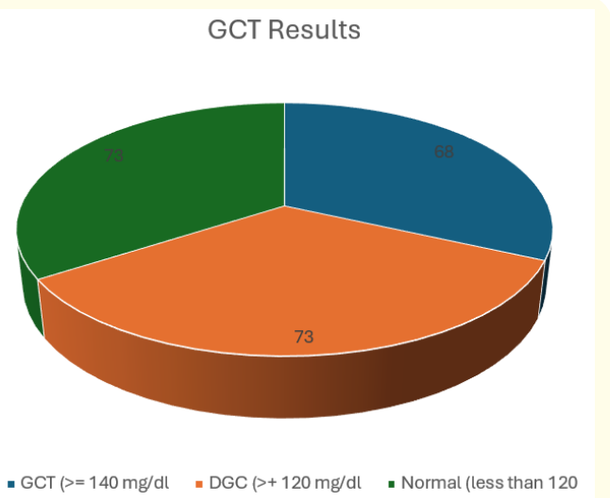

Figure 2

Table 3: Distribution of BMI.

BMI (*weight/meter*^{2})	Frequency	Percent
Underweight (<18.5)	6	2.8
Normal (18.5–24.9)	80	37.4
Overweight (25.0–29.9)	82	38.3
Obese (>30)	46	21.5
Total	214	100.0

Table 4: Correlation of GCT and Vitamin D.

Pearson Correlation	Sig.(2-tailed)
.004	.958

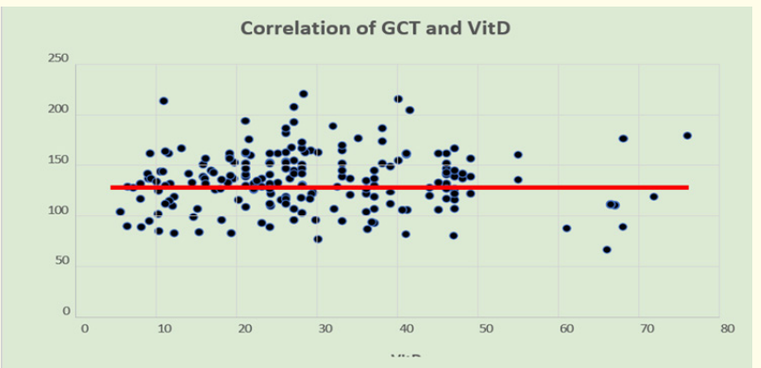

Figure 3

In the present study we observed that there is a weak correlation between GCT and Vitamin D deficiency.

Table 5: Associations of GCT and Vitamin D.

Vitamin D	Criteria for Diabetes			Total	Chi Square Value	df	P value
	Normal	DGCT	GDM				
Deficient	21(38.2%)	23(41.8%)	11(20.0%)	55(100.0%)	9.911	4	0.042
Insufficient	20(28.2%	19(26.8%)	32(45.1%)	71(100.0%)			
Sufficient	32(36.4%)	31(35.2%)	25(28.4%)	88(100.0%)			
Total	73(34.1%)	73(34.1%)	68(31.8%)	214(100.0%)			

We used chi square test and found there is a significant difference between GCT values and Vitamin-D levels (p value is 0.042 at 95% confidence interval).

Discussion

Globally vitamin D deficiency is found in 54% of all pregnancies and in 75% of newborns, this affects pregnant women of all latitudes, not only those with lower exposure to sunlight. In Europe, the vitamin D deficiency prevalence is 57%, while it is 73% in newborns [11]. Despite the mentioned high frequency of vitamin D deficiency, there is no consensus about the need for 25(OH)D level evaluation or the requirement of supplementation in pregnancy [12].

Sahu M., *et al*. showed a prevalence of vitamin D deficiency of 74.1% from the north-eastern part of India [13]. In our study 214 women enrolled in the second trimester, had mean age of 30.06 +/- 3.71 years. All the participants belonged to urban population. On evaluation 55 (25.7%) pregnant women had vitamin D deficiency, 71 (33.2%) had insufficient vitamin D levels and the remaining 88 (41.1%) had normal vitamin D levels.

Poel., *et al*. in a meta analysis of four out of seven observational studies have reported a high incidence of vitamin D deficiency (>50%, 25(OH)D <50 nmol/L) in pregnant women with the risk of GDM with an Odds ratio of 1.61 [14].

Dwarkanath., *et al*. [16] noted the association of low maternal plasma vitamin D concentrations in early pregnancy with an increased risk of GDM consistent with findings from three separate meta-analysis of published studies [17-19], emphasizing the pivotal role of vitamin D in perinatal period. This association remained statistically significant even after adjusting for the confounding factors which is in accordance with recent meta analysis conducted by Hu., *et al*. which indicated a decrease in the levels of vitamin D in GDM mothers as compared to the control group [19].

Wei., *et al*. found an increase in the risk of GDM by 40-60% in women with vitamin D deficiency during second trimester of pregnancy [18]. Several, but not all, observational studies have found an association between low 25(OH)D level and increased risk of GDM. In a matched, case-control study of 54 Iranian women with GDM and 11 normoglycemic controls, Soheilykhah., *et al*. found that maternal 25(OH)D concentrations at 24–28 weeks of gestation were significantly lower in women with GDM [20]. They noted that 83% of GDM women had 25(OH)D levels <50 nmol/L (a cutoff often used to define vitamin D deficiency [21-24]) vs. 71% of controls. Clifton-Bligh and colleague studied 264 women in Australia and found that among the 32% of patients with GDM, 25(OH)D levels were significantly lower compared to normoglycemic women [25]. In another study of Iranian women at high risk for vitamin D deficiency, Hossein-Nezhad and colleagues found that 29% of 741 women had 25(OH)D levels <15 nmol/L and the prevalence of GDM in this subgroup was higher compared to women with 25(OH)D levels ≥35 nmol/L [26]. Likewise, Zhang., *et al*. found in a nested case-control study in the United States (Washington) of 57 cases of GDM, that maternal 25(OH)D levels at 16 weeks' gestation were 20% lower among women who later developed GDM [27].

However, other studies have not detected a statistically significant association between 25(OH)D level and GDM. Farrant., *et al*. [15] found no association between maternal vitamin-D status and risk of GDM in a cross-sectional study of 559 pregnant women from south-india at the gestational age of 30 weeks. Likewise, Makgoba and colleagues studied 90 cases of GDM and 158 controls in the United Kingdom and reported no association between first trimester blood samples and subsequent development of GDM [28]. Baker and colleagues conducted a nested case-control study in the United States (North Carolina) using routine first trimester serum aneuploidy screening blood samples, and in their comparison of 60 women who later developed GDM and 120 controls who did not, the investigators found no association between 25(OH)D level and the odds of GDM. Plasma levels of vitamin D may not be a contributing factor for the development of GDM in women with a low risk for GDM [10].

Conclusion

India has high predisposition for insulin resistance. Besides the regional factor, genetic predisposition adds to this too. Causal or not concomitant deficient vitamin D status adds to poor health outcome. Hence, regardless of whether optional vitamin D status can prevent GDM, limited trial data suggests that exploring an adjunctive role of vitamin D supplementation for females with established GDM may be fruitful in preventing adverse outcome in mother and fetus.

In our study we observed that there is a weak correlation between GDM and vitamin D deficiency. Additional observational studies with well-designed RCT's are required to have a conclusive relation between vitamin D and GDM.

Ethical Board Clearance

The study was initiated after approval by the institutional ethics committee. Study participants were explained purpose of study and written informed consent was taken in an approved consent format.

Conflicts of Interest

There are no conflicts of interest.

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