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Original Article

Severe 25(OH)vitamin-D deficiency: A risk factor for development of gestational diabetes mellitus

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ABSTRACT

Objective: To estimate the level of 25 (OH)vitamin D in gestational diabetes mellitus (GDM) and to find the correlation between level of 25(OH)vitamin D and GDM.
Materials and methods: The study was conducted on 50 diagnosed patients of GDM attending antenatal clinic in the obstetrics and gynecology department of Pt. B.D. Sharma PGIMS, Rohtak. 50 age and gestational age matched normoglycemic women were taken as control group. Procedure of study was explained to the participants and informed consent was taken.
Results: GDM women had higher age, BMI, and positive family history of type 2 DM as compared to pregnant women without GDM. The mean vitamin D in GDM women was 32.64 ± 24.33 nmol/L while in controls it was 39.90 ± 21.86 nmol/L(P = 0.033). The prevalence of severe vitamin D deficiency(<25 nmol/L) was found to be 44% among GDM women (22 out of 50 GDM women) and 20% among women with normoglycemia (10 out of 50 normoglycemic controls) with significant p value of 0.010 and odds ratio of 1.833. GDM women with BMI>25 kg/m^2 had 1.799 times chances to be severely deficit in vitamin D than women with BMI<25 kg/m^2 6 GDM women had mild vitamin D deficiency (>50 but <75 nmol/L) and 16 had moderate deficiency (>25 but <50 nmol/L). Only 6 GDM patients were found to be sufficient for vitamin D(>75 nmol/L).
Conclusion: Severe vitamin D deficiency in second trimester of pregnancy is significantly associated with elevated risk for GDM.

1. Introduction

Gestational diabetes mellitus (GDM) is defined as diabetes diagnosed in the second or third trimester of pregnancy that is not clearly either type 1 or type 2 diabetes [1]. This definition applies regardless of whether insulin or only diet modification is used for treatment. GDM affect maternal, fetal and neonatal well-being. In mothers, GDM is associated with higher risk of cesarean section and the later development of T2DM. For offspring, GDM is associated with macrosomia, birth trauma, respiratory distress syndrome, jaundice, polycythemia, fetal growth disturbance and hypoglycemia. Children born to women with pregnancies complicated by GDM are also at increased risk for future development of glucose intolerance and obesity. Various risk factors found to be associated with development of GDM include overweight/obesity, family history of diabetes etc. In recent past it had been found that Vitamin D deficiency during early pregnancy significantly increases the risk for GDM in later pregnancy [2]. Vitamin D is known to influence insulin secretion and insulin resistance [3,4]. Data on vitamin D status in gestational diabetes is unclear, conflicting and scarce especially in India. Only few studies have been carried out before and no study has been conducted in Haryana before. The present study was conducted to evaluate the correlation of Vitamin D level in GDM.

2. Materials and methods

50 cases of GDM and 50 age and parity matched pregnant women with normal plasma glucose levels attending antenatal clinic in the obstetrics and gynecology department of Pt. B.D. Sharma PGIMS, Rohtak were recruited for this study. The procedure

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of study was explained to the participants and informed consent was taken and the study was approved by Institutional review board. A performa containing general information on demographic characteristics, socio-economic status, parity, family history of diabetes and/or hypertension and past history of GDM was filled up, history of hospitalization and/or urinary tract infection during present pregnancy was recorded. Personal history of smoking, alcohol consumption was also recorded. Blood was sampled under aseptic conditions and sent for estimation of serum vitamin D level. The vitamin D estimation assay used for this study was ELISA method using Calbiotech Vitamin D kit which provides intra assay variation of <6% and coefficient of variance of <8%.

Depending on the values obtained, the patients were categorized as having vitamin D sufficiency if its concentration is > 75 nmol/L or 30 ng/ml, insufficiency if levels are <75 but >50 nmol/L or <30 but >20 ng/ml, deficiency when levels are <50 but >25 nmol/L or <20 but >10 ng/ml and severe deficiency with levels <25 nmol/L or 0–10 ng/ml[5].

According to the objectives of the study, the collected data was compiled, tabulated and analyzed, using appropriate statistical tests. SPSS (Statistical Package for the Social Sciences) version 17 was used for calculations.

3. Results

The present cross-sectional study included 50 GDM (study group) and 50 age and gestation matched normoglycemic women (control group) attending ANC clinic at PGIMS Rohtak. The baseline characteristics of study and control population are summarized in Table 1. GDM women had higher age, BMI, and positive family history of type 2 DM as compared to pregnant women without GDM. The mean vitamin D in GDM women was 32.64 ± 24.33 nmol/L while in controls it was 39.90 ± 21.86 nmol/L(P = 0.033). The prevalence of vitamin D deficiency in study and control population is given in Table 2. On comparing 50 GDM cases and 50 normoglycemic controls, prevalence of severe vitamin D deficiency(<25 nmol/L) was found to be 44% among GDM women (22 out of 50 GDM women) and 20% among women with normoglycemia (10 out of 50 normoglycemic controls) with significant p value of 0.010 and odds ratio of 1.833. GDM women with BMI>25 kg/m^2 had 1.799 times chances to be severely deficit in vitamin D than women with BMI<25 kg/m^2 6 GDM women had mild vitamin D deficiency (>50 but <75 nmol/L) and 16 had moderate deficiency (>25 but <50 nmol/L). Only 6 GDM patients were found to be sufficient for vitamin D(>75 nmol/L). Mild and Moderate Vitamin D deficiency was not found to be more common in GDM women, Infact more women in the control group had moderate Vitamin D deficiency as compared to study group. Table 3 compares GDM women with severe vitamin D deficiency(<25 nmol/L) with rest of the study group.

Table 2
Showing serum 25(OH) Vitamin D Level of Study & Control Group (n = 50).

25(OH)Vit D(nmol/l)	Study Group		Control Group		P Value
	Frequency	%	Frequency	%	
<25	22	44%	10	20%	0.010
25–50	16	32%	29	58%	0.009
50–75	6	12%	6	12%	1.000
>75	6	12%	5	10%	0.749
Total	50	100%	50	100%	
Mean ± SD	32.64 ± 24.33		39.90 ± 21.86		0.033

4. Discussion

In the present study it was found that level of vitamin D were significantly lower in women with GDM than normoglycemic controls and severe Vitamin D deficiency(<25 nmol/L) is associated with GDM (p = 0.010; OR = 1.833) while no association was found with mild and moderate deficiency. The previous studies have not shown the association of GDM with mild moderate or severe vitamin D deficiency. In our study severe vitamin D deficiency was found in 44% of GDM women (22 out of 50) and 20% of normoglycemic women (10 out of 50) [p = 0.010].

A rising trend in prevalence of gestational diabetes mellitus has been suggested by studies done in various parts of world as well as India. The causes of GDM are an active area of investigation with growing interest in vitamin D deficiency as a potential cause [6,7]. Reduced availability of maternal vitamin D in pregnancy represents a plausible mechanism contributing to the development of insulin resistance leading to GDM. The association between 25(OH)vitamin D levels and GDM in the literature is not entirely clear and data relating vitamin D to the risk for GDM are sparse. Various studies conducted in past have concluded that maternal vitamin D deficiency is highly prevalent in early pregnancy and is an independent risk factor for GDM. In the present study the mean vitamin D in GDM women was significantly lower as compared to control population. These finding paralleled with observations made in various previous studies[2–3, 8–14]. A study by Zhang et al. [8] found that plasma levels of 25[OH]D among GDM women were significantly lower than control (24.4 vs. 30.1 ng/ml, p < 0.001). A study by Soheilykhah et al. [9] found that 83% of GDM women had 25(OH)D levels <50 nmol/L vs. 71% of controls(p = 0.03). Maghbooli et al. [10] found that Vitamin D levels were significantly lower in GDM (7% of the sample) and IGT (22% of the sample) groups, compared to women who were normoglycemic. Muthukrishnan et al. [2] found that serum 25-OH Vit D levels were significantly lower in GDM (24.7 ± 17.6 ng/ml) versus control group (45.8 ± 28 ng/ml, P = 0.0004). Jain et al. [11] found that serum 25(OH) D concentrations were significantly lower (46% less) in women who subsequently developed GDM compared with controls (11.93 ± 3.42 ng/ml vs. 22.26 ± 15.28 ng/ml, p < 0.001). Use of different criteria for Vitamin D deficiency/insufficiency/sufficiency or method of

Table 1
Baseline characteristics of study and control groups.

	Study Group	Control Group	P Value
Mean age ±SD	25.94 ± 4.90	23.28 ± 4.77	0.04
Mean BMI	25.52 ± 4.41	22.29 ± 1.99	0.05
Mean Age of Gestation (wk)	26.66 ± 1.59	26.18 ± 1.32	0.102
Housewife	46(92%)	47(94%)	0.695
Working	4(8%)	3(6%)	0.695
Mean Income/Month	6563.27 ± 3166.08	6136.00 ± 2464.92	0.455
Urban residence	9(18%)	16(32%)	0.106
Rural residence	41(82%)	34(68%)	0.106
Positive Family history of diabetes	9(18%)	3(6%)	0.03

Table 3
Showing Vitamin D status of GDM women (n = 50).

25(OH)Vit-D (nmol/L)	<25	25–50	50–75	>75	P Value
Number of Patients	22	16	6	6	
Age (Mean ± SD)	25.14 ± 4.72	27.44 ± 5.09	24.50 ± 5.47	25.04 ± 6.19	0.462
Income (Mean ± SD)	6890.91 ± 3543.86	6466.67 ± 3351.26	6666.67 ± 2804.76	5500 ± 1516.58	0.827
Housewife(N)	19	15	6	6	0.560
Working(N)	3	1	0	0	0.560
Education > Sr sec (N)	6	4	3	1	0.310
Urban(N)	5	3	1	0	0.645
Rural(N)	17	13	5	6	0.645
Family history of diabetes(N)	4	3	0	2	0.516

Vitamin D estimation are factors that can be responsible for different observed results. In the present study, we categorized GDM women according to current definitions of Vitamin D deficiency as suggested by Holick MF [5]. In the present study although severe Vitamin D deficiency was found to be associated with GDM, the mild and moderate Vitamin D Deficiency was comparable between the two groups and this might be due to the high background prevalence of Vitamin D deficiency among general population from India. Similar observations had been made by Farrant et al. [12] in their study and they concluded that although Vitamin D insufficiency is common in Indian mothers, it is not associated with gestational diabetes or variation in newborn size.

In the present study the mean BMI of women who developed GDM was significantly higher than normoglycemic controls. It was observed that GDM women with BMI>25 kg/m^2 had 1.799 times chances to have severe Vitamin D deficiency as compared to women with BMI<25 kg/m^2. Results were comparable to previous studies by Makgoba et al. [13] and Zhang et al. [8].

Several limitations merit discussion and consideration in our study. First, a single measurement of plasma 25-(OH)vitamin D concentrations is not likely to provide a time integrated measure of maternal vitamin D status during the entire study pregnancy. Longitudinal studies with serial measurements of maternal plasma 25-(OH)vitamin D concentrations, indices of insulin sensitivity and secretion are needed to elucidate the mechanisms and pathophysiological consequences of maternal vitamin D deficiency during pregnancy. Second, our study is relatively small and thus, large prospective studies are needed to confirm our results.

In conclusion, our study provides data indicating that severe vitamin D deficiency in second trimester of pregnancy is significantly associated with elevated risk for GDM. Such evidence is valuable in view of the limited prospective data on the relation of circulating vitamin D status to impaired glucose tolerance in either pregnant or non-pregnant individuals.

Conflicts of interest

No conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.01.004.

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