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Original Research Article

Relationship of vitamin D deficiency and gestational diabetes mellitus in pregnant women

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common metabolic disorder among pregnant women. It is important to be diagnosed and treated early to minimize complications for both the mother and the foetus. Recent studies found that deficiency of vitamin D is a risk factor for GDM and its supplementation may be helpful in prevention of GDM. Objectives were to assess vitamin D status in pregnant women with or without GDM and to find out the association between vitamin D deficiency and GDM.
Methods: A total of 400 patients were included in the study, 200 pregnant women diagnosed with GDM and 200 normoglycemic pregnant women. Serum 25 (OH) vitamin D concentration in these women were compared.
Results: Only 6.75% of women were found to have normal vitamin D levels, all others having either insufficiency 18.5% or deficiency 74.75%. In case group around 79% of women had vitamin D deficiency, 70.5% in control group. In case group around 14.5% of women had vitamin D insufficiency, 22.5% in control group. In both case and control group around 6.5% and 7% of women were within the normal range respectively. Mean vitamin D is 14.3 ng/ml in case group and 15.4 ng/ml in control group.
Conclusion: Prevalence of vitamin D deficiency is alarmingly high in pregnant women in India and has become a re-emerging public health issue and needs to be addressed.

Keywords: Vitamin D deficiency, Gestational diabetes mellitus

INTRODUCTION

Diabetes mellitus with the first onset in pregnancy-gestational diabetes mellitus (GDM) is a common complication of pregnancy.[1] The frequency of GDM may reach up to18% depending on the population and diagnostic criteria used.[2] Even the normal pregnancy is characterized by a marked reduction in maternal insulin sensitivity in the second and third trimesters. However, the reduced β cells reserve or their maladaptation to higher insulin demands may lead to the development of GDM. Resulting abnormal metabolic situation during pregnancy might adversely influence the fetal development (resulting most often in macrosomia with subsequent delivery complications and possibly also the postnatal health status of offspring due to the fetal programming). Moreover, GDM is a significant predictor of woman's predisposition to the development of diabetes mellitus type 2 later in life as documented by epidemiological studies.[3,4] In addition, GDM strongly predicts cardiovascular disease in the future life. The risk is increased by 70% in women with a previous history of GDM compared to women without this history.[5]

Several studies have consistently shown that 1,25 (OH)2 D concentration increases progressively during gestation being twice as high in late pregnancy as in postpartum or in non-pregnant controls.[6,7] The active form 1,25 (OH)2D

is also produced by placenta during pregnancy with possible autocrine or paracrine function.[8,9]

A number of studies focused on putative role of vitamin D deficiency in various pregnancy pathologies including GDM.[10] Observational studies revealed correlation between low vitamin D levels and preeclampsia or GDM.[11] 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.[12] Whether this association is causal remains however unclear.[13] Furthermore, several studies found inverse correlation between 25(OH)D and fasting plasma glucose (FPG), 1 hour after load plasma glucose in oral glucose tolerance test (OGTT) and glycated haemoglobin.[14]

Nowadays, GDM is a common metabolic disorder among pregnant women. It is important to be diagnosed and treated early to minimize or avoid complications for both the mother and the foetus. Recent studies found that deficiency of vitamin D is a risk factor for GDM and this risk factor differs from population to population. Therefore, levels of vitamin D in GDM women compared to controls give us knowledge about our population status and the strategies to reduce or avoid hypovitaminosis D and GDM. Vitamin D supplementation to pregnant women may be helpful in the prevention strategy of GDM and the serious complications which can affect both the mother and the baby in the future.

Aims and objectives

Aims and objectives were to assess vitamin D status in pregnant women with or without GDM and to find out the association between vitamin D deficiency and GDM.

METHODS

The present case-control study was conducted in the Postgraduate Department of Obstetrics and Gynecology, Lalla Ded Hospital, an associated hospital of GMC, Srinagar after obtaining the ethical clearance from the institutional ethical committee between July 2020 to January 2022.

Inclusion criteria

All low-risk pregnant mothers visiting as out patients or admitted in labor ward were selected, gestational diabetes mothers as study group (group-A) and normoglycemic mothers as control group (group-B). Vitamin D concentration in these women were compared.

Exclusion criteria

Exclusion criteria included women with chronic hypertension, renal disease, hypothyroidism, collagen vascular disease, diabetes mellitus and multiple pregnancy, other complications (PIH, anemia, preeclampsia) not willing for study, on steroids, metformin, any drug that interferes with vitamin D metabolism like anti-epileptics and nifedipine.

Statistical methods

The recorded data was compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of statistical package for the social sciences (SPSS) version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. Student's independent t-test was employed for comparing continuous variables. Chi-square test was applied for comparing categorical variables. A p value of less than 0.05 was considered statistically significant.

RESULTS

Data regarding age, socio-economic class, educational status, parity, body mass index were recorded. Details regarding previous history of GDM, family history of diabetes mellitus, previous pregnancy outcome was recorded. Thorough clinical examination was done and vitals like blood pressure and pulse rate were recorded. Venous blood samples for 25(OH) vitamin D estimation were collected after 12 hours overnight fasting, protected from light, centrifuged and stored at – 200°C until analysis. 25 (OH) vitamin D estimation were done using chemiluminescent immunoassay (CLIA). Value of 25 (OH) vitamin D ≤20 ng/ml was the cut off to define vitamin D deficiency.

Table 1: Comparison based on BMI in cases and controls.

BMI	Cases		Controls		P value
	No.	%	No.	%	
<18.5	1	0.5	3	1.5	0.002*
18.5-24.9	93	46.5	101	50.5	
25.0-29.9	79	39.5	89	44.5	
≥30.0	27	13.5	7	3.5	
Total	200	100	200	100	
Mean±SD	25.7±4.19		24.5±3.47		

*Statistically significant difference (p value<0.05); p value by student's independent t-test

Mean age of case group is 27.3±6.54 and that of controls is 26.9±5.83. Majority of patients fall between 21-30 years. Mean body mass index (BMI) of cases is 25.7±4.19 kg/m^2 and that of controls is 24.5±3.47 kg/m^2. It is observed that the difference in BMI between two groups is statistically significant (p value=0.002). Mean gestational age of cases was 32.7±3.97 weeks and of controls were 33.2±3.42 weeks. Mean sun exposure of cases is 4.6±1.83 hours and that of controls is 4.8±1.54 hours. Mean vitamin D levels of cases is 14.3 ng/ml and that of controls is 15.4 ng/ml. In cases 158 (79%) had vitamin D deficiency (0-20

ng/ml), 29 (14.5%) had insufficiency (21-30 ng/ml) and 13 (6.5%) had normal levels (>30 ng/ml). While in controls 141 (70.5%), 45 (22.5%) and 14 (7%) had deficiency, insufficiency and normal levels.

Table 2: Vitamin D status of cases and controls.

Duration (hours)	Cases		Controls		P value
	No.	%	No.	%	
Deficiency (0-20 ng/ml)	158	79.0	141	70.5	0.107
Insufficiency (21-30 ng/ml)	29	14.5	45	22.5	
Normal (>30 ng/ml)	13	6.5	14	7.0	
Total	200	100	200	100	

Table 3: Comparison based on vitamin D levels (ng/ml) in cases and controls.

Group	N	Mean	SD	95% CI	P value
Cases	200	14.3	6.53	12.71-19.52	0.112
Controls	200	15.4	7.19	13.95-21.09	

Table 4: Comparison based on gestational age in cases and controls.

Gestational age (weeks)	Cases		Controls		P value
	No.	%	No.	%	
32	87	43.5	65	32.5	0.178
33	53	26.5	54	27.0	
34	60	30.0	81	40.5	
Total	200	100	200	100	
Mean±SD	32.7±3.97		33.2±3.42		

Table 5: Duration of sun exposure in cases and controls.

Duration of sun exposure (hours)	Cases		Controls		P value
	No.	%	No.	%	
0-4	73	36.5	61	30.5	0.238
4-8	126	63.0	136	68.0	
8-12	1	0.5	3	1.5	
Total	200	100	200	100	
Mean±SD	4.6±1.83		4.8±1.54		

DISCUSSION

Of the 400 antenatal women included in the study, only 6.75% of women were found to have normal vitamin D levels, all others having either insufficiency 18.5% or deficiency 74.75%. In India there is a very high prevalence of low level of vitamin D among pregnant women in spite of our country being tropical. Mean exposure to sun in case group is 4.6±1.83 and control group is 4.8±1.54. The Vitamin D status is analysed. It is observed that, in case group around 79% of women had vitamin D deficiency, whereas it is 70.5% in control group. In case group around 14.5% of women had vitamin D insufficiency whereas it is 22.5% in control group. In both case and control group around 6.5% and 7% of women were within the normal range respectively. Mean vitamin D is 14.3 ng/ml in case group and 15.4 ng/ml in control group. The association between GDM and vitamin D deficiency is controversial. Savvidou et al investigated maternal serum 25(OH) D levels at 11^{+0}-13^{+6} weeks of gestation in three groups of complicated pregnancies including women who had type 2 diabetes, women who subsequently developed GDM and non-diabetic women who delivered macrosomic neonates, and they failed to find a significant difference in vitamin D levels compared to those in non-diabetic controls.[15] Similarly, Makgoba et al examined first-trimester maternal serum 25(OH) D levels and GDM in a case-control study of 90 pregnant women and did not find an evidence of an association in women with GDM compared to 158 controls.[16] On the other hand, there are several studies which reported a significant association between vitamin D deficiency and GDM. Recently, Zuhur et al studied 234 cases of GDM and 168 controls in Turkey and reported that only severely deficient maternal serum 25(OH)D levels (<5.2 ng/ml) were significantly associated with an elevated relative risk of GDM.[17] Likewise, Maghbooli et al studied maternal vitamin D deficiency and GDM in a cross-sectional study of 741 pregnant women at 24-28 weeks gestation and found significantly lower levels of 25(OH)D in women with GDM compared to normoglycaemic controls.[18] They reported higher rate of severe vitamin D deficiency (<10 ng/ml) (70.6%) compared to that in our study (44.6%) and suggested that severe vitamin D deficiency might contribute to insulin resistance. Zhang et al studied vitamin D deficiency in early pregnancy (mean gestational age: 16 weeks) and found a 2.66-fold increased risk of GDM in women with vitamin D deficiency.[19] The prevalence of vitamin D deficiency (<20 ng/ml) was found to be high in 20% of women in this cohort. In a study by Farrant et al the participants with vitamin deficiency received vitamin D and calcium supplementation at the 30th week; no association was found between vitamin D deficiency and gestational diabetes. However, it should be noted that this study was limited to women admitted to the hospital and its results could not be generalized to the whole population, and is also in line with our results. Clinical trials in different part of world have shown that the effect of vitamin D supplementation in pregnant women increases birth weight and height.[20]

Limitations

There are some limitations that should be noted. The sample size taken was small and hence a large randomized controlled trial is necessary to determine the vitamin D

levels in pregnancy and to draw guidelines regarding screening and supplementation.

CONCLUSION

Based on our study, there are many women who are deficient in vitamin D and many others who are insufficient. Prevalence of vitamin D deficiency is alarmingly high in pregnant women in India and has become a re-emerging public health issue. Due to lack of vitamin D level screening, many women go undetected and are suffering from adverse outcomes including in newborn. So, there is a need to identify them early in pregnancy and supplementing pregnant women with vitamin D and to decrease the likelihood of them developing complications. We would like to conclude this study saying that in a country like India where the prevalence of vitamin D deficiency among pregnant women is high, adequate sun exposure, dietary intake and supplementation is necessary. Only viable option is fortification of food products and supplementation of vitamin D to population at risk. Policies and recommendations should be drawn up by the Government of India to combat the pandemic that's rising silently.

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