e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(6); 1620-1623

Original Research Article

Study of Preventing Development of Gestational Diabetes Mellitus in Role of Vitamin D Supplementation

Preeti Singh[1], Priyanka[2], Pratima[3], Kumari Bibha[4]

[1]Assistant Professor, Department of Obstetrics and Gynaecology, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar

[2]Senior Resident, Department of Obstetrics and Gynaecology, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar

[3]Assistant Professor and HOD, Department of Obstetrics and Gynaecology, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar

[4]Professor, Department of Obstetrics and Gynaecology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar

Received: 25-01-2024 / Revised: 23-02-2024 / Accepted: 26-03-2024

Corresponding Author: Dr. Pratima

Conflict of interest: Nil

Abstract:

Background: Adverse pregnancy outcomes such as infertility, gestational diabetes mellitus (GDM), preeclampsia, higher rate of cesarean delivery, bacterial vaginosis, newborn hypocalcaemia, fetal growth restriction (FGR), and neonatal convulsions have all been linked to hypovitaminosis D. It was recently suggested that low vitamin D status may raise the risk of GDM. Clinical quantification of the effect of vitamin D supplementation on women at increased risk of GDM development is necessary. The purpose of this research is to determine how vitamin D supplementation can help high-risk pregnant women avoid developing gestational diabetes mellitus.

Methods: In a randomised, double-blind, interventional study, 178 antenatal women with biochemically diagnosed vitamin D deficiency having at least one risk factor for GDM with gestational age 13-24 weeks were randomised into intervention group (86 participants) and control group (92 participants). Women in the intervention group were given vitamin D supplementation, in the form of oral cholecalciferol sachet 60,000 IU per week till 26th week. Women in both intervention and control groups continued to receive iron, calcium and vitamin B, C supplement from second trimester till delivery. Oral Glucose Tolerance Test (OGTT) between 26th-28th weeks was carried out and GDM was determined.

Results: Among 86 patients in intervention group, 13.95% developed GDM while 86.05% did not develop GDM. On the other hand, 32.61% patients in control group developed GDM, while 67.39% did not develop GDM. The difference observed in development of GDM after supplementation with vitamin D was statistically significant ($p<0.001$).

Conclusion: It was found that vitamin D supplementation for high-risk pregnant women in the second trimester is useful in preventing development of gestational diabetes mellitus. Investigations to diagnose vitamin D deficiency in pregnant patients and timely supplementation during pregnancy can significantly improve the feto-maternal outcome. Vitamin D could become a new generation drug which is safe, cheap, simple and easily available with additional pleiotropic effects in prevention of GDM.

Keywords: Gestational diabetes mellitus; Vitamin D supplementation; Cholecalciferol.

Introduction

Hypovitaminosis D has been associated with adverse pregnancy outcomes like infertility, GDM, preeclampsia, increased rate of caesarean section, bacterial vaginosis, neonatal hypocalcaemia, FGR, neonatal seizures. [1,2] As per The Endocrine Society (USA), vitamin D deficiency is defined as 25-Hydroxy vitamin D concentration less than 20 ng/ml, while concentration between 20-30 ng/ml is considered as vitamin D insufficiency. [3]Recently, poor vitamin D status was proposed as a contributor to increased GDM risk. Pregnant women are at high risk of vitamin D deficiency, leading to nearly two fold increased risk of GDM by factors regulating the production of vitamin D in the skin. [1] Several mechanisms may explain the observed association between vitamin D deficiency and GDM risk. Vitamin D may directly or indirectly modulate pancreatic β-cell function and secretion, can promote insulin sensitivity and may also regulate extracellular calcium, thus ensuring normal calcium

influx through cell membranes and an adequate intracellular cytosolic calcium pool, which is essential for insulin-mediated intracellular processes in insulin-responsive tissues. [4]

Many researchers have shown the relationship between vitamin D deficiency and GDM, but little is known about the effect of taking vitamin D supplementation in preventing GDM. There is a need to clinically quantify the impact of vitamin D supplementation in the second trimester on women at higher risk of developing GDM, thus generating evidence in this field of research. Only then can a simple measure like vitamin D supplementation be routinely advised to patients at high risk for GDM. The current study was designed to illuminate the impact of vitamin D supplementation in second trimester on women who are at higher risk of developing GDM.

Materials and Methods

This randomised, double-blind, interventional study was conducted in the Department of Obstetrics and Gynaecology at Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar from January 2023 to December 2023. Written informed consent was taken from all the study subjects. Women attending antenatal OPD, who were vitamin D deficient (25-Hydroxy Vitamin D concentration less than 20ng/ml), aged between 18-40 years, with gestational age 13-24 weeks and had at least one of the risk factors for GDM (BMI > 25kg/m^2, history of macro some neonate, positive family history for diabetes, history of GDM in previous pregnancies, glycosuria in morning urine sample) were included in the study. Patients with who already had diabetes before pregnancy, with diagnosed GDM at the time of first visit at OPD, history of vitamin D supplementation within six months prior to the study, history of intake of drugs that interfere with glucose metabolism like glucocorticoids, thiazide diuretics, beta blockers, etc and with chronic medical illness were excluded in this study.

Total 178 antenatal women (n=178) with above mentioned criteria were randomised into intervention group (86 participants, n1=86) and control group (92 participants, n2=92). Women in the intervention group were given vitamin D supplementation, in the form of oral cholecalciferol sachet 60,000 IU per week till 26th week, which was dissolved in water and taken under supervision. Women in both intervention and control groups continued to receive iron, calcium and vitamin B, C supplement from second trimester till delivery. Every month all the women recruited in the study were examined. OGTT was performed according to the ADA/IADPSG (American Diabetes Association and the International Association of the Diabetes and Pregnancy Study Group) Guideline. Threshold values for venous plasma glucose are as follows.

- Fasting - ≥ 92 mg/dl
- 1st hour - ≥ 180 mg/dl
- 2nd hour - ≥ 153 mg/dl

One or more of such values would indicate gestational diabetes mellitus. Those who were diagnosed to be gestational diabetes mellitus patients were then referred to Medicine OPD for diabetic control and they were managed conservatively. All the patients were followed up until delivery.

Results

The predominant age group was 21-25 years both in the intervention group (45%) and the control group (47%). Sixty four percent participants in intervention group and 62% participants in control group were burkha clad. The difference observed in religion (p value 0.98), type of complexion (p value 0.14) and socioeconomic status (p value 0.62) was not statistically significant making the groups comparable.

Of all the participants, 27.91% participants in interventional group and 40.22% participants in control group had BMI more than 25 kg/m^2. Also, 39.06% patients in interventional group and 39.62% patients in control group had macrosomia in previous pregnancies. Total 42.19% participants in interventional group and 43.39% patients in control group had history of GDM in previous pregnancies. Ninety three percent patients in interventional group had no glycosuria in morning urine sample which was comparable to controls (91%). Moreover, 69% participants in interventional group had family history of diabetes.

On the other hand, in control group, 53% had family history of diabetes. The difference between the incidence of BMI ≥ 25 kg/m^2 (p value 0.08), macrosomia in previous pregnancies (p value 0.98), history of GDM in previous pregnancies (p value 0.12), glycosuria in morning urine sample (p value 0.67) among intervention and control groups was not statistically significant (Table 1). However, the difference between the incidence of family history of diabetes among the two groups was statistically significant (p value 0.04).

Table 1: Distribution of participants in intervention and control groups according to risk factors

Risk Factors	Intervention group (n1=86)		Control group (n2=92)		Overall (n=178)		p Value
	Number	Percentage	Number	Percentage	Number	Percentage	
BMI > 25	24	27.91	37	40.22	61	34.27	0.08
Macrosomia	25	29.07	21	22.83	46	25.84	0.95

History GDM	37	43.02	23	25.00	60	33.71	0.12
Glycosuria	6	6.98	8	8.70	14	7.87	0.67
Family H/O Diabetes	59	68.60	49	53.26	108	60.67	0.04

In this study, among 86 patients in interventiongroup, 13.95% developed GDM while 86.05% did not develop GDM.

On the other hand, among 92 patients in controlgroup, 32.61% developed GDM, while 67.39% did not develop GDM (Table 2). The difference observed in development of GDM after supplementation with vitamin D was statistically significant (p <0.001).

Odds of participants in intervention group developing GDM after supplementation with vitamin D as compared to participants not developing GDM after vitamin D supplementation was 0.34 (95%C.I.:0.158–0.709).

Table 2 : Distribution of participants in intervention and control groups according to development of GDM in present pregnancy (n=178)

GDM	Intervention group (n1=86)		Control group (n2=92)		p- Value
	Number	Percentage	Number	Percentage	
Yes	12	13.95	30	32.61	< 0.001
No	74	86.05	62	67.39	
Total	86	100.00	92	100.00	

In the intervention group, 12 participants developed GDM in present pregnancy, out of which 83.33% were treated with Metforminand16.67%weretreatedwithInsulin,after detection of GDM (Table 3). Among the control group, 30 participants developed GDM, 76.67% of them were treated with Metformin and 23.33% were treated with Insulin. The difference observed in treatment of GDM was not statistically significant (pvalue0.634).

Table 3: Distribution of participants who developed GDM in intervention and control groups according to treatment taken for GDM (n=42)

Treatment	Intervention group		Control group		p Value
	Number	Percentage	Number	Percentage	
Metformin	10	83.33	23	76.67	
Insulin	2	16.67	7	23.33	0.634
Total	12	100.00	30	100.00	

Discussion

Vitamin D deficiency is an emerging risk factor for development of GDM, however there is paucity of literature pertaining to association between hypovitaminosis D and gestational diabetes mellitus from sun-rich country of India. [5] In a study by Pleskacova A. et al. positive history of GDM in previous pregnancies was significantly more frequent in GDM group compared to controls (p = 0.0491, Fischer's exact test). [6] Similarly in the present study, history of GDM in previous pregnancy was present in around 58% participants in interventional group.

In the present study, 39.06% patients in interventional group and 39.62% participants in control group had macrosomia in previous pregnancy. There was no statistical difference (p >0.05) between the incidence of confounding high risk factor of macrosomia in previous pregnancy among the two groups. Shahgheibi et al. found that history of macrosomia was present in almost 11% of participants both in vitamin D supplemented and non-supplemented groups. [7] In the present study, 69% participants in interventional group and 53% in control group had family history of diabetes. A p value of 0.04 makes this difference statistically significant. No positive family history of any form of diabetes (p=0.0018, Fisher's exact test) was found in the study by Pleskacova A.et al. [6]

This might be due to high prevalence of diabetes in India. In the given study, the difference between the incidence of confounding high risk factor of glycosuria in morning urine sample among the two groups was not statistically significant (p value 0.67). Glycosuria was present in 8.5% participants in vitamin D supplemented group and 4.4% participants in placebo group in the randomised placebo controlled trial by Shahgeibi et al. [7]

In the present study, the difference observed in development of GDM after supplementation of vitamin D was statistically significant (p <0.05). In a study by Muthukrishnan J. et al., it was found that supplementing vitamin D reversed GDM in11.7% of patients with vitamin D deficiency, which was statistically similar othose in normal vitamin D group (17.6%) following a similar advice on diet and lifestyle modification. Results from a study by Shahgheibi S.et al.in 2016 showed that vitamin D supplementation in the first and second trimester shows as an effect on GDM, in which

significantly higher percentages of positive glucose tolerance test (34.8%vs11.4%) and glucose challenge test (35.6% vs 10.9%) were observed in the control group compared with participants in the vitamin D supplementation group; both P<0.01. [7] Thus, the study results showed that pregnant women in the first trimester who received vitamin D had less GDM than women who received placebo, and this is statistically significant (P =0.009). In a study by Jahanjoo F. et al. the estimated overall effect demonstrated a statistically significant difference in the FPG (Fasting plasma glucose) serum level in women taking vitamin D supplements, meaning that intake of vitamin D supplements in women with GDM led to a significantly lower FPG serum level (MD–12.54mg/dL,95%CI–15.03to–10.05, p <0.001). [9] Thus in most studies, the results were similar to this study which shows that vitamin D supplementation in antenatal women resulted in less occurrence of GDM. However, in a study by Farrant HJ et al., percentages of women with gestational diabetes were similar in women with and without hypovitaminosis D (7% in both groups). [10] 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.

Conclusion

Vitamin D supplementation reduces risk of maternalco-morbidities like GDM and helps improve neonatal outcomes. Investigations to diagnose vitamin D deficiency in pregnant patients and timely supplementation during pregnancy can significantly improve the fetomaternal outcome. The present interventional study was carried out to illuminate the impact of vitamin D supplementation in second trimester on women who are at higher risk of developing GDM. The study concluded that vitamin D supplementation for high-risk pregnant women in the second trimester is useful in preventing development of gestational diabetes mellitus.

References

1. Yazdchi R, Gargari BP, Asghari-Jafarabadi M, Sahhaf F. Effects of vitamin D supplementation on metabolic indices and hs-CRP levels in gestational diabetes mellitus patients: a randomized, double-blinded, placebo-controlled clinical trial. Nutr Res Pract 2016;10 (3):328-35.
2. Barrett H, Mc Elduff A. Vitamin D and pregnancy: an old problem revisited. Best Pract Res Clin Endocrinol Metab 2010; 24(4):527-39.
3. Marilyn Urrutia-Pereira, DirceuSolé. Vitamin D deficiency in pregnancy and its impact on the fetus, the newborn and in childhood. Rev Paul Pediatr 2015; 33(1):104–113.
4. B Draznin, K E Sussman, R H Eckel, M Kao, T Yost. Possible role of cytosolic free calcium concentrations in mediating insulin resistance of obesity and hyperinsulinemia. J Clin Invest 1988; 82(6):1848–1852.
5. Kumari A, Mitra S, Tiwari H, of RS-IJ. Hypovitaminosis D in pregnancy and its correlation with preeclampsia and gestational diabetes mellitus. Int J ReprodContraceptObstetGynecol 2017; 6(3):890-896.
6. Pleskačová A, Bartáková V, Pácal L, et al. Vitamin D Status in Women with Gestational Diabetes Mellitus during Pregnancy and Postpartum. Biomed Res Int 2015; 2015:260624.
7. Shahgheibi S, Farhadifar F, Pouya B. The effect of vitamin D supplementation on gestational diabetes in high-risk women: Results from a randomized placebo-controlled trial. J Res Med Sci 2016; 28:21-2.
8. Muthukrishnan J, Dhruv G. Vitamin D status and gestational diabetes mellitus. Indian J Endocrinol Metab 2015; 19(5):616-9.
9. Jahanjoo F, Farshbaf-Khalili A, Shakouri SK, Dolatkhah N. Maternal and Neonatal Metabolic Outcomes of Vitamin D Supplementation in Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. Ann NutrMetab 2018; 73(2):145-159.
10. Farrant HJ, Krishnaveni GV, Hill JC, Boucher BJ, Fisher DJ. Vitamin D insufficiency is common in Indian mothers but is not associated with gestational diabetes or variation in newborn size. Eur J ClinNutr 2009; 63(5):646-52.