ORIGINAL ARTICLE

Role of Vitamins D Supplements in Preventing Development of Gestational Diabetes Mellitus

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ABSTRACT

Aim: To evaluate the role of vitamin D supplements in prevention of gestational diabetes mellitus. **Study Design:** Cross sectional.

Place and duration: Study was carried out at obstetrics and gynecology department of Roshan Suleman Medical College, Tando Adam, from June 10, 2021 to November 09, 2021.

Methodology: Initially 125 pregnant women were enrolled in study and 15 women refused to give consent and study was conducted on 110 pregnant women. Main variables of study were age of women, parity, education status, occupation and previous mode of delivery. Outcome of study was gestational diabetes at 28 weeks of glucose tolerance test. SPSS version 23 was used for data analysis, mean and SD for numerical data and frequency percentages for categorical data were calculated. Test of significance was chi square test and p value ≤0.05 was significant.

Results: Of the total patients, 40.9% had \leq 20 ng/ml and 59.1% had \geq 20 ng/ml level of vitamin D. It was seen that 44.4% patients had \leq 20 ng/ml as well as GDM. About 35.6% had normal OGTT with \leq 20 vitamin D level. On the other hand, most of the patients 60.0% had normal OGTT as well as \geq 20 ng/ml vitamin D level. The difference had statistically significant, (p=0.005).

Conclusion: use of vitamin D supplements in high risk pregnant women till 28 weeks of pregnancy has positive effect on prevention of gestational diabetes.

Keywords: Gestational diabetes, Vitamin D, 25-hydroxyvitamin D, gestational diabetes mellitus, GDM, pregnancy.

INTRODUCTION

Vitamin D a fat soluble vitamin has so many characteristics in human body along with bone health¹. It has a vital role in prevention of cell proliferation in prostate, colorectal and breast cancer and also famous for control of autoimmune disease. In some stages of life increased ratio of vitamin D is required especially during pregnancy for the purpose of fetal growth, at embryonic growth². Studies conducted on relationship between vitamin D and pregnancy concluded a strong association between pregnancy outcomes and vitamin D deficiency³. Its deficiency also associated with increased incidence of cesarean section, preeclampsia and gestational diabetes mellitus⁴.

Reverse relationship between risk of diabetes type II and vitamin D concentration also proved⁵. Direct effects of vitamin D concentration on glucose metabolism and pancreatic beta cells were observed thus later on a reverse mechanism with HbA1c/glycosylated hemoglobin was found⁶. Deficiency of vitamin D is also related to insulin concentration changes and blood glucose level. Gestational diabetes mellitus is also known as glucose intolerance in gestation which has similarity of pathophysiology with type II diabetes⁷.

Development of GDM have both maternal (infection, premature birth, hypertension and hydramnios) and fetal (altered fetal growth, death birth, respiratory distress syndrome, metabolic disorders, diabetes and obesity) complications⁸. During antenatal period vitamin D deficiency is a common phenomenon that causes

increased insulin sensitivity glucose tolerance. Many studies have shown a strong association between vitamin D deficiency and GDM but only fewer studies evaluated that role of vitamin D supplementation in prevention of GDM⁹.

Although number of observational studies proved the effect of vitamin D deficiency on gestational diabetes but role of vitamin D supplements and dose calculation in prevention of GDM is unknown yet^{10,11}. It was observed in vivo studies that vitamin D supplements improved the insulin secretion and glucose tolerance and very small authors reported its role in control of glucose in gestational age¹². Looking at vitamin D deficiency in Pakistani population, specifically in pregnant women and its adverse effects on pregnancy outcomes, this study was planned to investigate the role of vitamin D supplements during pregnancy on GDM in high risk women.

METHODOLOGY

Study was carried out at obstetrics and gynecology department of Roshan Suleman Medical College, Tando Adam from June 10, 2021 to November 09, 2021. Study was started after ethical approval from departmental ethical committee. Written informed consent was obtained from patients. Non probability consecutive sampling technique was used and sample size was calculated by using openepi.com online software with confidence interval 95% and margin of error 0.5%. Pregnant women presented at outpatients department having at least one risk factor like

previous history of gestational diabetes, increased body mass index (above 25 kg/m²), family history of diabetes or gestational diabetes, glycosuria and history of macrosomic baby were included. Women with any chronic disease like rheumatic disease, renal disease, thyroid, hepatic, gestational diabetes at admission time, diabetic before pregnancy and women already using vitamin D supplements were excluded.

Glucose challenge test was performed on all women then blood sample was taken for measurement of vitamin D level. Women with vitamin D level ≤20ug/ml and >20ug/ml were recorded. All women were advised vitamin D supplements 5000 units per week till 28 weeks. All women were examined every month and oral glucose tolerance test at 26-28 weeks was done to determine the gestational diabetes. Oral glucose tolerance test was done with following approach: Baseline blood glucose was measured after that 75 g oral glucose was given and blood glucose level. Fasting blood sugar 100-120 mg/dl or 140 mg/dl after 1 hour of oral glucose was considered as normal, similarly blood glucose 140-200 mg/dl after 2 hours of oral glucose considered as impaired. Test was taken as positive when two continuous OGTT were impaired.

Collected data was entered in SPSS version 23 and analyze for mean and SD of continuous variables e.g age, Frequency and percentages were calculated for categorical variables like education status, occupation, parity, previous mode of delivery. Test of significance were applied and p value ≤ 0.05 was taken as significant.

RESULTS

One hundred and ten patients were included in this study. The mean age of the patients was 28.87±6.32 years. Majority of the patients (62.7%) between age group 18-30 years.

Table 1: Demographic characteristics of the patients

Characteristic	N (%)	
Age distribution (years)		
18-30	69 (62.7)	
31-35	20 (18.2)	
36-45	21 (19.1)	
Education status		
Uneducated	45 (40.9)	
Primary	26 (23.6)	
Secondary	16 (14.5)	
Higher	23 (20.9)	
Occupation		
House wife	69 (62.7)	
Working lady	41 (37.3)	
Parity		
Primi para	53 (48.2)	
Multi para	57 (51.8)	
Previous mode of delivery		
Normal vaginal delivery	73 (66.4)	
Caesarean section	37 (33.6)	
Gestational age (weeks)		
4-13	43 (39.1)	
14-26	40 (36.4)	
27-35	11 (10.0)	
36 and above	16 (14.5)	

Most of the patients (62.7%) were house wives and uneducated (40.9%). Primi para had (48.2%) patients and multipara had (51.8%) patients. Majority of the patients were delivered by normal vagina (66.4%). The mean gestational age of the patients was 24.41 ± 6.31 weeks. Most of the patients between 4-13 weeks of gestational age. (Table. I).

Of the total patients, (40.9%) had ≤ 20 ng/ml and (59.1%) had > 20 ng/ml level of vitamin D. It was seen that (44.4%) patients had ≤ 20 ng/ml as well as GDM. Out of total (35.6%) had normal OGTT with ≤ 20 vitamin D level. On the other hand, most of the patients (60.0%) had normal OGTT as well as > 20 ng/ml vitamin D level. The difference had statistically significant, (p=0.005). (Table. II).

Table 2: Association of Vitamin D level with oral glucose tolerance test

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Oral alugada	Vitamin D level		
toloronoo toot	≤20 mg	>20 mg	P-value
	N (%)	N (%)	
Normal	16 (35.6)	39 (60.0)	
Paired	9 (20.0)	15 (23.1)	
Gestational	20 (44.4)	11 (16.9)	0.005
diabetes millets			
Total	45	65	

DISCUSSION

In our study we observed higher proportion of gestational diabetes in women with low level of vitamin D (\leq 20 mg) as compare to those women with higher level of vitamin D. Similar results were reported by Lacroix et al¹³ that low level of vitamin D in 1st trimester of pregnancy is responsible for GDM. Women with low level of vitamin D concentration are 1.4 time more prone to GDM.

In our study we investigated final glucose tolerance test at 26-28 weeks. In a study conducted by Farrant et al¹⁴ and final tolerance test was done at 30th week of pregnancy. Results showed significant reduction in plasma glucose level and reduced rate of GDM at the end of pregnancy. Asemi et al¹⁵ conducted a study on effect of vitamin D supplements on reduction of gestational diabetes. Two groups' vitamin D supplements and placebo were compared and observed significant reduction in plasma glucose level after administration of supplements as compared to placebo group.

A study was conducted by Pittas¹⁶ and concluded that there is an association between vitamin D deficiency and gestational diabetes mellitus. Further studies on prescription of vitamin D supplementation during antenatal period are recommended to evaluate the incidence of GDM and effect of vitamin D deficiency. Hossein et al¹⁷ also conducted a study on 741 pregnant women and concluded strong association between vitamin D concentration and insulin sensitivity index.

Zhou et al¹⁸ carried out a study on pregnant women who were presented with low serum vitamin D level and at the end of pregnancy they were observed with adverse pregnancy outcomes like macrosomic baby, congenital anomalies, birth weight and gestational diabetes. In our study we didn't included various pregnancy outcomes except gestational diabetes. Rudnicki and Pedersen¹⁹ found a significant decrease in GDM when glucose tolerance test was performed at 28 weeks of pregnancy. Zhang et al²⁰ completed a case control study on US population and reported that in women with 20% lower 25(OH) D level at 16 weeks of pregnancy were developed GDM in later pregnancy days. In contrast to our conclusion some studies reported no significant association between vitamin D and gestational diabetes. Makgoba and colleagues²¹ observed a study on 90 GDM and 158 controls in UK population and concluded that there is no association between development of subsequent GDM and blood samples taken for serum vitamin D level.

Limitations: Patient's poor compliance to study drugs and advise of non gynecological medical specialists, Hakeem's and lay man to stop any medication during pregnancy are main limitations of our study.

Recommendations: Proper counseling and education about importance of supplementation of vitamin D is necessary. Further studies with larger sample size are recommended.

CONCLUSION

Our findings reveal that use of vitamin D supplements in high risk pregnant women till 28 weeks of pregnancy has positive effect on prevention of gestational diabetes.

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REFERENCES

- Corcoy R, Mendoza LC, Simmons D, Desoye G, Adelantado JM, Chico A et al. The DALI vitamin D randomized controlled trial for gestational diabetes mellitus prevention: No major benefit shown besides vitamin D sufficiency. Clin Nutr. 2020;39(3):976-984. doi: 10.1016/j.clnu.2019.04.006.
- Liu J, Dai Q, Li W, Guo Y, Dai A, Wang Y et al. Association of vitamin D receptor gene polymorphisms with gestational diabetes mellitus-a case control study in Wuhan, China. BMC Pregnancy Childbirth. 2021;21(1):142. doi: 10.1186/s12884-021-03621-y.
- Gao C, Sun X, Lu L, Liu F, Yuan J. Prevalence of gestational diabetes mellitus in mainland China: a systematic review and meta-analysis. J Diabetes Investig. 2019;10(1):154–62. doi: 10.1111/jdi.12854.
- Apaydin M, Beysel S, Eyerci N, Pinarli FA, Ulubay M, Kizilgul M, Ozdemir O, Caliskan M, Cakal E. The VDR gene Fokl polymorphism is associated with gestational diabetes mellitus in Turkish women. BMC Med Genet. 2019;20(1):82. doi: 10.1186/s12881-019-0820-0.
- Zhu B, Huang K, Yan S, Hao J, Zhu P, Chen Y et al. VDR Variants rather than Early Pregnancy Vitamin D Concentrations Are Associated with the Risk of Gestational Diabetes: The Ma'anshan Birth Cohort (MABC) Study. J Diabetes Res. 2019 Jun 24;2019:8313901. doi: 10.1155/2019/8313901.
- Ojo O, Weldon SM, Thompson T, Vargo EJ. The Effect of Vitamin D Supplementation on Glycaemic Control in Women with Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. Int J Environ Res Public Health. 2019 May 16;16(10):1716. doi: 10.3390/ijerph16101716.
- Gunasegaran P, Tahmina S, Daniel M. Role of vitamin Dcalcium supplementation on metabolic profile and oxidative stress in gestational diabetes mellitus: A randomized

controlled trial. J Obstet Gynaecol Res. 2021; 47(3):1016-1022.

- Tripathi P, Rao YK, Pandey K, Gautam KA. Significance of Vitamin D on the Susceptibility of Gestational Diabetes Mellitus - A Meta-Analysis. Indian J Endocrinol Metab. 2019;23(5):514-524. doi: 10.4103/ijem.IJEM_184_19.
- Yue CY, Ying CM. Sufficience serum vitamin D before 20 weeks of pregnancy reduces the risk of gestational diabetes mellitus. Nutr Metab (Lond). 2020;17:89. https://doi.org/10.1186/s12986-020-00509-0.
- Azzam EZ, El-Aghoury AA, Abd El-Naby EE, El-Maadawy SA. Studying the relation between vitamin D deficiency and glycemic state among pregnant women with gestational diabetes. Diabetes Metab Syndr. 2019 Mar-Apr;13(2):1505-1509. doi: 10.1016/j.dsx.2019.03.007.
- Yoon HK. Gestational Diabetes Mellitus, Fetal Growth and Vitamin D. J Bone Metab. 2017 Aug;24(3):155-159. doi: 10.11005/jbm.2017.24.3.155.
- Yu F, Wang C, Wang L, Jiang H, Ba Y, Cui L, Wang Y, Yu S, Li W. Study and evaluation the impact of vitamin D receptor variants on the risk of type 2 diabetes mellitus in Han Chinese. J Diabetes. 2017;9(3):275–84. doi: 10.1111/1753-0407.12413.
- Lacroix M, Battista MC, Doyon M, Houde G, Ménard J, Ardilouze JL, Hivert MF, Perron P. Lower vitamin D levels at first trimester are associated with higher risk of developing gestational diabetes mellitus. Acta Diabetol. 2014 Aug;51(4):609-16. doi: 10.1007/s00592-014-0564-4.
- Farrant HJ, Krishnaveni GV, Hill JC, Boucher BJ, Fisher DJ, Noonan K et al. Vitamin D insufficiency is common in Indian mothers but is not associated with gestational diabetes or variation in newborn size. Eur J Clin Nutr. 2009;63(5):646-52. doi: 10.1038/ejcn.2008.14.
- Asemi Z, Karamali M, Esmaillzadeh A. Effects of calciumvitamin D co-supplementation on glycaemic control, inflammation and oxidative stress in gestational diabetes: a randomised placebo-controlled trial. Diabetologia. 2014 Sep;57(9):1798-806. doi: 10.1007/s00125-014-3293-x.
- Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab. 2007 Jun;92(6):2017-29. doi: 10.1210/jc.2007-0298.
- 17. Hossein-Nejad A, Maghbooli J, Arzaghi S, Shafaei A, Rahmani M, Larijani B. Relationship between vitamin D deficiency and gestational diabetes mellitus. IJDLD. 2006;5:226–35.
- Zhou J, Su L, Liu M, Liu Y, Cao X, Wang Z et al. Associations between 25-hydroxyvitamin D levels and pregnancy outcomes: a prospective observational study in southern China. Eur J Clin Nutr. 2014 Aug;68(8):925-30. doi: 10.1038/ejcn.2014.99.
- Rudnicki PM, Mølsted-Pedersen L. Effect of 1,25dihydroxycholecalciferol on glucose metabolism in gestational diabetes mellitus. Diabetologia. 1997 Jan;40(1):40-4. doi: 10.1007/s001250050640.
- Zhang C, Qiu C, Hu FB, David RM, van Dam RM, Bralley A et al. Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. PLoS One. 2008;3(11):e3753. doi: 10.1371/journal.pone.0003753.
- Makgoba M, Nelson SM, Savvidou M, Messow CM, Nicolaides K, Sattar N. First-trimester circulating 25hydroxyvitamin D levels and development of gestational diabetes mellitus. Diabetes Care. 2011 May;34(5):1091-3. doi: 10.2337/dc10-2264.