CPQ Medicine (2018) 2:4
Mini-Review

The Role of Vitamin D in Gestational Diabetes Mellitus and its Therapeutic Implications

Parth Shah

USA

***Correspondence to:** Dr. Parth Shah, Orlando, Florida, USA

Copyright

Received: 02 August 2018

Published: 28 August 2018

Keywords: *Gestational Diabetes; Insulin Resistance; Vitamin D; Fasting Glucose*

Abstract

Incidence of diabetes since 1980s has doubled worldwide, affecting 422 million people globally in 2014. In the United States, gestational diabetes mellitus occurs in approximately ~9.2% of the pregnant women. Women with previous history of gestational diabetes mellitus are highly prone to developing type II diabetes mellitus in the long run. A strong inverse correlation has been found between the risk of developing gestational diabetes mellitus and vitamin D deficiency/insufficiency in pregnant women. Furthermore, in women who were previously diagnosed with gestational diabetes mellitus, markers of developing insulin resistance have been found associated with their vitamin D status. Appropriate vitamin D supplementation recommendations are needed as a possible preventative measure for gestational diabetes mellitus and to reduce the long-term risk of developing diabetes.

Introduction

The vitamin D deficiency, widely clinically defined as <30-32 ng/mL (normal 30-100 ng/mL [1] or 32-100 ng/mL [2]), is highly prevalent worldwide. As per the <30 ng/mL cut-off, the prevalence in adults worldwide has ranged from 5% (Jordanian men) to 97% (parts of India) [3]. In North America, the vitamin

D deficiency prevalence has ranged from 28% to 59% at <30 ng/mL vitamin D level cut-off. Furthermore, at the cut-off <20 ng/mL, highest rate of vitamin D deficiency can be seen in the United States (U.S.) blacks at 82.1% and Hispanics at 69.2% [3,4]. Recent studies have brought to light an association between the vitamin D status and insulin resistance in pregnant women.

As per the World Health Organization (WHO), the incidence of diabetes since 1980 in adults (18+ years) has doubled across each of the regions worldwide [5]. As per the World Health Organization, in 2014, an estimated 422 million (8.5%) people worldwide had diabetes [5,6]. Every year, 1.5 million Americans are diagnosed with diabetes, and in 2015, 84.1 million American adults had prediabetes [7]. The prevalence of gestational diabetes mellitus (GDM) is estimated to be as high as 9.2% in the United States [8]. Approximately 50% of women with previous history of GDM develop diabetes mellitus type II (DMII) [9]. Some known fetal complications of the GDM include increased birth weight, large for gestational age, and macrosomia [10]. Given that GDM can have poor maternal and fetal outcomes, it has become crucial to implement the preventative measures.

Vitamin D and Prevention of GDM

Correlations have been found between the blood levels of vitamin D and the development of GDM. A cross-sectional study in 155 pregnant women at 24-28 weeks gestation demonstrated significant inverse relationship between their vitamin D levels and their second trimester insulin and blood sugar 2-hours post ingestion of 75 g of glucose [11]. Another study in Saudi pregnant women found that from those who were vitamin D deficient (<20 ng/mL) in the first trimester, 27.7% developed GDM in the second trimester, and there was an inverse correlation between their fasting plasma glucose (FPG) and first trimester vitamin D levels [12]. In a study in women with recurrent miscarriages, assessment of vitamin D levels at baseline and insulin levels pre and post 75 g OGTT illustrated hyperinsulinemia in 58% of patients in the vitamin D deficient group (<50 nmol/L, <20 ng/mL), 38.7% in the insufficient group (50-74.9 nmol/L, 20-29.9 ng/mL), and 33.3% in the sufficient group (≥75nmol/L, ≥30 ng/mL) [13]. In assessing 4,718 second- and third-trimester pregnant women in China, a strong association was found between vitamin D deficient women (<50 nmol/L, <20 ng/mL) and the risk of developing GDM [14]. Overall, multiple studies done in different regions of the world have found an inverse association between the vitamin D status and the gestational markers of insulin resistance.

There have been studies pointing to the relationship between varying amounts of vitamin D ingestion and the risk of developing GDM. In a study involving 15,225 women with a total of 21,356 singleton pregnancies, pre-pregnancy vitamin D intake from food sources and supplements was followed for 10 years. An inverse relationship was found between the relative risk (RR) of GDM and vitamin D intake at levels 0, 1-399, and ≥400 IU/day as 1.00, 0.80, and 0.71, respectively [15]. In a randomized placebo-controlled trial, pregnant women with one risk factor for GDM were started on vitamin D 5,000 IU/day or placebo [16]. At week 26 of the pregnancy, an abnormal glucose challenge test (GCT) was significantly higher in the placebo group compared to the vitamin D group; furthermore, the incidence of diabetes in the control group was 34.8% versus only 11.4% in the vitamin D group [16]. At gestational age of 12-16 weeks, women with vitamin D levels <30 ng/mL were given either vitamin D 400 IU/day (group A) or 50,000 IU every two weeks (group B) until delivery [17]. The average vitamin D levels in group B were 37.9 ng/mL and in group A were 27.2 ng/mL with significant lower incidence of GDM of 6.7% in group B versus 13.4% in group A [17].

In a study where 24-28 weeks pregnant women with GDM were randomized to the placebo or vitamin D 50,000 IU every two weeks group, there was an improvement in the fasting blood glucose and HbA1C in the vitamin D group [18]. In a four-arm placebo-controlled trial, 24-28 weeks pregnant women with GDM were randomized into a placebo, vitamin D low dose (200 IU/day), vitamin D medium dose (50,000 IU/month), or vitamin D high dose (50,000 IU every two weeks) group [19]. It was found that vitamin D 50,000 IU every two weeks significantly improved insulin resistance in the GDM cohort [19]. As per the previously described studies, vitamin D dosages as high as 5,000 IU daily [16] have been used in pregnant women and an inverse correlation has been shown between the vitamin D dose and the risk of developing GDM.

Vitamin D and the Outcomes Post-GDM Diagnosis

Considering the 50% long-term risk of developing DMII in women with previous GDM, few studies have explored the association of vitamin D in this cohort. In women with previously diagnosed GDM, administration of 75g oral glucose tolerance test (OGTT) 1-2 years post-pregnancy illustrated that 53% of women had Vitamin D levels <50 nmol/L (<20 ng/mL) and 87% had vitamin D levels <75 nmol/L (29.9 ng/mL) [20]. Consequently, it was found that in women with previous GDM, vitamin D deficiency was associated with beta cell dysfunction and insulin resistance [20]. Yeow *et al.* randomized women with previous GDM and Vitamin D deficiency into the placebo or 4000 IU vitamin D group and followed them for 6 months [21]. The study concluded that a 6-month supplementation with 4000 IU vitamin D improved vitamin D levels and basal pancreatic beta-cell function [21]. Longer term assessments are needed to explore the consequences of the vitamin D deficiency/insufficiency in women who were previously diagnosed with GDM and develop appropriate vitamin D supplementation recommendations.

Conclusion

The current data illustrates that there is a significant inverse relationship between the vitamin D levels and development of the insulin resistance. Overall, there was a significant improvement in GDM incidence and insulin resistance in patients with or without GDM at higher vitamin D doses. More studies need to be conducted to establish recommendations for serum vitamin D levels with appropriate dosing for pregnant women as a preventative measure for GDM and to avoid development of DMII in the long run.

Conflicts of Interest

The author has no conflict of interests to report.

Bibliography

1. Holick, M. F., *et al.* (2011). Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab, 96*(7), 1911-30.

2. Hollis, B.W. (2005). Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr, 135*(2), 317-22.

3. Palacios, C. & Gonzalez, L. (2014). Is vitamin D deficiency a major global public health problem? *J Steroid Biochem Mol Biol, 144*(Part A), 138-145.

4. Forrest, K. Y. & Stuhldreher, W. L. (2011). Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res, 31*(1), 48-54.

5. WHO. (2016). *Global Report on Diabetes*, W. H. Organization, WHO Press.

6. (NC-RisC)., N.R.F.C. (2016). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4*4 million participants. *Lancet, 387*(10027), 1513-1530.

7. ADA. (2018). *Statistics About Diabetes.*

8. DeSisto, C. L., Kim, S. Y. & Sharma, A. J. (2014). Prevalence estimates of gestational diabetes mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. *Prev Chronic Dis, 11*, E104.

9. CDC. (2017). *Gestational Diabetes.*

10. Yang, Y., *et al.* (2018). The association of gestational diabetes mellitus with fetal birth weight. *J Diabetes Complications, 32*(7), 635-642.

11. Jafarzadeh, L., *et al.* (2015). A Comparison of Serum Levels of 25-Hydroxy Vitamin D in Pregnant Women at Risk for Gestational Diabetes Mellitus and Women without Risk Factors. *Mater Sociomed, 27*(5), 318-22.

12. Al-Ajlan, A., *et al.* (2018). Lower vitamin D levels in Saudi pregnant women are associated with higher risk of developing GDM. *BMC Pregnancy Childbirth, 18*(1), 86.

13. McCormack, C., *et al.* (2018). Association between vitamin D status and hyperinsulinism. *J Matern Fetal Neonatal Med*, 1-4.

14. Wen, J., *et al.* (2018). Association of maternal serum 25-hydroxyvitamin D concentrations in second and third trimester with risk of macrosomia. *Sci Rep, 8*(1), 6169.

15. Bao, W., *et al.* (2018). Prepregnancy habitual intake of vitamin D from diet and supplements in relation to risk of gestational diabetes mellitus: A prospective cohort study. *J Diabetes, 10*(5), 373-379.

16. Shahgheibi, S., Farhadifar, F. & Pouya, B. (2016). The effect of vitamin D supplementation on gestational diabetes in high-risk women: Results from a randomized placebo-controlled trial. *J Res Med Sci, 21*, 2.

17. Mojibian, M., *et al.* (2015). The effects of vitamin D supplementation on maternal and neonatal outcome: A randomized clinical trial. *Iran J Reprod Med, 13*(11), 687-96.

18. Yazdchi, R., *et al.* (2016). 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, 10*(3), 328-35.

19. Zhang, Q., *et al.* (2016). Effect of various doses of vitamin D supplementation on pregnant women with gestational diabetes mellitus: A randomized controlled trial. *Exp Ther Med, 12*(3), 1889-1895.

20. Shaat, N., *et al.* (2017). Glucose homeostasis, beta cell function, and insulin resistance in relation to vitamin D status after gestational diabetes mellitus. *Acta Obstet Gynecol Scand, 96*(7), 821-827.

21. Yeow, T. P., *et al.* (2015). Impact of Vitamin D Replacement on Markers of Glucose Metabolism and Cardio-Metabolic Risk in Women with Former Gestational Diabetes--A Double-Blind, Randomized Controlled Trial. *PLoS One, 10*(6), e0129017.