Review of gestational diabetes mellitus and vitamin D

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Abstract

Most of what we know about the link between vitamin D levels and GDM comes from observational studies with different results. Two well-conducted meta-analyses published recently from this work found evidence of a small link between low 25(OH)D levels and an increased risk of GDM. It is yet uncertain, though, if a vitamin D deficit affects the pathophysiology that leads to the development of GDM. To our knowledge, there hasn't been a published major randomized trial of different vitamin D doses in women at high risk for getting GDM or who already have GDM. RCTs are needed to prove that getting enough vitamin D helps prevent or treat GDM because the only studies done so far are encouraging but not conclusive. 7–14% of pregnancies are complicated by gestational diabetes mellitus (GDM). Pregnancy also frequently results in vitamin D insufficiency. However, it is unknown whether vitamin D supplementation can prevent GDM. New research indicates that vitamin D delivery can increase insulin sensitivity and glucose tolerance. Observational studies provide conflicting evidence regarding the association of low serum 25(OH)D levels with GDM. According to two recent systematic evaluations, vitamin D insufficiency raises the risk of GDM. However, the observational and varied nature of the included studies restricts these reviews. The biggest worry is that we don’t know how significant confounding factors like obesity and race/ethnicity might influence the association. Only a few randomized controlled trials have been conducted. Still, they are necessary to determine if extra vitamin D supplements, beyond what is usually found in prenatal vitamins, can help GDM patients with glucose tolerance.

Keywords: GDM; Gestational diabetes; 25-hydroxyvitamin D; Pregnancy; Vitamin D

1. Introduction

Vitamin D, also called calciferol, comes in two primary forms that are functionally the same: vitamin D2 (ergocalciferol), which is made in a lab and added to foods and supplements, and vitamin D3 (cholecalciferol), which is found in animal-based foods and made by the human skin when sunlight converts 7-dehydrocholesterol. Both forms are prohormones that are inactive biologically until they are hydroxylated twice, once in the liver to produce 25hydroxyvitamin D (25(OH) D) and again in the kidney to produce calcitriol (1,25-dihydroxy vitamin D). The most accurate predictor of one’s total vitamin D status is 25(OH) D, the main form of vitamin D that circulates and is coupled in plasma to albumin and vitamin D binding protein (DBP). The parathyroid hormone strictly controls the production of calcitriol in the kidney. Calcitriol controls gene expression (VDR) by changing gene transcription when it comes into contact with a vitamin D receptor in the nucleus. Calcitriol is usually used to balance calcium and phosphate in the blood and keep bones healthy. But the fact that VDRs are found in tissues that don’t have anything to do with calcium or phosphate metabolism suggests that calcitriol could be used for more than just keeping bones healthy. Since many human genes involved in cell differentiation and growth have vitamin D-responsive elements (VDRE), vitamin D has been looked at as a possible treatment or prevention for cancer and autoimmune diseases like type 1 diabetes mellitus. Vitamin D and type 2 diabetes mellitus have been the subject of several observational and experimental studies with people. Some studies...
suggest that vitamin D supplementation or optimal 25(OH)D levels may help with type 2 diabetes. In rodent models, calcitriol has been shown to affect insulin synthesis, secretion, and actions. Such discoveries have sparked more research on the connection between vitamin D levels and GDM. GDM, which complicates 7–14% of pregnancies. It is rising because more people are overweight or obese.[1],[2],[3],[4].

GDM increases the risk of adverse health outcomes for mothers and infants. Women with GDM who have had cesarean sections are more likely to get type 2 diabetes mellitus. Children whose mothers have diabetes are more likely to have congenital disabilities, macrosomia, birth trauma, respiratory distress syndrome, jaundice, and low blood sugar. Several things, like a mother’s age, being overweight, having a family history of diabetes, or being of a certain race, have increased the risk of GDM. However, it is still unclear how these things affect a woman’s risk of getting GDM. Vitamin D deficiency has been acknowledged as a potential factor in recent years. It is still unknown if vitamin D deficiency affects a mother’s risk of getting GDM, despite epidemiologic research consistently linking vitamin D deficiency to a higher risk of type 2 diabetes and obesity to both GDM and vitamin D deficiency. Researchers from many fields are interested in studying vitamin D status and health outcomes because vitamin D has many effects, vitamin D receptors are typical in the body, and the epidemiology of vitamin D deficiency is very interesting. Whether or not they are caused, low vitamin D levels are linked to several health risks. Notably, in the United States, African Americans and people who are overweight or obese are more likely to have low 25(OH) D levels. Black and white Americans continue to experience significant health disparities. People are always interested in finding out if vitamin D deficiency could cause racial differences in health outcomes, especially in pregnancy. Disparities, however, are not just limited to black-white inequalities in the case of GDM. Compared to white women, Asian and Hispanic women had higher rates of GDM, and there were fewer differences in vitamin D status between them and black and white people. Contrarily, obesity is unquestionably linked to GDM and vitamin D insufficiency. It is unclear if not getting enough vitamin D makes you more likely to get GDM. It may be hard to tell this possibility apart from other risk factors that could act as confounding variables and impact measure modifiers. For instance, it is unknown if vitamin D insufficiency impacts the risk of GDM differently in obese women compared to lean women. Based on the few human studies that have looked at vitamin D supplementation during pregnancy, vitamin D makes insulin more sensitive and supports the idea of a threshold effect. Also, the small number of trials suggests that it might be worth looking into the role of vitamin D supplements for women who already have GDM, even if optimal vitamin D levels can’t prevent GDM. Even though there will be more observational studies on the topic, well-designed RCTs are needed to answer these and other vital questions about the link between vitamin D and GDM.[5],[6],[7],[8],[9].

2. Conclusion

Most of what we know about the link between vitamin D levels and GDM comes from observational studies with different results. Two well-conducted meta-analyses published recently from this work found evidence of a small link between low 25(OH) D levels and an increased risk of GDM. It is yet uncertain, though, if a vitamin D deficit affects the pathophysiology that leads to the development of GDM. To our knowledge, there hasn’t been a published major randomized trial of different vitamin D doses in women at high risk for getting GDM or who already have GDM. RCTs are needed to prove that getting enough vitamin D helps prevent or treat GDM because the only studies done so far are encouraging but not conclusive.7–14% of pregnancies are complicated by gestational diabetes mellitus (GDM). Pregnancy also frequently results in vitamin D insufficiency. However, it is unknown whether vitamin D supplementation can prevent GDM. New research indicates that vitamin D delivery can increase insulin sensitivity and glucose tolerance. Observational studies provide conflicting evidence regarding the association of low serum 25(OH) D levels with GDM. According to two recent systematic evaluations, vitamin D insufficiency raises the risk of GDM. However, the observational and varied nature of the included studies restricts these reviews. The biggest worry is that we don’t know how significant confounding factors like obesity and race/ethnicity might influence the association. Only a few randomized controlled trials have been conducted. Still, they are necessary to determine if extra vitamin D supplements, beyond what is usually found in prenatal vitamins, can help GDM patients with glucose tolerance.

Compliance with ethical standards

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Disclosure of conflict of interest

There are no conflicts of interest declared by the authors.

Statement of ethical approval

This evaluation does not require ethical approval because no patient data will be collected. Plagiarism, confidentiality, malfeasance, data falsification and/or falsification, double publishing and/or submission, and duplication are among the ethical problems examined in this study.

References

[9] Aghajafari F, Nagulesapillai T, Ronksley PE, et al. Association between maternal serum 25hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and metaanalysis of observational studies. BMJ. 2013; 346:f1169. [PubMed: 23533188] Another recently published systematic review of vitamin D status and pregnancy outcomes including a metaanalysis of 10 studies of 25(OH)D levels and the risk of GDM. They concluded that women with 25(OH)D levels <75 nmol/L had higher odds of GDM (Figure 1.)