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Review Article

**THE RELATIONSHIP BETWEEN VITAMIN D AND
GESTATIONAL DIABETES-A REVIEW ARTICLE**Fateme parooei ¹, Zohreh Mahmoodi ², Mohammad Reza Havasian ³, Mahmood Anbari ⁴, Elaham poorgholam ⁵, Morteza Salarzai ^{1*}, Alireza Abrishami ⁶¹ Medical student, Student Research Committee, zabol University of Medical Sciences, zabol, Iran² Department of Cardiology, Faculty of Medicine, Zabol University of Medical Sciences, Zabol, Iran.³ Department of Periodontics, School of Dentistry, Ilam University of Medical Sciences, Ilam, Iran.⁴ zabol University of Medical Sciences, zabol, Iran⁵ Student Research Committee, zabol University of Medical Sciences, zabol, Iran⁶ Department of orthopedics Faculty of Medicine, Zabol University of Medical Sciences, Zabol, Iran.**Abstract:**

Introduction: Gestational diabetes manifests itself as not having glucose tolerance, and is seen in around 2-13% of all cases of pregnancy. One of the important factors in the development of gestational pregnancy is vitamin D deficiency. so, this study is designed to determine the relationship between low levels of vitamin D in pregnancy and gestational diabetes mellitus.

Methods: In this review article, the databases Medline, Cochrane, Science Direct, and Google Scholar were thoroughly searched to identify the studies investigating the relationship between vitamin D and gestational diabetes.

Results: vitamin D deficiency will definitely leave harmful effects on the pregnant women's health and on their infants, in a way that vitamin D deficiency condition during pregnancy is accompanied by the development of gestational diabetes, mother's blood pressure disorder, the embryo's skeletal growth disorder, brain growth and development disorders, and disorders in the functioning of the embryonic immune system.

Discussion and conclusion: Given that pregnancy is diabetogenic and that the incidence of gestational diabetes in the society is high, paying more attention to providing adequate amounts of vitamin D can be an important factor in this area.

Key words: Vitamin D, Gestational Diabetes

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INTRODUCTION:

Gestational diabetes manifests itself as not having glucose tolerance, and is seen in around 2-13% of all cases of pregnancy(1). The incidence of gestational diabetes in the world varies depending on the investigated population and diagnostic protocols, in a way that the incidence of gestational diabetes varies from 1 to 14 % among different racial groups(2). According to the studies conducted on Indian Immigrants in the United States, gestational diabetes is more common among Asian women compared with white American women(3). Given the seriousness of gestational diabetes and its consequences, numerous studies have investigated the factors affecting this condition.

METHODS:

In this review article, the databases Medline, Cochrane, Science Direct, and Google Scholar were thoroughly searched to identify the studies investigating the relationship between vitamin D and gestational diabetes. In this review, the papers published until early January 2017 that were conducted to study the relationship between gestational diabetes and vitamin D were selected. In searching for the articles, only those English papers were selected that had investigated the consumption of vitamin D before and during pregnancy in healthy pregnant women who, during the pregnancy period, had not shown any of the unpleasant consequences of pregnancy other than gestational diabetes.

RESULTS:**The effects of gestational diabetes on the mother:**

Diabetes and pregnancy significantly affect each other, in a way that can strongly put the mother's health into risk(4). Preventing maternal complications is important as preventing embryonic complications. Observational studies have shown that gestational diabetes increases the risk of the development of polyhydramnios, pregnancy hypertension, chronic hypertension, pyelonephritis, and cesarean delivery(5). Pregnancy hypertension and preeclampsia are twice as common in mothers with gestational diabetes as in healthy women, and the relationship remains to exist even after the mother's weight is matched(6). In addition to chronic hypertension, pregnancy hypertension and preeclampsia are both clearly more common among women with gestational pregnancy(7). Insulin resistance may have a role in the development of preeclampsia and pregnancy hypertension, a factor which can justify the high incidence of the disorder despite the improvement in controlling blood glucose(8). Cesarean delivery occurs in 13 to 32 percent of pregnant women, and

the highest rate cesarean delivery is seen in women who receive insulin.

The effects of gestational diabetes on the embryo:

The embryo in the body of a mother with gestational diabetes develops in an environment totally different from the embryo in the body of a healthy mother(9). Glucose, alanine, and free fatty acids are transferred to the embryo in high amounts from the mother's blood circulation(10). As a result, insulin concentration of amniotic fluid is increased, which is an indicator of the embryo's compensatory response in order to increase these substances. Clear hyperglycemia in the first three months of pregnancy increases the risks of congenital malformations and prenatal mortality around delivery(11).

The harmful effects of gestational diabetes on the embryo include the following:

1. An increased risk of the development of macrosomia, which results in complications like shoulder dystocia and arm muscle damage. All organs of the embryo develop macrosomia except for the brain. These infants' macrosomia is closely related to the infant hypersensitivity resulting from maternal hyperglycemia(12).
2. Neonatal hypoglycemia and severe decrease in plasma glucose concentration after delivery are found in infants of mothers with gestational diabetes. This condition is attributed to hyperplasia of the embryonic pancreas B cells due to mother's chronic hyperglycemia(13).
3. Hyperbilirubinemia: Pathogenesis of hyperbilirubinemia is not clear in infants of mothers with gestational diabetes, but prematurity, poly septicemia, and hemolysis have been reported as factors affecting this condition(14).
4. Heart hypertrophy: These infants may develop hypertrophic cardiomyopathy, which gradually advances to congestive heart failure. These infants are specifically macrosomic, and hyperinsulinemia in pathogenesis is considered to be responsible(15).
5. Hypocalcaemia: In addition to hypoglycemia, hypocalcaemia is another common complication among infants of mothers with gestational pregnancy(16).
6. Polycythemia: It is believed that polycythemia is the result of chronic intrauterine hypoxemia that results in increased erythropoietin and the production of red blood cells(17).
7. Obesity: These infants are exposed to an increased risk of obesity, impaired glucose intolerance, and the development of diabetes in late adolescence and early youth(18).
8. The death of a dead baby (stillbirth): The birth of a dead baby without explainable reason is a process seen exclusively in pregnant women with gestational diabetes, since factors like obvious placental insufficiency, placenta decollement, and oligohydramnios have not been

found responsible for this. These infants are specifically large for to the length of pregnancy and die prior to birth around the 35th week of pregnancy or later(19).

One of the important factors in the development of gestational pregnancy is vitamin D deficiency(20). Vitamin D is the key factor in the formation of bones, extracorporeal actions like the coordination of the immune system, preventing malignancy, blood pressure, and maintaining a normal glucose homeostasis(21). Vitamin D is an essential and unique micronutrient whose main function is to maintain calcium homeostasis and skeletal health. In the case of vitamin D deficiency, only 10-15% of calcium and 60% of phosphorus in the food can be absorbed, while correcting Vitamin D results in absorbing 30-40% of the calcium and 80% of the phosphorus(22). Physiologically speaking, there are two active forms of vitamin D that are collectively called calciferol, and include vitamins D2 and D3. Vitamin D2 (ergocalciferol) is made by plants, while vitamin D3 (cholecalciferol) is made by the ultraviolet irradiation of 7-dehydrocholesterol beneath the skin(23). This vitamin is found as D2 or D3 in supplements. Vitamin D3 is three times as effective as vitamin D2. Since vitamin D has a short half-life, receiving adequate amounts of this vitamin is needed to ensure a stable level of circulation in the body(24). The two forms of vitamin D (D2 and D3) have a common metabolism; they are first hydroxylated in the liver and are then transformed into 25 hydroxy or calcidiol and are then transformed into 1 and 25 in hydroxy vitamin D or calcitriol in the kidney in response to levels of parathyroid hormone. Although the two forms of 1 and 25 dihydroxy vitamin D are active forms in circulation, measuring their levels cannot be useful since they are quickly and strongly modified by the kidneys, and only 25 (OH) D can be used as the criterion to diagnose the deficiency of this vitamin(25). Almost all body cells have vitamin D receptors. Therefore, the actions of this macronutrient seem to be beyond metabolism adjustment of calcium and phosphorus. Around one third of human genome is directly or indirectly are controlled by 1 and 25 dihydroxy vitamin D, in a way that the significant effect of various variants of the gene receiving vitamin D (rs757343) on polycystic ovary syndrome phenotype has be emphasized(26).

DISCUSSION AND CONCLUSION:

Lower-than-normal levels of vitamin D are one of the problems of the 21st century. Some people are more exposed to the risks of the deficiency of this vitamin(21). The most obvious group is pregnant women, because pregnancy may increase the need for vitamins. On the other hand, it seems that vitamin D has multidimensional effects on pregnancy that are beyond the known activities of

calcium and the metabolism of the bones(23). A low level of vitamin D during pregnancy is related to health problems and several consequences like egg implantation and the diseases of adulthood. It has now been confirmed that vitamin deficiency on the part of the mother affects the mother's and the infant's calcium homeostasis and also affects the bone development of the embryo(27). Vitamin D deficiency in pregnant mothers is likely in later stages of pregnancy due to the quick growth and development of the embryo, especially bone calcification. Since the embryo and the infant depend on the amounts of vitamin D found in the mother's blood and milk, adequate stores of vitamin D in the mother's body is quite vital(28). Vitamin D deficiency is not limited to pregnant women of certain racial groups or from certain regions; it is quite widespread all around the world, and the incidence of vitamin D deficiency in women at reproductive ages and pregnant women is very high. For example, serum levels of 25 (OH) D lower than 25 nanograms/ml during pregnancy has been reported to be 17-18% in Caucasia, 61% in New Zealand, 32-42% in Indian, 59-84% in Kuwait, 84% in Iran, and 75% in the United Arab Emirates(29). Such a widespread deficiency will definitely leave harmful effects on the pregnant women's health and on their infants, in a way that vitamin D deficiency condition during pregnancy is accompanied by the development of gestational diabetes, mother's blood pressure disorder, the embryo's skeletal growth disorder, brain growth and development disorders, and disorders in the functioning of the embryonic immune system(30). Therefore, given that preeclampsia is one of the three main causes of death among pregnant women and that the harmful effects of diabetes on pregnancy like macrosomia and baby delivery trauma are obvious and that bacterial vaginosis is accompanied by preterm labor and that the maternal and embryonic risks of cesarean is more than natural baby delivery, vitamin D deficiency and especially severe cases of vitamin D deficiency is a risk factor for insulin resistance during pregnancy and, as a result, gestational diabetes. Given that pregnancy is diabetogenic and that the incidence of gestational diabetes is the society is high, paying more attention to providing adequate amounts of vitamin D can be an important factor in this area.

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