The relationship between vitamin D3 deficiency and gestational diabetes mellitus

Zahra Barzegarjahani¹, Nasrin Jalilian¹,*, Mansour Rezaei²

1. Maternity research center obstetrician and gynecologist, Kermanshah University of medical sciences, Kermanshah, Iran
2. Biostatistics & epidemiology department, school of public health, Social development & health promotion research center, Kermanshah University of medical sciences, Kermanshah, Iran

*Corresponding Author email: njalilian@yahoo.com

ABSTRACT: Vitamin D3 (VD3) deficiency during pregnancy period is a common phenomenon. The results of some studies indicated that VD3 can have a significant effect on the secretion and function of insulin. The aim of this study is to investigate the relationship between VD3 deficiency and gestational diabetes mellitus (GDM) so as to decrease resistance to insulin during pregnancy with treatment of VD3 deficiency. The case control study includes 150 pregnant women (75 GDM and 75 non-GDM) who referred to clinic of Imam Reza hospital or private office of obstetricians in Kermanshah from 2012 to 2014. For cases included in the study screening test of pregnancy was done in the 24-28 weeks of pregnancy using OGTT with 75gr glucose. All centrifuged blood samples were transferred to reference lab for measuring fast glucose and 25-hydroxy-VD3 through immunoassay method and IDS Kit. All data were saved and analyzed employing SPSS 16.0 software. The mean body mass index was 29.21 and 27.55 (kg/m²) in case and control group (P=0.002), respectively. The gestational age, parity, educational level and occupation were not different in two groups. The mean of VD3 level in case and control group were 14.98±11.2 and 16.88±10.7, respectively (P=0.070). The results of our study showed that there was no relationship between VD3 deficiency and GDM risk. In addition, it was shown that in GDM woman there was a reverse relationship between VD3 and BMI. In addition, cohort studies in future can response to this question that how much dose of VD3 can has positive effect on the prevention or exacerbation of GDM.

Keywords: Vitamin D3, Gestational diabetes mellitus.

INTRODUCTION

Vitamin D3 (VD3) deficiency during pregnancy period is a common phenomenon particularly in darkskinned women. Potential short term consequences (such as neonatal hypocalcemia and seizure) and longer term complications (like failure to thrive and rickets) are common complications and consequences for the new born baby. Also, in adults this complication (Vitamin D deficiency) is associated with increased risk of some cancers, autoimmune disease (including type 1 diabetes) and infectious diseases (1).

Pregnancy is a diabetogenic condition. The concentration of fast insulin increases physiologically during pregnancy (2). Although the exact cause of this change is unknown, low sensitivity of cells to insulin during pregnancy can be due to high production of diabetogenichormones (placental lactogenic, progesterone and cortisone) (3). Thus, the stress on pancreatic B-cell function increases to levels typically associated with type 2 diabetes. Compared with normal pregnant woman, woman with gestational diabetes mellitus (GDM) have impaired B-cell function and reduced B-cell adaptation (4). Usually insulin resistance increases in mid-pregnancy and through the third trimester (5). For this reason, it is recommended that screening for GDM be done between 24 to 28 weeks of pregnancy. Untreated hyperglycemia allows glucose to travel freely from mother to the fetus forcing the fetus to increase its own production of insulin. Excess insulin production by the fetus increases the risk of embryopathy, fetal macrosomia, birth trauma and perinatal death (1-4). In recent years trend has raised to investigate antioxidant Vitamins and disease prevention (6). One of the most important antioxidant Vitamin is VD3 which has been noticed by physicians during past decade, because of its variouseffects on human health. VD3 increases intestinal absorption of phosphor and calcium and decreases them from kidneys. It also affects bone metabolism and helps
cellular growth through transcription of nucleargenes(7). Some studies show that VD3 has effect on secretion and dysfunction of insulin(8,9). Most tissues including special pregnancy tissue like decidua and placenta and pancreatic cells have neutral receptors for VD3 and hydroxylase enzymes(9).

This enzyme converts 25-hydroxy (25(OH))VD3 to activated form 1.25(OH) VD which increases calciumabsorptioninintestine. Serum concentration of 1.25(OH) VD increases 50-100% in second trimester and up to 100% in third trimester. These compatibilitiespave the background for translation of 25-30 gr calcium from mother to fatal bone(6). Thereby, low VD3duringpregnancy can be harmful for mother and fetus(10,11). Some studies show that VD3 can affect on secretion and insulin dysfunction (12,13) and low serum of VD3 is more common among diabetes mellitus patients. GDM and pregnant woman(14,15,16) and VD3 replacement can lower resistance to it(17). Since VD3 deficiency and diabetes mellitus have high frequency during pregnancy, the study of the relation between two diseases help better understand pathogeneses, as no specific study has been done on the relationship between insulin disorder and Vitamin deficiency during pregnancy. The objective of this study is to investigate the relationship between VD3 deficiency and diabetes mellitus during pregnancy so as to provide decrease resistance to insulin during pregnancy and to prevent it.

MATERIALS AND METHODS

This study was a case control. The population of the study includes all pregnant women who referred to clinic of Imam Reza hospital of Kermanshah (referral center of high risk pregnancy) or referred to private office of obstetricians from 2012 to 2014. Patients with the history of GDM, Patients suffered from diabetes mellitus, patients having members of their family suffering from diabetes mellitus and patients had child birth weight more than 4 kg were excluded from the study.

In the beginning of the study all patients were examined by the obstetricians physically. Demographic information such as mother age, gestational age, the number of pregnancy, height, weight, level of education, job, previous suffering from diabetes mellitus before pregnancy, previous suffering from diabetes mellitus in the previous pregnancy, previous suffering from diabetes mellitus among family were gathered from the patients via questionnaire.

For cases included in the study screening test of pregnancy was done in the 24-28 weeks of pregnancy using oral glucose tolerance test (OGTT) with 75 gr glucose. To do that the participants were advised to eat 150 gr carbohydrates daily at least for 3 days. In 4th day we tested serum glucose when they fast for 8-12 hours and took their blood samples in 0, 1, &2 hours after 75 gr glucose consumption. Patients who had one or more abnormal test were included in the study. Normal glucose for each sample in 0, 1, &2 hours was less than 92, 180, &152 mg/dl, respectively. The sampling procedure was convenience, and in which only available cases were included in the study. Based on the Zhang study(17), in which he mentioned the lowest VD3 deficiency in GDM women and control group as 33% and 14%, respectively, we determined the minimum sample size needed for each group were 75 cases, with employing Cochrane formula and using 95% confidence level and 80% power of test. Like Zhang study, 75 GDM women were chosen as case group and 75 non-GDM women as control group.

All centrifuged blood samples, from both groups, were transferred to reference lab for measuring fast glucose and 25(OH) VD3 through immunoassay method and Immunodiagnostic Systems (IDS) Kit. VD3 equal to or lower than 10 ng/ml was considered as VD3 Deficiency.

All data were saved and analyzed employing SPSS16.0 software. First, to determine the normality of the quantitative data, Kolmogorov-Smirnov (KS) test was employed. To compare the normal variables such as weight, height, age, and BMI in each group, Leven and independent samples T-test (parametric tests) and to compare non normal variables such as OGTT and VD3 in each group Mann-Whitney u test (non-parametric tests) were employed. In addition, to compare qualitative variables such as job, level of education, pregnancy age category and parity in both groups Chi-square ($\chi^2$) test was employed. Spearman and Pearson correlation coefficient was utilized for relationship determination. P-value less than 0.05% was considered as significant.

RESULTS

Mean age in case and control groups were 31.9±5.6 and 30.2±5.3, respectively. Two groups were not significant different with regards to age ($P=0.060$), height ($P=0.058$) and weight ($P=0.058$). The mean of gestational age of pregnant women who suffered from GDM was 27.0±0.9 weeks. The mean BMI was 29.2±3.4 (kg/m$^2$) in case group and 27.6±3.1 (kg/m$^2$) in control group ($P=0.002$). The means in gestational age ($P=0.549$), parity ($P=0.591$), educational level ($P=0.276$) and occupation ($P=0.840$) were not significant different in two groups.
Results of screening test of pregnancy in the 24-28 weeks of pregnancy using OGTT with 75gr glucose calculated. After eating 150 gr carbohydrates daily at least for 3 days, in 4th day serum glucose when they fast for 8-12 hours tested in 0, 1, & 2 hours after 75gr glucose consumption (fig. 1).

Vitamin D3 mean level in case group and control group (fig. 2) were 14.98±11.2(ng/ml) and 16.88±10.7(ng/ml), respectively (P=0.070). VD3 deficiency (VD3≤10 ng/ml) in 34.7% and 22.7%, VD3 insufficiency (10<VD3≤30 ng/ml) in 57.3% and 66.7%, and VD3 sufficiency (VD3>30 ng/ml), in 8% and 10.7% observed in case and control group, respectively (P=0.104). In general, VD3 deficiency, insufficiency, and sufficiency were 28.7%, 62.0% and 9.3%, respectively (table 1).

![Figure 1. Comparison of the OGTT rate in case group](image1)

![Figure 2. Comparison of vitamin D3 level in case and control groups](image2)
VD3 deficiency was common in both groups though it was high in case group and there was no meaningful difference between both groups. In control group there was no relationship between VD3 and the other variables. In case group there was a reverse relationship between VD3 and BMI (P=0.026, R=-0.256), and in case group there was no relationship between VD3 level and other variables.

**DISCUSSION**

Vitamin D3 deficiency is a common problem among pregnant women. VD3 deficiency has a proved effect on the bone density, calcium level during and rickets during childhood. That 41% of the women suffered from GDM in the study done by Lau, et al is a sign of high frequency of this problem(1). In this study, 90.7% of pregnant woman hadn’t deficiency VD3 (VD3<30 ng/ml) which shows a high frequency of this disease in Iran among pregnant women. In other studies VD3 deficiency was common in pregnant women which are in line with the results of the current study. In this study sever VD3 deficiency was detected (VD3<10 ng/ml) in 34.7% of case group and 22.7% of control group. 57.3% of case and 66.7% of control group had VD3<30 ng/ml.

Hannah and colleagues reported that 66% of women had VD3 insufficiency (VD3<50 ng/ml). They showed that VD3 deficiency was common in 30th week of pregnancy but it didn’t increase the risk of diabetes (18). Results of this study are similar to their study. In other studies done by Baker, et al and McLeod, it was found that VD3 deficiency was common in the first trimester of pregnancy but no specific relationship between VD3 deficiency and GDM (19,20). They also mentioned that we need more studies particularly among individuals with lower VD3 deficiency.

Makgoba, et al in a case control study reported that there is a reverse relationship between VD3 and OGTT (2 hours) and direct relationship with HDL cholesterol level, but there was no difference between GDM patient and normal individuals in mean level of VD3(21). The results of our study are agreed with the results of the above-mentioned studies. In a study done by Hoseinnejad, et al it was found that there is a relation between VD3 metabolism and risk of GDM or exacerbation of Iteven after adjusted the effects of variables such as age and BMI(22). The study was done by Rudnick among women suffering from GDM it was shown that vascular injection of 25(OH) was accompanied by decrease of insulin using GTT test while the insulin level was decreased(23). Zhang, et al in their study after equalizing patients in age, race, family history of diabetes and BMI before pregnancy, reported that VD3 deficiency has a meaningful relationship with the increased risk of GDM(17). The results of our study are not in line with those of the above-mentioned study. This disagreement may be due to the difference in the type or method of the study. In our study the mean of VD3 level in case group was less than that of control group but this difference was not statistically significant. Our study demonstrated that VD3 deficiency in pregnant women (with or without GDM) is common. Despite this fact that most of studies have shown a high frequency of VD3 deficiency among pregnant women, some studies have controversial results.

In our study due to this fact that variables such as sun effect, physical activity and diets enriched with VD3 and calcium have not been dealt with, our study may show results different from other studies. It also may show the limitation of our study. In addition it may lead us to this belief that we need large sample for our study to help prove the above results. Alzaym, et al suggested that VD3 prophylaxis during pregnancy is needed so as to deal with its effect on GDM prevention(24). In addition, cohort studies in future can response to this question that how much dose of VD3 can have positive effect on the prevention or exacerbation of GDM(25).

**Table1.** Comparison of the demographic information and vitamin D3 in two groups (mean±SD) or frequency (percent)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case (n=172)</th>
<th>Control (n=75)</th>
<th>Total (n=247)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>31.89±5.56</td>
<td>30.21±2.27</td>
<td>31.05±5.46</td>
<td>0.060</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>29.22±3.44</td>
<td>27.56±3.13</td>
<td>28.39±3.39</td>
<td>0.002</td>
</tr>
<tr>
<td>Parity</td>
<td>1.8±1.0</td>
<td>1.83±0.94</td>
<td>1.81±1.0</td>
<td>0.591</td>
</tr>
<tr>
<td>Gestational age (w)</td>
<td>27.05±0.91</td>
<td>26.95±0.88</td>
<td>27.02±0.90</td>
<td>0.469</td>
</tr>
<tr>
<td>Vitamin D3 (ng/ml)</td>
<td>14.99±11.21</td>
<td>16.88±10.74</td>
<td>15.93±10.98</td>
<td>0.070</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under diploma</td>
<td>14(18.7)</td>
<td>15(20.0)</td>
<td>29(19.3)</td>
<td>0.276</td>
</tr>
<tr>
<td>Diploma</td>
<td>32(42.7)</td>
<td>40(53.3)</td>
<td>72(48.0)</td>
<td></td>
</tr>
<tr>
<td>Over diploma</td>
<td>29(38.7)</td>
<td>20(26.7)</td>
<td>49(32.7)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housekeeper</td>
<td>59(78.7)</td>
<td>60(80.0)</td>
<td>119(79.3)</td>
<td>0.840</td>
</tr>
<tr>
<td>Employed</td>
<td>16(21.3)</td>
<td>15(20.0)</td>
<td>31(20.7)</td>
<td></td>
</tr>
<tr>
<td>Vitamin D3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficiency</td>
<td>26(34.7)</td>
<td>17(22.7)</td>
<td>43(28.7)</td>
<td>0.104</td>
</tr>
<tr>
<td>Sufficiency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficiency</td>
<td>43(57.3)</td>
<td>50(66.7)</td>
<td>93(62.0)</td>
<td></td>
</tr>
<tr>
<td>Sufficiency</td>
<td>6(8.0)</td>
<td>8(10.7)</td>
<td>14(9.3)</td>
<td></td>
</tr>
</tbody>
</table>
CONCLUSION

The results of our study showed that there was no relationship between VD3 deficiency and GDM risk. In addition, it was shown that in GDM woman there was a reverse relationship between VD3 and BMI.

ACKNOWLEDGEMENTS

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