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*Research Article*

# Concentration of Maternal Serum 25-Hydroxy Vitamin D and Gestational 2 Diabetes Mellitus Risk

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**ABSTRACT**

***Background:*** The present study was designed to primarily investigate the association between serum 25 (OH) vitamin D levels and gestational diabetes mellitus (GDM) in a sample of Iranian woman.
***Methods:*** In the present cross-sectional study 136 pregnant women (68 with GDM and 68 non GDM) who were referred to a university hospital clinic of the Tabriz University of Medical Sciences during July to September 2016 were studied. All pregnant women were assessed for GDM and also serum vitamin D was assessed in all participants.
***Results:*** The mean serum 25(OH) D of pregnant women was 13.42±7.78 ng/mL. In the term of the mean serum 25(OH) D level, there was not significant differences between GDM (14.45±8.73) and non-GDM (12.38±6.62) pregnant women (p=0.12). Totally 83.8% of participants were vitamin D deficient and 11.8% of them had insufficient amount of serum vitamin D. Only 4.4% of participants were vitamin D sufficient. The results of logistic regression analysis showed no significant association between GDM and vitamin D status in both unadjusted and adjusted (for mother`s age, parity, BMI and gestational week) models.
***Conclusion:*** The results of the present study could not show any association between serum vitamin D and GDM. It seems that other factors rather than serum level of 25 (OH) vitamin D level likely explain the growing prevalence of GDM.

## Introduction

Gestational diabetes mellitus (GDM) is defined as of glucose intolerance with onset or first recognition during pregnancy. It complicates about 14% of pregnancies.[1] It affects both maternal and neonatal well-being. Previously it has been shown that the risk of cesarean section and development of Type 2 diabetes in GDM mothers is higher than non GDM mothers.[2,3] Moreover the risk of macrosomia, respiratory distress syndrome, birth trauma , jaundice and hypoglycemia in neonates from GDM mothers are also higher.[4] Considering the high burden of GDM on maternal and children, investigators attempt to find the underlying causes of GDM. Factors including obesity, family histories of type 2 DM, maternal age shown to play a significant role in GDM incidence. Nowadays, there is increasing interest in the contribution of hypovitaminosis D to GDM. Vitamin D has been shown to affect insulin sensitivity or beta cell function.[5,6] Since GDM is correlated with insulin resistance in peripheral tissues, it is postulated that hypovitaminosis D may have a role in pathogenesis of it.[7]

Although previous reports relating hypovitaminosis D with diabetes, there is conflicting results regarding association between GDM and maternal serum vitamin D levels. In a cross-sectional study in Iran, serum 25-[OH] D concentrations were significantly lower in GDM women compared with non GDM pregnant women.[8] In a study conducted in mothers,[9] there was a significant inverse relationship between maternal serum 25-[OH] D concentrations and fasting glucose. on the other hand there was no significant association between serum vitamin D concentrations and GDM in Indian population.[10]

In a prospective study in UK, no significant

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association between the serum concentration of 25-Hydroxyvitamin D and GDM development was observed.[11]

Considering these conflicting results, the present study was designed to primarily investigate the association between serum 25 (OH) vitamin D concentration and gestational diabetes in a sample of Iranian woman.

## Materials and Methods

In the present cross-sectional study, one hundred thirty six pregnant women (68 with GDM and 68 nonGDM) were recruited from a university hospital from April to September 2016. The pregnant woman who sought prenatal care and have not type 1 and type 2 diabetes mellitus were included in the present study. The ethics approval for this study was taken from ethics committee of Tabriz University of medical sciences.

The sample size was calculated using prior information about the relationships between GDM and serum vitamin D level [8] with 80% power and alpha error of 5%, which necessitated at least 68 cases in each group.

After taking the informed consent, for measuring blood glucose and also serum vitamin D concentration, the fasting blood was obtained. The universal screening tool for GDM was used to assess the pregnant women. Between the twenty-fourth and 28 weeks of pregnancy, oral glucose challenge test and oral glucose tolerance test were performed. Furthermore, the demographic information including age and parity were obtained through questionnaire. Furthermore, the gestational age was calculated and also the earlier obstetrics histories were taken. The seca weighing scale was used for measuring body weight and height was measured using a stadiometer according to standard methods.

All pregnant women were assessed for GDM. A diagnosis of GDM can be made in women who meet either of the following criteria: FBS≥92 mg/dL but FBS<126 mg/dL at any gestational age OR at 24 to 28 weeks of gestation: 75 gram GTT (glucose tolerance test) with at least one abnormal result: FBS≥92 mg/dL , but <126 mg/dL or one hour ≥180 mg/dL or two hour ≥153 mg/dL.

The serum level of 25(OH) D was measured using chemiluminescent immunoassay technology (25 OH Vitamin D Total Assay, DiaSorin, Saluggio, Italy). The hypovitaminosis D was defined as having a serum concentrations of 25(OH)D <20 nmol/l.

SPSS v18 statistical computer software was used for all statistical analyses. The Kolmogorov-Smirnov test was used to assess the normal distribution of data. Between-group comparisons were made by independent t-test or chi-squared test. Moreover ANCOVA used for comparison of the mean serum glucose and vitamin D between two groups Adjusted for, mothers age, BMI, parity, gestational week. The binary logistic regression analysis was used to assess the cross-sectional associations between serum 25-hydroxy-vitamin D (categorical variable) and GDM status in two models. Model 1 is unadjusted and model 2 is adjusted for age, parity, Body mass index and gestational age. A significance level of 0.05 was used and confidence intervals (CIs) were calculated at 95% level.

## Results

Table 1 presents the demographic characteristics of participants stratified by GDM status. According to results, the mean age of the pregnant women was 30.41±5.82 years and the mean gestational age was 22.57 weeks. There was a significant differences in gestational age of GDM (20.26 weeks) and non-GDM (24.88 weeks) women (p=0.001).

Table 2 depicted the biochemical characteristics of participants. Statistically significant differences were observed between GDM and non-GDM mothers in the term of serum levels of FBS, GTT-1 hour and GTT-2 hour. Moreover, the mean serum 25(OH)D of mothers was 13.42±7.78 ng/mL. There was not significant differences in the mean serum 25(OH)D level between GDM (14.45±8.73) and non-GDM (12.38±6.62) pregnant women (p=0.12).

Table 3 presents the vitamin D status in GDM and non-GDM women. Totally, 83.8% of participants were vitamin D deficient and 11.8% of them had insufficient amount of serum vitamin D. Only 4.4% of participants were vitamin D sufficient. The results of logistic regression analysis showed no significant association between GDM and serum vitamin D level in both unadjusted and adjusted (for mother`s age, parity, BMI and gestational week) models.

**Table 1.** Socio-demographic characteristics of participants (n=136).

| Variable | Total | Non GDM (n=68) | GDM (n=68) | p-value* |
|---|---|---|---|---|
| **Age (Years)** | 30.41±5.82 | 29.66±6.09 | 31.16±5.48 | 0.13 |
| **Gestational age (weeks)** | 22.57±8.52 | 24.88±6.76 | 20.26±9.50 | 0.001 |
| **BMI (kg/m$^2$)** | 29.42±5.45 | 29.06±5.66 | 29.78±5.23 | 0.14 |
| **Parity n (%)** | | | | 0.11≠ |
| **Nulliparous** | 81 (56.9) | 36 (52.9) | 45 (66.2) | |
| **parous** | 55 (40.4) | 32 (47.1) | 23 (33.8) | |

*P-value of independent t-test
≠ p-value of chi-square

**Table 2.** Biochemical characteristics of participants (n=136).

| Variable | Total | Non-GDM (n=68) | GDM (n=68) | p-unadjusted≠ | p-adjusted* |
|---|---|---|---|---|---|
| **FBS (mg/dl)** | 89.68±13.70 | 79.51±7.14 | 99.71±10.93 | <0.001 | <0.001 |
| **GTT 1h (mg/dl)** | 146.73±42.85 | 125.66±32.11 | 182.48±34.38 | <0.001 | <0.001 |
| **GGT 2h (mg/dl)** | 116.06±41.56 | 97.84±29.97 | 148.61±39.78 | <0.001 | <0.001 |
| **Serum vitamin D (ng/mL)** | 13.42±7.78 | 12.38±6.62 | 14.45±8.73 | 0.12 | 0.17 |

≠Independent t-test
* ANCOVA: Adjusted for, mothers age, BMI, parity, gestational week.

**Table 3.** Comparison of the vitamin D status in GDM and non-GDM mothers.

| Variables | Total | Non-GDM (n=68) | GDM (n=68) | Odds Ratio (95% CI) | |
|---|---|---|---|---|---|
| | | | | Unadjusted model | Adjusted model* |
| **Vitamin D deficiency** | 114 (83.8) | 62 (91.2) | 52 (76.5) | 0.44 (0.04, 4.81) | 0.28 (0.02, 3.54) |
| **Vitamin D insufficiency** | 16 (11.8) | 5 (7.4) | 11 (16.2) | 0.16 (0.01, 1.48) | 0.15 (0.01, 1. 44) |
| **Vitamin D sufficiency** | 6 (4.4) | 1 (1.5) | 5 (7.4) | 1 | 1 |

*Logistic regression: Adjusted for, mothers age, BMI, parity, gestational week.

## Discussion

Vitamin D status of pregnant mother is essential to fetal bone, lung and immune functions development. However, vitamin D deficiency during pregnancy is a worldwide epidemic. In this regard, the results of present study showed that a high proportion (83.8%) of mothers recruited from the hospital clinic in Tabriz-Iran had hypovitaminosis D, according to recognized criteria. It has been reported that the prevalence of hypovitaminosis D in pregnant women was 40%–100% in Sweden,[12] Australia,[13] Pakistan, India,[14] Japan[15] and China.[16] The prevalence of vitamin D deficiency in pregnant women in Yazd was reported to be 78.4% [17] and in Tehran it was 70.6%.[8] The difference in prevalence of vitamin D in pregnant women in different regions may be due to season of sampling, different methods of assaying serum vitamin D level, ethnics and genetic characteristics of the participants, geographical factors and other biologic factors that may affect on the heterogeneity of the results.

Previously, it has been shown that the serum level of vitamin D is correlated with function of the pancreatic cell.[5] In clinical studies, vitamin D deficiency has been reported to be associated with diabetes and obesity. In-vitro and animal studies have reported that hypovitaminosis D have impact on insulin secretion and the expression of insulin receptors.[18] Besides, due to anti-inflammatory properties, studies demonstrate that vitamin D deficiency may associated with metabolic syndrome and diabetes development.[5] There is a large scientific evidence linking vitamin D deficiency with diabetes. However, in the case of gestational diabetes, conflicting results were reported. In a case–control study, Zhang et al, showed that in 16-week pregnant women with lower level of serum 25(OH)D, the risk of GDM was higher.[19] In another case–control study in Iran, it has been shown that women with GDM were 2.7 times more likely to display the low level of serum 25(OH)D.[17] In two other studies Baker et al and also Farrant et al , reported no association between serum 25(OH)D levels and the GDM development among pregnant women.[20,10] In a retrospective study, Makgoba reported no significant differences in serum level of vitamin D in GDM and non-GDM pregnant women.[11] These situations are consistent with the findings of the current study. Indeed, we could not find any association between the maternal serum 25(OH) D status and the risk of GDM. This may be due to high prevalence of vitamin D deficiency in our pregnant women population (83.8%). Moreover, these conflicting results between serum level of 25(OH) D and GDM may be due to differences in study design, sample size, the gestation age in which vitamin D measured, sampling season and ethnic and genetic characteristics of the participants.

The results of the current study should be interpreted considering the limitations including cross-sectional design of the study which restricts examining causal associations. Moreover, we did not assess dietary intake and supplements use of the participants that may influence both on GDM and also serum 25(OH)D level. Moreover, in the present study, the serum level of 25(OH) D was measured using RIA method. Previous study showed that the most sensitive and specific method for measuring serum 25(OH) D concentrations is LC-MS, but because of its high equipment cost, its use in clinical practice is very limited.

## Conclusion

In conclusion, the preliminary hypothesis of the present study was not supported by these results. So, it seems that other factors rather than serum level of 25 (OH) vitamin D level likely explain the growing prevalence of GDM. However, for certain conclusion, there is a need for well-designed and well-conducted study to assess the correlation

between 25(OH) D and GDM.

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## Conflict of interests

The authors claim that there is no conflict of interest.

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