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Comparison of serum calcium and 25-hydroxyvitamin D levels among pregnancies with gestational diabetes mellitues, impaired glucose tolerance and normal glucose tolerance

Abstract

We aimed to assess the serum calcium and 25-hydroxyvitamin D levels among the pregnant who has gestational diabetes, impaired glucose tolerance and normal glucosetolerance. We included 151 pregnant who underwent oral glucose tolerance test between November 2014 and April 2015. Fasting blood glucose level, oral glucose tolerance test with 50 g of glucose and serum levels of 25-hydroxyvitamin D were performed to whom BMI was ≤30 at between 24-28 weeks of pregnancy. Patients with abnormal response to challenge test underwent standard 100 g, 3-hour oral glucose tolerance test (OGTT). There were three groups as follows: group 1 with impaired glucose tolerance, group 2 gestational diabetes mellitus and group 3 normal glucose levels. Serum levels of 25-hydroxyvitamin D did not demonstrate statistically significant difference between gestational diabetes mellitus, impaired glucose tolerance and normal glucose tolerance groups. There was no statistically significant difference in serum calcium levels between the groups. The main parity was statistically significantly higher in gestational diabetes mellitus group than impaired glucose tolerance and normal glucose tolerance groups. The fasting blood glucose levels of the control group were significantly lower than those of impaired glucose tolerance and gestational diabetes mellitus groups. We did not detect any significant difference between subjects with gestational diabetes, impaired glucose tolerance and normal glucose tolerance test results. Further extensive researches are required to determine the underlying mechanism.

Keywords: *gestational diabetes, calcium, 25-hydroxyvitamin D*

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Introduction

Diabetes mellitus (DM) is a metabolic disease that organs are exposed to hyperglycemia for a long period of time, as a result of insulin deficiency or insulin insensitivity of tissues[(1)]. Gestational diabetes mellitus (GDM) is a major disease causing serious negative fetal and maternal outcomes. GDM occurs 2-13% of all pregnancies.

It is asserted for GDM that, maternal age and weight gain, obesity, GDM history of previous pregnancies and family, fetal mortality and macrosomic infant history, ethnical risk and hypo vitamin-D level are the risk factors[(2)].

Vitamin D increases vitamin D receptor and 25-hydroxyvitamin D hydroxylase expression, by affecting pancreatic B-cells. Vitamin D increases insulin secretion and decreases insulin resistance. Vitamin D decreases insulin resistance via intracellular calcium level which is active in glucose transport. Vitamin D also affects systemic inflammation which is connected to diabetes mellitus and insulin resistance[(3)]. Vitamin D increases insulin production from pancreatic B-cells and activates transformation of proinsulin to insulin[(4)]. Hypo-vitamin D level is a risk factor for metabolic syndrome and type 2 DM and vitamin D deficiency is related to insulin resistance and pancreatic B-cells dysfunction[(5)].

There is no consensus on the optimal vitamin D serum levels of all humans, pregnant and non-pregnant women. Vitamin D deficiency is serum 25(OH)D vitamin level under <25 nmol/l (10 ng/ml), and vitamin D insufficiency is serum 25(OH)D vitamin level between 25-50 nmol/l (10-20 ng/ml)[(6)].

Statistically significant difference in 25-hydroxyvitamin D vitamin levels is determined between pregnants who have GDM and normal glucose tolerance. It is determined that, serum vitamin D level is lower at pregnants who have GDM[(7-10)].

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We aimed to assess the serum calcium and 25-hydroxyvitamin D levels among the pregnants who has gestational diabetes, impaired glucose tolerance and normal glucose tolerance.

Methods

In this retrospective study, between November 2014 and April 2015, 151 pregnants between 24-28 gestational weeks who accepted GDM scan were included to the study. There are three groups as group 1 with impaired glucose tolerance, group 2 with GDM and group 3 with normal glucose levels.

Gestational age is determined according to latest menstrual date and ultrasonographic evaluation made during first trimester. Pregnants who have Type I and Type II diabetes, fetal and/or chromosomal anomalies and liver, kidney and endocrinopathic diseases were excluded. Preprandial blood glucose, 50 g oral glucose tolerance test (OGTT), serum 25-hydroxyvitamin D and calcium levels were examined. Hypertension, diabetes, proteinuria histories of previous pregnancies were questioned. Prepregnancy height, weight, body mass index (BMI) value (BMI ≤30 were included), parity, number of live birth, abortus and curettage were recorded. For 50 g OGTT, 1 hour threshold was accepted as 140mg/dl and pregnant who have higher blood glucose level are suggested 100 g OGTT. For 100 g OGTT, preprandial 95, 1 hour 180, 2 hour 155 and 3 hour 140 mg/dl issue. In 100 g OGTT, participants who seamy value exceeds the relevant threshold, are qualified as impaired OGTT. Participant who set two values exceed the relevant threshold are accepted as GDM. The study was approved by the Ethics and Clinical Investigation Committee of Fatih Sultan Mehmet Research and Training Hospital in Istanbul.

During the evaluation of the findings obtained by the study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) software was used for statistical analyses. Normality of sample data and parameters was tested by Shapiro Wilks test. During the evaluation of the sample data, besides the descriptive statistical methods (mean, standard deviation), the comparison of quantitative data, intergroup comparison of normally distributed parameters was conducted by one way ANOVA test and the group causing discrepancy was detected by running Tukey HDS test. In the intergroup comparison of non-normally distributed parameters Kruskal Wallis test and the group causing discrepancy was detected by using Mann Whitney U test. Two-sample comparison of normally distributed parameters was held by running Student t test. The comparison of qualitative data was held by using Chi-Square test. Analyses of the data were held by using correlation analysis. Statistical significance level was determined as $p < 0.05$.

Results

The demographical characteristics of the participant patients are shown in Table 1. There was no significant difference among groups according to age, number of abortus, BMI or previous birth method ($p > 0.05$).

Table 1 Assesment of parameters according to groups

Mean±SD	Impaired glucose tolerance (n:33)	GDM (n:30)	Control (n:88)	P
Age	30.27±4.16	30.60±4.05	28.80±5.14	[1]**0.113**
Parity	0.79±1.11 (0)	1.47±1.11 (1,5)	0.94±0.95 (1)	[2]**0.012***
Abortus	0.27±0.57 (0)	0.33 ±0.76 (0)	0.2±0.57 (0)	[2]**0.613**
Gestational week	25.88±1.22 (26)	26.17±1.26 (26)	25.45±1.3 (25)	[2]**0.012***
BMI	23.55±2.3	23.87±2.09	23.34±2.41	[1]**0.557**
Delivery	n (%)	n (%)	n (%)	
Vaginally	6 (18.2%)	9 (30%)	26 (29.5%)	[3]**0.488**
CS	12 (36.4%)	13 (43.3%)	29 (33%)	

[1]*One-Way ANOVA* [2]*Kruskal Wallis Test* [3]*hChi-square Test* **p<0.05*

There was statistically significant difference between the parity means of the cases among groups (p=0.012; p<0.05). The result of paired comparisons for identification of the reason of difference shows that, the parity mean of GDM group was significantly higher than the means of impaired OGTT and control groups (p<0.01, p<0.05). There was no statistically significant difference between number of parity of impaired OGTT and control groups.

For the third group, statistically significant difference was estimated for the means of pregnancy week and OGTT was examined. The result of paired comparisons for identification of the reason of difference showed that, the pregnancy week mean of GDM group was significantly higher than the mean of control group. There was no statistically significant difference between other two groups with regard to the gestational week (p>0.05).

Serum 25-hydroxyvitamin D levels, serum calcium levels and preprandial blood glucose levels among groups are presented in Table 2. There was no statistically significant difference among groups with regard to serum 25-hydroxyvitamin D levels and serum calcium levels (p>0.05).

There was statistically significant difference among the groups with regard to the preprandial blood glucose levels of the cases. The result of paired comparisons for identification of the reason of difference showed that, the mean of preprandial blood glucose of the control group was significantly lower than the mean of BGT and GDM groups. Preprandial blood glucose level means of BGT and GDM groups were between 80-100 and there was no significant difference (p>0.05).

The serum 25-hydroxyvitamin D, calcium and preprandial blood glucose levels of GDM diagnosed pregnants whose blood glucose level was regulated by diet or by insulin are shown in Table 3.

There was no significant difference with regards to serum 25-hydroxyvitamin D, calcium and preprandial blood glucose levels, between GDM diagnosed patients who receive diet or insulin treatment (p>0.05).

The 25-hydroxyvitamin D level ranges are presented in Table 4.

There was no statistically significant difference among 3 groups with regard to vitamin 25(OH)D serum levels (p>0.05).

Table 2 Assesment of glucose, calcium and 25 OH vitamin D levels regard to groups

Mean±SD	Impaired glucose tolerance (n:33)	GDM (n:30)	Control (n:88)	p
25-OH-VitaminD (ng/ml)	10.39±4.78	10.45±5.98	10.86±5.42	**0.887**
Calcium (mg/dl)	9.03±0.32	8.87±0.48	8.89±0.38	**0.181**
Glucose (mg/dl)	88.24±7.46	94.47±9.90	82.86±11.80	**0.001****

One-Way ANOVA ***p<0.01*

Table 3 Comparing to glucose, calcium and 25OH vitamin D levels between patients with gestational diabetes

Mean±SD	On diet (n:22)	With insulin treatment (n:8)	P
25-OH vitamine D	9.48±3.89	13.10±9.58	**0.146**
Calcium	8.88±0.52	8.85±0.37	**0.875**
Glucose	94.05±9.85	95.63±10.60	**0.706**

Student t Test

Table 4 Comparing to 25 OH vitamine D levels between groups

25-OH vitamine D levels	Impaired glucose levels (%) (n:33)	GDM (%) (n:30)	Control (%) (n:88)	P
0-10 (ng/ml)	18 (54.5%)	17 (56.7%)	47 (53.4%)	0.941
10-20 (ng/ml)	14 (42.4%)	11 (36.7%)	35 (39.8%)	
>20 (ng/ml)	1 (3%)	2 (6.7%)	6 (6.8%)	

Chi-square Test

Table 5 Assesment of parameters according to BMI

Mean±SD	BMI < 25 (n:118)	BMI ≥ 25 (n:33)	p
Age	29.34 ± 5.03	29.97 ± 3.76	0.505
Parity	1.01 ± 0.98	1.03 ± 1.24	0.915
Abortus	0.26 ± 0.65	0.18 ± 0.47	0.503
Gestational Week	25.92 ± 1.31	25.73 ± 1.38	0.472
25-HO-Vit D	9.96 ± 4.81	13.22 ± 6.50	0.002*
Serum Ca	8.92 ± 0.39	8.92 ± 0.39	0.907

*Student t Test, *p<0.05*

The demographical characteristics of normal weight and overweight cases according to body mass index are given in Table 5.

There was no statistically significant difference between normal weight and overweight cases according to age, parity, abortus, gestational week and serum calcium levels.

There was statistically significant difference between normal weight and overweight cases according to serum 25-hydroxyvitamin D levels. Serum 25-hydroxyvitamin D levels of overweight cases were estimated significantly higher than other group (p:0.013; p<0.05).

Discussion

It is indicated that, vitamin D increases the functional capacity of β cells, insulin secretion and glucose intake of muscle and fat tissues by stimulating the insulin receptors[11,12]. Besides the effects of vitamin D to insulin excretion, it is also indicated via human and animal experiments that, vitamin D deficiency is related to impaired insulin excretion and it returns normal by using 1,25(OH)D3[11]. Vitamin D does not only increase the productive capacity of β cells, but also it accelerates the proinsulin-insulin transformation[4].

In the study of Makgoba et al. the concentrations of serum 25-hydroxyvitamin D was found 18.9 ng/ml in GDM group and 19.0 ng/ml in normoglycemic pregnants, and there was no statistically significant difference between groups(13). Also in our study, similarly, the means of serum 25-hydroxyvitamin D concentrations were determined for GDM and for normal glucose tolerance, and no statistically significant difference was detected.

In the study of Farrant et al. no statistically significant difference was detected between serum 25(OH) D vitamin concentrations and maternal age, height and BMI[14]. The occurrence of hypovitaminosis D was similar for GDM diagnosed and normal glucose tolerance cases (7% for both). According to the results of our study, there was no correlation between serum 25(OH)D vitamin concentrations and BMI. However, the serum 25-hydroxyvitamin D levels of the overweight cases were found significantly higher than the normal weight patients. Inclusion of onlyBMI ≤30 cases and the exclusion of obeses, constitutes the constraints for the study.

In the study of Baker et al. the difference of two groups which first trimester maternal 25(OH)D values were <50nmol/L and ≥75nmol/L was not correlated with GDM. (OR1.25; 95%CI, 0.39-4.05). It was determined for GDM diagnosed pregnant that, BMI was significantly higher than the control group[15]. Likewise in our study, in accordance with the study of Baker et al. no statistically significant difference was found for the 25-hydroxyvitamin D means among the groups. In addition, contrary to the study of Baker et al. there was no statistically significant difference BMI means of the cases among groups. It is considered that, inclusion of only BMI ≤30 pregnants and adoption of 24-28 gestational weeks as measurement timing instead of first trimester might be the reasons behind this results.

Zhang et al. determined that 25-hydroxyvitamin D concentration of GDM diagnosed pregnants was statistically significantly lower than the control group (24.2 vs. 30.1 ng/ml). It was also determined in this study that, deficiency of serum 25-hydroxyvitamin D (<20 ng/ml) increases the risk of GDM 2.66 times and every 5 ng/ml decline in 25(OH)D vitamin level increases the risk of GDM 1.29 times[10]. We consider that the result of statistical insignificance found among groups in our study might be because of the lower population mean.

According to the study of Soheilykhah et al., 25-hydroxyvitamin D3 deficiency diagnosed pregnants (<15 ng/ml) was determined to have 2.66 times higher GDM risk than the control group[9]. (95% CI, 1.26-5.6). No correlation is found between serum 25-hydroxyvitamin levels and maternal age, parity, BMI and preprandial blood glucose levels. According to the results of our study, there was no statistically significant difference among the 25-hydroxyvitamin D means of the cases (p>0.05). Compatible with the results of the study of Soheilykhah et al., statistically significant difference was detected between the age and BMI averages of the groups in this study. It was considered that inclusion of only BMI ≤30 pregnants and the limited sample size may be the reasons of statistical indifference.

In the study of Kostoglou-Athanassiou et al. serum 25-hydroxyvitamin D concentrations was found lower than control group(16). The means of serum 25-hydroxyvitamin D concentrations of patient group and control group were determined as 19.26 ± 0.94 ng/ml and 25.48±1.02 ng/ml respectively (p<0.001). Unlike these results, according to our study, there was no statistically significant difference between 25-hydroxyvitamin D averages of the cases.

In the study of Al-Rowaily et al. it was showed that multiparous women have 8.29 times more risk than the nulliparous women[17]. We also estimate that, the parity mean of GDM group was significantly higher than the parity means of impaired glucose tolerance and control groups. There was no statistically significant difference between parity numbers of impaired glucose tolerance and control groups.

In the study of Clifton-Bligh et al. the negative correlation between lower 25-hydroxyvitamin D concentrations and preprandial plasma glucose levels was indicated (r=-0.20, -0.31 to -0.08)[7]. According to our results, the preprandial blood glucose mean was statistically lower than the means of impaired glucose tolerance group and GDM group. There was no statistically significant difference between the preprandial blood glucose means of impaired glucose tolerance group and GDM group.

Maghbooli et al. showed that the total vitamin D deficiency (<25 nmol/L) prevalence of the pregnants was 70.6 %. They found that serious vitamin D insufficiency (<12.5 nmol/L) prevalence was higher for GDM pregnants than the normoglycemic pregnants. (GDM (44.2%), impaired glucose tolerance (33.3%) and normoglycemic (23.5%) (8.) In our study, it was determined that 94% of the pregnants' 25-hydroxyvitamin D levels WEre lower than >20ng/ml. When the 25-hydroxyvitamin D cut-off values are assumed as 0-10, 10-20, >20ng/ml, there was no statistically significant difference among groups with regard to 25-hydroxyvitamin D levels. It was considered that, the indifference among groups might be because of the endemic serum of 25-hydroxyvitamin D deficiency or insufficiency of the Turkish population. The exclusion of use of pregestational and gestational 25-hydroxyvitamin D vitamin and calcium adjuvant from the study constitutes as a restriction for this study. Since the study was achieved in the winter, seasonal factors, low level of sunshine utilization and covered clothing might have also affected the results.

In the study of Muscoguiri et al. it was found that lower serum 25-hydroxyvitamin D levels and higher BMI were correlated (p:0.048)[18]. According to the results of our study, the serum 25-hydroxyvitamin D levels of overweight cases were paradoxically statistically higher than the levels of normal weight cases. It was considered that, inclusion of only BMI ≤30 pregnants, adoption of 24-28 gestational weeks as measurement timing and the limited sample size might have affected the results of this study.

Conclusions

According to the results of this study, there was not statistically significant difference between serum 25-hydroxyvitamin D and calcium levels among the pregnants who have GDM, impaired glucose tolerance and normal glucose tolerance.

There was no statistically significant difference among groups with regards to age, gestational week, abortus, BMI, mode of delivery and preprandial blood glucose averages. Parity mean of GDM was significantly higher than the means of impaired glucose tolerance group and control group. Preprandial blood glucose mean of the control group was estimated statistically lower than the means of impaired glucose tolerance group and GDM group. There was no statistically significant difference between impaired glucose tolerance group and GDM group with regard to preprandial blood glucose averages. ■

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