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Relationship between gestational diabetes, vitamin D levels, and maternal age

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Abstract

Our study aimed to determine the vitamin D level of pregnant women was associated with gestational diabetes mellitus (GDM) and whether maternal age affects this. This cohort study retrospectively examined the electronic records of 200 pregnant women. The patients were divided into two groups: the GDM group (n: 35) as the case group and the healthy group (n: 165) as the control group. Pregnant women aged 19-44 years were included in the study. Vitamin D levels are deficient at <12 ng/mL, insufficient at 12-20 ng/mL, and sufficient at>20 ng/mL. Results found a statistically significant association between vitamin D levels and GDM in women (p <0.05). The vitamin D level in the GDM group (M=16.19; SD=5.59) was lower than the vitamin D level in controls (M=25.48; SD=10.01). The percentage of women whose vitamin D was within the acceptable range in GDM was 11% compared to 63% of healthy pregnant women. There was no statistically significant association between age and GDM (p>0.05). Results showed that the vitamin D levels in the GDM group were significantly lower than in the control group.

Keywords: Gestational diabetes mellitus, vitamin D, pregnancy, advanced maternal age

1. Introduction

Gestational diabetes mellitus (GDM) is defined as impaired *glucose* tolerance (IGT) and insulin resistance, first diagnosed during pregnancy. GDM affects 6-25% of pregnant women (1, 2). GDM usually has no symptoms but is associated with a higher risk of neonatal and pregnancy complications (3). Based on the performed studies, the reduction of vitamin D levels leads to an increase in the risk of GDM by 45%(4).

Epidemiological factors such as the rising maternal age and increasing background rates of obesity among women of reproductive age lead to a continually increasing prevalence of GDM worldwide. Recently, the World Health Organization has allocated GDM to global health research priorities in terms of its sudden increasing prevalence among women of reproductive age and its relationship with increased risk of neonatal complications, birth difficulties, and abnormal intrauterine growth, including neonatal hypoglycemia, macrosomia, fetal demise, neonatal respiratory distress syndrome, hyperbilirubinemia, the cardiovascular disease after pregnancy, and the onset of type 2 diabetes (1).

Vitamin D is a vitamin soluble in fat that contributes to the mineralization of bone, phosphorus, and calcium intake, immune system function, and parathyroid status (5). The role of vitamins in women's health is one of the main topics in various research (6, 7). Vitamin D deficiency may be due to different factors, including gender, age, BMI, time of sun exposure, level of sun exposure, season, diet, skin type, and sleep pattern (8). Possible mechanisms to adjust glucose homeostasis by vitamin D may include stimulating physiological insulin secretion in interaction with insulin-like growth factor, increasing duodenal intake and calcium renal reabsorption, and facilitating insulin intracellular signal transmission (9).

The high-income countries have an increased rate of women giving birth over the age of 35 over time, raising concern about the effect of advanced maternal age (AMA) on pregnancy outcomes (10). There is an association between AMA and extensive adverse pregnancy outcomes, including stillbirth, chromosomal abnormalities, miscarriage, fetal growth restriction (FGR), preterm labor, GDM, preeclampsia, and increased cesarean section rates (CS). In developing countries, we see an increase in the age of marriage and childbearing among women every year. This issue requires more studies on the increased risks for the baby and the mother.

Information on the role of vitamin D in glucose metabolism in pregnancy and its relationship with the development of GDM is insufficient and contradictory. The study aimed to determine the vitamin D level of pregnant women was associated with gestational diabetes mellitus (GDM) and

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whether maternal age affects this.

2. Materials and Methods

The Ethics Committee of Medipol University Non-Interventional Clinical Research Ethics Committee approved this retrospective study (Date:13.9.2022 Decision no:789). All procedures were carried out by the ethical rules and the principles of the Declaration of Helsinki. Two hundred women participated in this study between July 2018 and May 2022.

Maternal ages were divided into four groups; 18-21, 22-35, 36-40, and >40 years old. Pregnant women whose 25 (OH) vitamin D levels were checked in the first trimester and had an oral glucose tolerance test (OGTT) at 24-28 were included in the study. The study did not include pregestational diabetic women who did not have the recommended OGTT or whose result was not in the file. Pregnant women who had OGTT but were not screened for vitamin D levels in the first trimester and for whom no vitamin D was screened were excluded from the study.

The pregnant women included in the study were screened for GDM with the two-stage diagnostic approach recommended by the American Diabetes Association (11). In the two-stage diagnostic approach, if the plasma glucose level is ≥140 mg/dL 1 hour after drinking 50 g of glucose liquid randomly during the day, it is suspicious for diabetes. A 3-hour OGTT with 100 g glucose should be performed to confirm the diagnosis in pregnant women with a positive 50 g screening test. In our study, the evaluation of 100gr OGTT was evaluated according to the Carpenter-Coustan criteria in the "American College of Obstetricians and Gynecologists" (ACOG) and "American Diabetes Association" (ADA) guidelines. Fasting, first, second, and 3rd-hour cut-off values in the Carpenter-Coustan assessment are ≥95 mg/dL - ≥180 mg/dL - ≥155 mg/dL - ≥140 mg/dL, respectively. Those with two positive values out of four were diagnosed with GDM, and those with one positive value on the OGTT were called a single pathological value in the OGTT. A diagnosis of 'impaired glucose tolerance' was made. Two-step tests 24-28 were applied during pregnancy weeks. It was determined that pregnant women with a high risk for GDM were screened with 100 g OGTT in earlier weeks.

Vitamin D levels are deficient <12 ng/mL, insufficient 12-20 ng/mL, and sufficient >20 ng/mL(12-14).

2.1. Statistical Analysis

SPSS 26.0 package program was used for statistical analysis. Evaluation of the data, percentage distributions, mean(M), standard deviation (SD), Kolmogorov Smirnov test as a normality test, Mann-Whitney U test, and Kruskal-Wallis H test were used.

We utilized the GPower 3.1 program to calculate the example size. The two groups' total mean was calculated based on the Mann-Whitney test with a power of 80%, an effect size of 50%, and a beta/alpha ratio of 1 for at least 30 patients for each group (15).

3. Results

Two hundred women were divided into pregnant women with gestational diabetes (n=35) and healthy pregnant women (n=165). Table 1 shows descriptive statistics of study parameters in women. The mean age and BMI of women were 31.6 ± 7.89 and BMI 25.01±2.05, respectively.

Table 1. Descriptive statistics of study parameters in women

	Study parameters	Median (range) Mean ± SD or n (%)
Maternal characteristics	Age(years)	32 (19-44) 31.6±7.89
	BMI (kg/m2)	32 (18-30) 25.01±2.05
Laboratory values	HbA1c(%)	5.24 (4.51-6.2) 5.27±0.23
	FPG	83 (69-135) 84.23±7.7
	Plasma glucose at 60-minute time (mg/dL)	145 (13-252) 145.8±36.93
	Plasma glucose at 120-minute time (mg/dL)	113 (13-223) 117.59±30.95
	Vitamin D (ng/ml)	25.65 (5-48) 23.85±10.02
Age groups	18-21	47(23.5)
	22-35	60(30)
	36-40	57(28.5)
	>40	36(18)
Cigarette	Yes	18(9)
	No	182(91)
Vitamin D	Deficiency	23(11.5)
	Insufficient	69(34.5)
	Sufficient	108(54)
Insulin	Yes	2(1)
	No	198(99)
GDM	Yes	35(17.5)
	No	165(82.5)

BMI: Body mass index, SD: standard deviation, HbA1c: Hemoglobin A1c, FPG: fasting plasma glucose, GDM: gestational diabetes mellitus

Table 2 compares GDM positive as a case group and healthy women as a control group on age and Vitamin D values.

Table 2. Comparison of case and control groups regarding age and vitamin D

Study parameters	GDM positive (n=35) median (range) mean ± SD	Healthy (n=165) median (range) mean ± SD	*p*
Age (years)	32 (19-44) 30.89±8.46	16 (6-31.1) 16.19±5.59	0.521*
Vitamin D (ng/ml)	16 (6-33.1) 16.18±5.59	31 (5-48 25.48±10.01	<0.001*
HbA1c (%)	5.5 (5.1-6.2) 5.52±0.25	5.2 (4.51-5.67) 5.21±0.18	<0.001*
FPG	90 (79-135) 92.37±11.2	82 (69-97) 82.5±5.37	<0.001*
Plasma glucose at 60-minute time (mg/dL)	197 (127-252) 196.97±25.57	139 (13-215) 134.95±29.02	<0.001*
Plasma glucose at 120-minute time (mg/dL)	159 (83-223) 157.63±37.42	112 (13-174) 109.09±21.39	<0.001*

*A Mann-Whitney U test

As stated in Table 2, a statistically significant association was found between the case and control regarding age (p>0.05).

As stated in Table 2, a statistically significant association was found between the case and control regarding Vitamin D (p<0.05). The serum vitamin D was significantly higher in the healthy group (Mean=16.18 vs. 25.48). There was a significant difference between the two groups in terms of HbA1c, FPG, and plasma glucose at 60 and 120 minutes (p<0.05).

Fig. 1 shows the serum vitamin D levels in women with gestational diabetes and healthy women.

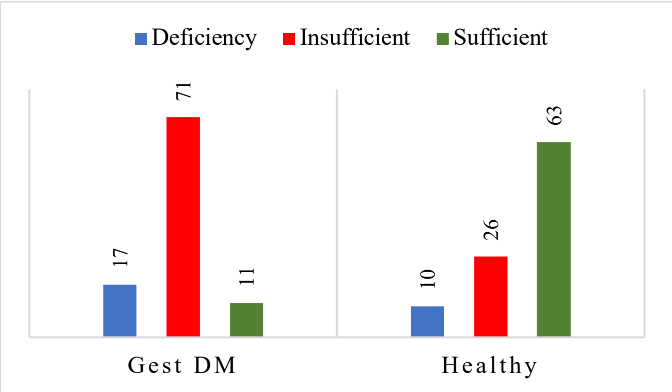

Fig. 1. The serum vitamin D levels in women with gestational diabetes and healthy women [Values in the figure are in percentages (%)]

In the GDM group, the frequency for the serum 25-hydroxyvitamin D (vitamin D) <12 ng/ml interval is 6 (17.1%). The frequency for vitamin D (12-20 ng/ml) and vitamin D (>20 ng/ml) was 25 (71.4%) and 4 (11.4%), respectively. In the control group, the frequency for the serum 25-hydroxyvitamin D (vitamin D) <12 ng/ml interval is 17 (10.3%). The frequency for vitamin D (12-20 ng/ml) and vitamin D (>20 ng/ml) was 44 (26.7%), and 104 (63%), respectively.

As stated in Table 3, a statistically significant association was found between age and the serum vitamin D level in the case group (p<0.05). As stated in Table 3, a statistically significant association was found between age and the serum vitamin D level in the control group (p<0.05).

Table 3. Comparison of serum vitamin D level according to age groups in women with gestational diabetes and healthy women

Study parameters		GDM positive (n=35) Median (range) Mean±SD	*p*	Healthy (n=165) Median (range) Mean±SD	*p*
Age groups	18-21	16.75 (14-19) 16.57±1.62	0.002	32 (24.8-41) 31.98±3.05	<0.001
	22-35	18.5 (14.6-31.1) 21.43±6.66		33.2 (24.8-48) 34.07±3.78	
	36-40	14 (6-22) 13.7±5.17		15 (5-23) 15.43±3.68	
	>40	12 (9-14) 11.83±2.04		14.5 (5-34.2) 18.62±10.61	

Age groups were tested by a Kruskal Wallis U test

Fig. 2 shows the serum vitamin D levels in age groups in the case and control groups. The mean of Vitamin D levels in each age group is presented in this figure.

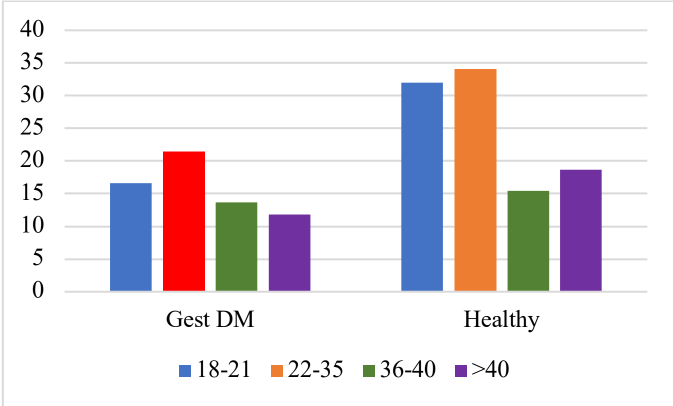

Fig. 2. The serum vitamin D levels in age groups in two groups

4. Discussion

The present study compared the relationship between vitamin D serum levels and GDM. There was a significant association between Vitamin D levels and GDM. The percentage of women whose vitamin D was within the acceptable range in pregnant women with diabetes was 11% compared to 63% of healthy pregnant women. There was a significant association between GDM and healthy groups in terms of HbA1c, FPG, and plasma glucose at 60 and 120 minutes and the age of women. Age groups the difference in vitamin D levels in healthy women in all age groups are more significant than in women. However, this difference decreases in women older than 36 years. Healthy women also face a decrease in vitamin D levels with age.

Previous studies have shown the ability of vitamin D in glucose homeostasis by regulating plasma calcium levels, which causes the regulation and secretion of insulin (16). Also, vitamin D improves the sensitivity of insulin target cells such as fat, liver, and skeletal muscles to insulin(17). Although the role of vitamin D in the pathogenesis of type 1 and type 2 diabetes has been proven, its role in GDM is still debated. We reviewed the literature and found that many studies have compared vitamin D levels and GDM. Some studies (8, 18-20) have documented no significant differences between vitamin D levels and GDM, and some studies (21-28) have indicated that vitamin D levels and GDM association were statistically significant. Milajerdi et al. (29) and Wang et al. (30), in two systematic reviews, reported a significant association between vitamin D deficiency and an increased risk of GDM.

Muthukrishnan et al. (18) found that serum Vitamin D levels were significantly higher in the control (45.8 ng/ml) versus the GDM group (24.7 ng/ml). Mosavat et al. (8) found that low maternal 25 (OH)-vitamin D in the second trimester of pregnancy is associated with GDM. The results of this study reported BMI, race, and ethnicity as influential factors in this association. Rajput et al. (19) said that severe vitamin D deficiency was significantly higher in GDM women, 44% versus 20% of healthy women. A meta-analysis by Zhang et al. (20) found that vitamin D deficiency increases GDM and the use of supplements during pregnancy helps reduce the risk of GDM. Further studies showed that vitamin D deficiency was not only a problem in mothers, but in a 9-year follow-up, it was shown that the children of these mothers showed more resistance to insulin and were, therefore, at a higher risk for diabetes(31).

Ismail et al. (22) reported no significant difference in the mean vitamin D concentration between GDM and normal pregnancies(14.43±5.27 versus 15.45±5.29). This study believes that the lower average vitamin D in GDM is outdoor activity and ethnicity in the third trimester of pregnancy. Jafarzadeh et al. (21) found that vitamin D levels in the first and second trimesters of pregnancy were similar in GDM and healthy women. Makgoba et al. (23) reported no association between the development of GDM and low vitamin D. Lou et al. (24) found no association between maternal vitamin D levels and GDM. Keller et al. (25) found that women whose diet is enriched with vitamin D have a lower risk of GDM. Although this finding was insignificant, it was close to significance (p=0.0.8). Farrant et al. (26) reported the relationship between vitamin D concentration, age, and BMI, and there was no increase in the risk of GDM. Park et al. (27) reported no relationship between the serum level of vitamin D in the first and second trimesters and GDM and fetal growth. Baker et al. (28) confirmed the absence of such a relationship.

GDM is a multifactorial disease. Therefore, despite many studies in this field, regional, economic, racial, ethnic, and lifestyle differences are the most critical factors that have caused the findings of studies to contradict each other. On the other hand, the design and sample size of many studies differ, which can be another reason for the differences in the results.

One of the strengths of this study is the statistical population with sufficient size. However, considering the multifactorial nature of gestational diabetes, the study participants should be evaluated in terms of lifestyle and diet.

As a result, there is a significant relationship between vitamin D and GDM. In most studies that did not report a meaningful relationship, vitamin D levels are still lower in diabetic women. It is necessary to replace vitamin D with proper nutrition and supplements. Age does not affect GDM due to vitamin D deficiency. However, the effect of vitamin D on GDM has yet to be proven. It requires more studies focusing on the characteristics such as lifestyle, ethnicity, and diets of the studied women.

Ethical statement

The Ethics Committee of Medipol University Non-Interventional Clinical Research Ethics Committee approved this retrospective study (Date:13.9.2022 Decision no:789). All procedures were carried out by the ethical rules and the principles of the Declaration of Helsinki.

Conflict of interest

The authors have no conflicts of interest to declare.

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None to declare.

Authors' contributions

Concept: A.Ş.K., Design: A.Ş.K., Data Collection or Processing: A.Ş.K., Analysis or Interpretation: A.Ş.K., Literature Search: A.Ş.K., Writing: A.Ş.K.

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