Maternal 25 Hydroxyvitamin D Level and Its Correlation in Thai Gestational Diabetes Patients

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Objective: *To identify 25 hydroxyvitamin D (25OHD) levels in Thai pregnant women with gestational diabetes and non-gestational diabetes.*
Material and Method: *This prospective study was conducted on 197 pregnant women at Rajavithi Hospital, a tertiary care medical center in Bangkok from October 2010 to July 2011. Plasma 25 hydroxyvitamin D concentration and HbA1c level during the 75 g OGTT in gestational diabetes mellitus (GDM) and non-GDM were evaluated. The recommendations of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) were used for diagnosis of GDM in the present study.*
Results: *In the selected 197 Thai pregnant women aged from 18 to 49 years, the mean age was 32.1 years, and the mean plasma 25OHD level was 34.3 ng/dl. The percentages of patients classified as having 25OHD deficiency (< 20 ng/dl), 25OHD insufficiency and normal 25OHD were 3.1%, 22.3% and 74.6%, respectively. Among the 197 women, 70 patients (34.8%) had GDM. In the GDM group, 29 patients (41.4%) had abnormal 25OHD level of which 5.7% had 25OHD deficiency and 35.7% had 25OHD insufficiency. Among those with GDM, plasma 25OHD concentration was significantly lower than in the non-GDM subjects (32.3 $\pm$ 10.3 vs. 35.5 $\pm$ 6.7 ng/dl, p = 0.001). Fasting blood glucose and HbA1C independently predicted low 25OHD levels in Thai GDM subjects after applying regression model and adjusting for age, BMI, trimester and family history of DM (p = 0.031, p = 0.014 respectively). Higher pre-pregnancy BMI was associated with GDM and lower 25OHD level.*
Conclusion: *Thai pregnant women with GDM had lower levels of 25OHD compared to those without GDM. Only fasting plasma glucose independently predicted low 25OHD levels in GDM subjects.*

Keywords: *Gestational diabetes mellitus, 25 Hydroxyvitamin D, Fasting plasma glucose, Hemoglobin A1c*

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Vitamin D is a secosteroid which is synthesized in the skin and metabolized in the liver and kidneys. It has been known to play a role in bone and calcium metabolism. Rather, it is a highly-regulated steroid hormone system with the potential to regulate up to 3% of the human genome[1]. There are two forms: vitamin D2 and vitamin D3. There is considerable evidence that low maternal levels of 25 hydroxyvitamin D are associated with adverse outcomes for both mother and fetus in pregnancy as well as for the neonate and child[2]. Vitamin D deficiency during pregnancy has been linked with a number of maternal problems including preeclampsia, gestational diabetes and an increased rate of cesarean section[2]. For the child, there is an association with small size, impaired growth and skeletal problems in infancy, type 1 diabetes, lower immune tolerance, neonatal hypocalcemia and seizures, and an increased risk of HIV transmission[2].

Vitamin D binds with vitamin D receptor (VDR), a classical steroid receptor of the nuclear retinoid X receptor (RXR) family. This receptor has been found in 37 different human tissues including those involved in the regulation of glucose metabolism, skeletal muscle, skin, the cardiovascular system, and components of the immune system[3]. There is evidence of the role of vitamin D in maintaining normal glucose homeostasis.

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There are two broad mechanisms by which vitamin D may have a role in glucose tolerance: through regulation of insulin release and/or insulin sensitivity[2]. The pancreatic beta cells have both VDR and 1 alpha hydroxylase, providing possible pathways for vitamin D, including 1, 25-$(OH)_2$ D3 produced locally. A study in 2009 found that circulating concentration forms of vitamin D were significantly and inversely related to the risk of type 2 diabetes[3]. It has long been known that vitamin D deficiency is prevalent among pregnant women[4,5]. Data from pregnant women in the northern United States showed that vitamin D deficiency occurred at a rate of 29.2% in black women and 5% in white women[6]. Data about the role of vitamin D in glucose homeostasis during pregnancy, and the development of gestational diabetes mellitus are scant and inconsistent.

In the present study, the authors evaluated the association between maternal plasma vitamin D concentrations in pregnancy, the risk of gestational diabetes and the outcome of obstetric and neonatal complications in Thai pregnant women according to their vitamin D status.

Material and Method

This prospective study was conducted on 197 pregnant women attending the antenatal care clinic at Rajavithi Hospital between October 2010 and July 2011 Thai pregnant women aged 18-49 years old who attended in the antenatal care unit (ANC) during this time period were legible to participate in the present study. Patients were excluded if they: 1) had gestational age > 28 weeks; 2) were aged < 18 years old; 3) did not plan to deliver at Rajavithi Hospital; 4) had pregestational diabetes; or 5) refused enrollment into the investigation.

Details of covariates were obtained by reviewing maternity medical records for maternal age, height, pre-pregnancy weight, pre-pregnancy BMI, medical histories, medical histories of first-degree family members, and smoking and alcohol history prior to pregnancy. Body mass index was calculated as weight in kilograms divided by the square of height in meters. After delivery, maternal and infant medical records were abstracted for information on the course and outcome of pregnancy on obstetric and neonatal complications. Infants' birth weight and blood glucose were also recorded.

In accordance with the recommendations of the American Diabetes Association, pregnant women were screened at 24-28 weeks gestation using a 50 gram 1-hour oral glucose challenge test. Those who had an abnormal screening test (glucose $\geq$ 140 mg/dl) were then tested with a 75 gram oral glucose tolerance test (OGTT). The plasma 25 hydroxyvitamin D concentration and HbA1c levels during the 75 g OGTT at first ANC in GDM and non-GDM subjects were collected and evaluated. Women were diagnosed with GDM if one or more of the glucose levels exceeded the criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) i.e. fasting $\geq$ 92 mg/dl (5.10 mmol/l); 1 hr $\geq$ 180 mg/dl (10 mmol/l); and 2 hr $\geq$ 153 mg/dl (8.49 mmol/l)[7].

A study of independent cases and controls with 2 controls per case was planned. Pregnant women aged 18-49 years old who fulfilled the inclusion criteria mentioned above were screened with 50 gram glucose challenge test at gestational age 24-28 weeks. If the result was abnormal the pregnant women were then tested with 75 gram oral glucose tolerance test (OGTT). Those with abnormal result of the OGTT were considered to be GDM. Prior data indicated that the rate of low vitamin D (25 (OH) d < 20 ng/ml) in GDM was 33% and the rate of low vitamin D (25 (OH) d < 20 ng/ml) in Non-GDM was 14%[8]. The authors indicated 85% of power and p-value less than 0.05 was statistical significant. In calculation for the case group, 64 case patients and 10% drop out (6 cases), 70 cases patients were recruited. Based on 2 controls per case, 140 control patients were recruited into the present study. The number derived from sample size calculation[9] based on 2 controls per 1 case:

$$n = \frac{\{Z_{\alpha/2}\sqrt{(k+1)\bar{P}(1-\bar{P})} + Z_{\beta}\sqrt{kP_1(1-P_1)+P_2(1-P_2)}\}^2}{k(P_1-P_2)^2}$$

giving k = 2, $Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.842$, $P_1 = 0.33$[8], $P_2 = 0.14$[8], $P = (0.33+0.14)/2$; sample size

$$n = \frac{\{Z_{\alpha/2}\sqrt{(2+1)0.235(1-0.235)} + 0.842\sqrt{2x0.33x(1-0.33)+0.14(1-0.14)}\}^2}{2(0.33-0.14)^2} = 60 \text{ and } 15\%$$

The present study was approved by the Ethics Committee of Rajavithi Hospital, and all patients provided written informed consent.

Biochemical measurement

Serum 25 hydroxyvitamin D was measured using the DiaSorin enzyme immunoassay reagents and procedure. Serum fasting plasma glucose, 1-hr and 2-hr glucose level after 75 g OGTT and HbA1c were measured. The authors categorized plasma 25OHD according to the criteria of the Endocrine Society Clinical Practice Guideline 2011. Three levels were defined as follows: Vitamin D deficiency < 20 ng/dl, Vitamin D insufficiency 20-29 ng/dl and Vitamin D

sufficiency ≥ 30 ng/dl[8].

Statistical analysis

Results of continuous data were presented by mean ± SD, and categororical data were expressed as proportions (%). A statistically significant difference was considered at a p-value of less than 0.05. Differences in clinical characteristics between the two groups were tested using a Student's t-test for continuous data and Chi-square (χ^2) for categorical data. Pearson correlation analysis was used to test for univariate linear relationships between 25OHD and other normal distribution variables. Regression models were used to analyze affected variables that probably involve the change of 25OHD with glycemic parameters. All statistical analyses were carried out using the statistical software SPSS version 17.0.

Results

According to the present study, pregnant women were enrolled from October 2010 to July 2011 if they plan to deliver at Rajavithi Hospital, age over 18 years old, gestational age less than 28 weeks, no history of diabetes and had an abnormal 50 gm glucose challenge test. From the calculated sample size, the authors need 70 pregnant women in GDM group and 140 pregnant women in the non GDM group. In total 197 pregnant women were recruited, 70 pregnant women had GDM and 127 were none GDM. Due to time limitation, the authors were able to recruit only 127 non GDM pregnant women. Three pregnant women were excluded.

In general, women who developed gestational diabetes were heavier with higher pre-pregnancy BMI (p = 0.011, Table 1). There were no significant differences in age or systolic blood pressure in the GDM and non-GDM groups. Other demographic characteristics and biochemical parameters of the subjects are shown in Table 1.

In the present study based on the IOM criteria 2011, the prevalence of vitamin D insufficiency (20-29 ng/ml) in Thai pregnant women at Rajavithi Hospital was 44 (22.3%) and vitamin D deficiency (< 20 ng/ml) was 6 (3.1%). The prevalence of hypovitaminosis D in Thai pregnant women at Rajavithi Hospital was found to be 50 (25.4%). In those 197 pregnant women, 70 (34.8%) had gestational diabetes. Approximately 4 (5.7%) of GDM cases compared with 2 (1.5%) of non-GDM cases had plasma 25OHD concentration consistent with a diagnosis of vitamin D deficiency (p < 0.001). And 25 (35.7%) of GDM cases compared with 19 (14.9%) had 25OHD concentrations consistent with vitamin D insufficiency. It was clear that those with GDM had a higher percentage with lower vitamin D status. Maternal plasma 25OHD concentration was significantly lower in the GDM group compared to the non-GDM group (31.82 ± 9.93 ng/ml in the GDM vs. 35.70 ± 6.80 ng/ml in non-GDM; p = 0.001). This difference in maternal plasma 25OHD concentration remained statistically significant after logistic regression was applied (ln 25 OHD level 3.42 ± 0.31 ng/ml in GDM vs. 3.55 ± 0.21 ng/ml in non-GDM, p ≤ 0.001).

As expected, maternal plasma 25OHD concentration was inversely associated with maternal adiposity as estimated by pre-pregnancy BMI (Table 2). The pre-pregnancy BMI were 34.57 ± 12.87, 25.16 ± 5.76 and 23.84 ± 5.86 kg/m^2 (p = 0.002) in the vitamin D deficiency, insufficiency, and sufficiency status groups respectively. The pre-pregnancy BMI was statistically significantly higher in the vitamin D deficiency group.

Table 1. Characteristics of GDM and Non GDM participants (n = 197)

	GDM n = 70	Non-GDM n = 127	p-value
Age (years)	32.80 ± 5.68	31.60 ± 6.1	0.161
BW (kg)	62.20 ± 16	55.50 ± 14.83	0.011*
Height (m)	1.56 ± 0.06	1.54 ± 0.054	0.104
Pre-pregnancy BMI (kg/m^2)	26.30 ± 6.93	23.30 ± 5.70	0.004*
Systolic BP (mmHg)	116.50 ± 11	113.70 ± 9.53	0.099
Diastolic BP (mmHg)	73.00 ± 10.3	69.70 ± 8.4	0.029*
OGTT fasting (mg/dl)	90.40 ± 26.14	76.30 ± 5.65	0.029*
OGTT 1 hr (mg/dl)	196.60 ± 35	141.10 ± 21.93	<0.001*
OGTT 2 hr (mg/dl)	168.70 ± 38.80	126.80 ± 118.56	<0.001*
HbA1c (%)	5.79 ± 0.94	5.33 ± 0.37	<0.001*
25 OHD (ng/dl)	31.82 ± 9.93	35.70 ± 6.80	0.001*

No obstetric complications such as increase of pre-eclampsia, cesarean section, neonatal admission into NICU or shoulder dystocia were found to significantly correlate with vitamin D status. As for neonatal complications, only hyperbilirubinemia was found to be significantly higher in newborns with vitamin D sufficiency (p = 0.049) (Table 2). According to the present study, the regression model for association of glycemic parameters with maternal. ln 25 OHD (ng/ml) in the GDM group, the fasting plasma glucose and ln HbA1c after adjustment for age, pre-pregnancy BMI, trimester and family history of DM was significantly associated with ln 25 OHD level (95% CI, -0.017, -0.001) and (95%CI, -3.783, -0.472), (p-value = 0.031 and 0.014, respectively). The analysis was done using a regression model (Table 3).

Discussion

A number of case-control and observational studies have suggested vitamin D deficiency is associated with an increased risk of type 2 diabetes mellitus[9] and gestational diabetes, confounded by the association of vitamin D deficiency with ethnic groups who have high prevalence of both type 2 and gestational diabetes. In a cross-sectional study of 741 pregnant women, the prevalence of severe vitamin D deficiency (< 12.5 nmol/L) was found to be higher in those with GDM (44% vs. 23.5%) and there was a correlation between insulin resistance and vitamin D level (p = 0.002)[11].

In the present study, maternal plasma 25OHD levels in pregnancy were significantly lower in the Thai GDM group compared to the non-GDM group. 25 OHD

Table 2. Vitamin D status according to baseline characteristics, obstetric and neonatal outcomes

	Vitamin D deficiency	Vitamin D insufficiency	Vitamin D sufficiency	p-value
Age	28.67 ± 3.2	32.34 ± 5.98	32.23 ± 5.91	0.338
BW (Kg)	65.12 ± 16.0	60.47 ± 14.72	57.06 ± 15.68	0.372
Height (m)	1.59 ± 0.7	1.56 ± 0.5	1.54 ± 0.5	0.130
Pre-pregnancy BMI (kg/m^2)	34.57 ± 12.87	25.16 ± 5.76	23.84 ± 5.86	0.002*
SBP (mmHg)	116.00 ± 10.98	118.03 ± 9.0	113.79 ± 10.24	0.115
DBP (mmHg)	73.50 ± 7.93	74.47 ± 9.87	69.87 ± 8.94	0.041*
OGTT fasting	96.83 ± 27.11	86.23 ± 21.27	79.26 ± 15.04	0.005*
OGTT 1 hr	176.17 ± 26.22	172.39 ± 42.82	156.38 ± 36.15	0.029*
OGTT 2 hr	152.67 ± 18.29	176.93 ± 199.5	130.59 ± 36.23	0.025*
Obstetric outcome (%)				
Preeclampsia	0	2 (1%)	3 (1.5%)	0.533
Cesarean section	2 (1%)	16 (8%)	58 (29%)	0.977
Neonatal ICU	0	0	8 (4%)	0.284
Shoulder dystocia	0	1 (0.5%)	1 (0.5%)	0.580
Neonatal outcome (%)				
Hyperbilirubinemia	2 (1%)	8 (4%)	16 (8%)	0.049*
Pre-mature delivery	0	5 (2.5%)	17 (8.6%)	0.459
Neonatal hypoglycemia	1 (0.5%)	6 (3%)	18 (9%)	0.933

Table 3. Regression model for association of glycemic parameter with maternal ln 25 OHD (ng/ml)

Model*	GDM			Non-GDM		
	β	95% CI	p-value	β	95% CI	p-value
A. Fasting PG	-0.009	-0.017, -0.001	0.031*	0.004	-0.005, 0.013	0.394
B. 1 hr OGTT	-0.002	-0.006, 0.002	0.360	0.000	-0.002, 0.002	0.757
C. 2 hr OGTT	-0.002	-0.005, 0.002	0.303	-0.001	-0.003, 0.002	0.560
D. ln HbA1c	-2.127	-3.783, -0.472	0.014*	0.044	-0.931, 1.018	0.929

Adjusted by Age, BMI, Trimester and family history of DM

is regarded as the best indicator of vitamin D status in the body because it is the substrate for renal and non-renal production of 1,25 $(OH)_2$ D3 and has a longer biological half-life and higher concentrations in circulation than 1,25 $(OH)_2$D3. Several mechanisms may explain the observed association between vitamin D deficiency and GDM risk. Firstly, vitamin D may directly or indirectly modulate pancreatic beta cell function and secretion by binding its circulating active form, 1,25 $(OH)_2$D3, to beta cell vitamin D receptor and regulating the balance between the extracellular and intracellular beta cell pools[12,13]. Secondly, vitamin D can promote insulin sensivitiy by stimulating the expression of insulin receptors and enhancing insulin responsiveness for glucose transport. It also regulates extracellular calcium and thus ensures normal calcium influx through cell membranes and an adequate intracellular cytosolic calcium pool, which is essential for insulin-mediated intracellular processes in tissues[14]. Lastly, other impacts of major endogenous and exogenous sources of vitamin D can have an effect on glucose homeostasis through other pathways. In three studies, 25 OHD concentration was correlated with insulin sensivitiy[15-17]. Data relating vitamin D to the risk for GDM are sparse and inconsistent. The authors findings are similar to those from a cross-sectional study, where 25 OHD was significantly lower in GDM groups compared to normal groups[18]. A study done in Iran, the prevalence of severe vitamin D deficiency (< 5 ng/ml) in GDM was higher than normoglycemic pregnancies and the regression model revealed a strong correlation between the HOMA index and serum level of vitamin D[19]. In another study serum 25OHD was significantly and inversely associated with fasting glucose, even though the association with GDM risk was not statically significant[20]. In the present study, fasting plasma glucose and HbA1c in the GDM group was inversely associated with vitamin D level after being adjusted for age, pre-pregnancy BMI, trimester measurement of 25 OHD, and family history of DM. In a study of an Indian population, no significant association between 25 OHD and GDM risk was observed[21].

In another study, BMI was the most powerful predictor of 25 OHD concentration ($p < 0.01$)[22]. It may be that the well-documented association between obesity and low vitamin D is the primary relationship, and that insulin sensitivity is related primarily to the obesity rather than the vitamin D level. In the present study, the BMI inversely correlated with vitamin D status.

Vitamin D deficiency had been associated with elevated risk of pregnancy complications such as pre-eclampsia and caesarean section. Low vascular endothelial growth factor (VEGF) and increased pro-inflammatory cytokines have been associated with preeclampsia. Vitamin D has been shown to influence their expression which could underlie the association[23-25]. In a study of 253 women, 28% of women with a low vitamin D level (14.8 ng/ml) had a cesarean section, compared with only 14% of women with a vitamin D level of 15.0 ng/ml or greater ($p = 0.012$)[26]. Unlike other studies, the present study did not find any of those complications to be associated with vitamin D status. Hyperbilirubinemia was significantly common in the maternal group with vitamin D sufficiency. This result conflicts with the finding by Maimburg's study that suggests neonatal vitamin D deficiency could be responsible for some cases of neonatal jaundice and autism[27]. Until more studies are done, hyperbilirubinemia should not be linked to vitamin D level. One study by Ruth Coleman et al[28] concluded that an excess of vitamin D can lead to a high blood calcium level, but not jaundice.

Vitamin D deficiency during pregnancy has been linked with a number of fetal and neonatal health problems, such as small size, neonatal hypocalcemia, seizures, impaired growth, skeletal problems and other possible disease associations include type 1 diabetes, asthma, atopy, an increase risk of HIV transmission and schizophrenia[2]. In the present study, neonatal complications were not found to be associated with low vitamin D status. But in previous studies, low maternal 25 OHD has been correlated with low birth weight, birth length and growth to one year[29].

Among women who developed GDM, plasma 25 OHD at an average of 16 wks was significantly lower than in controls (24.2 vs. 30.1 ng/ml, $p < 0.001$). This difference remained significantly (3.62 ng/ml) lower on average in GDM cases than in controls ($p = 0.018$) after the adjustment for maternal age, race, family history of diabetes, and pre-pregnancy BMI. Approximately 33% of GDM cases, compared with 14% of controls ($p < 0.001$), had maternal plama 25 OHD consistent with a pre-specified diagnosis of vitamin D deficiency (< 20 ng/ml). After adjustment for the a fore mentioned covariates including BMI, vitamin D deficiency was associated with a 2.66 fold (OR (95%CI): 2.66 (1.01-7.02) increased GDM risk. From the present study, it suggested that maternal vitamin D deficiency in early pregnancy is significantly associated with an elevated risk of GDM[23].

There were several limitations in the present

study. Firstly, only a single measurement of plasma 25 OHD was performed, and it might be unlikely to reflect the maternal vitamin D status during the entire pregnancy period. Secondly, calcium and PTH level were not measured. Lastly, the present study was relatively small, so larger prospective studies are needed to determine the mechanism and consequences of vitamin D deficiency during pregnancy.

Conclusion

The present study provides data indicating that vitamin D insufficiency and deficiency are found in approximately 25% of our Thai pregnant women and 41% among Thai GDM women living in Bangkok. Thai pregnant women with GDM had a significantly lower concentration of 25OHD compared to the non-GDM group. Pre-pregnancy BMI was found to be inversely associated with 25OHD status. Only fasting plasma glucose independently predicted a low level of 25OHD level in GDM.

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Potential conflicts of interest

None.

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ระดับ 25 ไฮดรอกซีไวตามินดีของมารดาและความสัมพันธ์ในผู้ป่วยเบาหวานระหว่างตั้งครรภ์

นวพร นภาทิวาอำนวย, สถิตย์ นิรมิตรมหาปัญญา, ชัยชาญ ดีโรจนวงศ์, ทองคำ สุนทรเทพวรากุล, วีระศักดิ์ ศรินนภากร

วัตถุประสงค์: *เพื่อศึกษาระดับ 25 ไฮดรอกซีไวตามินดีในหญิงที่เป็นเบาหวานและไม่เป็นเบาหวานระหว่างตั้งครรภ์*

วัสดุและวิธีการ: *ศึกษาแบบไปข้างหน้าในหญิงตั้งครรภ์ 197 ราย ที่มารับบริการที่โรงพยาบาลราชวิถีระหว่างเดือนตุลาคม พ.ศ. 2553 ถึง กรกฎาคม พ.ศ. 2554 โดยวัดระดับ 25 ไฮดรอกซีไวตามินดีและระดับ ฮีโมโกลบินเอวันซีในเลือด ระหว่างทดสอบการรับประทานกลูโคส 75 กรัม (75 g OGTT) ในหญิงที่เป็นเบาหวาน และไม่เป็นเบาหวานระหว่างตั้งครรภ์โดยใช้คำแนะนำของ the international association of diabetes and pregnancy study groups (IADPSG) ในการวินิจฉัยเบาหวานระหว่างตั้งครรภ์*

ผลการศึกษา: *หญิงตั้งครรภ์ 197 ราย อายุระหว่าง 18 ถึง 49 ปี อายุเฉลี่ย 32.1 $\pm$ 5.9 ปี มีระดับ 25 ไฮดรอกซีไวตามินดีในเลือดเฉลี่ย 34.3 $\pm$ 8.3 นาโนกรัม/มล. พบว่า 3.1% ของหญิงตั้งครรภ์ทั้งหมดมีภาวะขาดไวตามินดี (ระดับไวตามินดีน้อยกว่า 20 นาโนกรัม/มล.) 22.3% มีภาวะพร่องไวตามินดี (ระดับไวตามินดี 20-29 นาโนกรัม/มล.) และ 74.6% มีระดับไวตามินดีปกติ หญิงตั้งครรภ์ 70 ราย (34.8%) เป็นเบาหวานระหว่างตั้งครรภ์ โดยในกลุ่มนี้ 29 ราย (41.1%) มีระดับ 25 ไฮดรอกซีไวตามินดีผิดปกติ ซึ่งแบ่งเป็นภาวะขาดและภาวะพร่องไวตามินดี 5.7% และ 35.7% ตามลำดับ ในหญิงที่เป็นเบาหวานระหว่างตั้งครรภ์พบว่า ระดับ 25 ไฮดรอกซีไวตามินดีในเลือดมีค่าน้อยกว่าหญิงที่ไม่เป็นเบาหวานอย่างมีนัยสำคัญ (32.3 $\pm$ 10.3 และ 35.5 $\pm$ 6.7 นาโนกรัม/มล., $p = 0.001$) เมื่อวิเคราะห์ความถดถอยโดยปรับค่าอายุ body mass index (BMI) อายุครรภ์และประวัติเบาหวานในครอบครัวพบว่าระดับน้ำตาลในเลือดหลังอดอาหาร และระดับฮีโมโกลบินเอวันซี เป็นตัวทำนายอย่างอิสระของการมีระดับ 25 ไฮดรอกซีไวตามินดีในเลือดต่ำในหญิงที่เป็นเบาหวานระหว่างตั้งครรภ์ ($p = 0.031$ และ 0.014 ตามลำดับ) ค่า BMI ก่อนตั้งครรภ์ที่สูง มีความสัมพันธ์กับการเป็นเบาหวานระหว่างตั้งครรภ์ และการมีระดับ 25 ไฮดรอกซีไวตามินดีในเลือดต่ำ*

สรุป: *หญิงที่เป็นเบาหวานระหว่างตั้งครรภ์มีระดับ 25 ไฮดรอกซีไวตามินดีในเลือดต่ำกว่าหญิงที่ไม่เป็นเบาหวาน ระดับน้ำตาลในเลือดหลังอดอาหาร และระดับฮีโมโกลบินเอวันซี เป็นตัวทำนายอย่างอิสระของการมีระดับ 25 ไฮดรอกซีไวตามินดีในเลือดต่ำในหญิงที่เป็นเบาหวานระหว่างตั้งครรภ์*