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BRIEF COMMUNICATION

Body size modifies the relationship between maternal serum 25-hydroxyvitamin D concentrations and gestational diabetes in high-risk women

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Abstract

Obesity increases the risk of low 25-hydroxyvitamin D (25(OH)D) concentrations and gestational diabetes (GDM). We explored whether the association between GDM and change in 25(OH)D concentrations measured in the first (7–18 wk) and second (20–27 wk) trimesters of pregnancy is dependent on maternal BMI. The study was a prospective study of 219 women with BMI of ≥30 kg/m^2, a history of GDM, or both. The participants were stratified by first-trimester BMI: BMI of <25.0, 25.0–29.9, 30.0–34.9, and ≥35 kg/m^2. In the BMI group ≥35 kg/m^2, those who did not develop GDM during the follow-up showed higher increase in serum 25(OH)D concentrations compared with women who developed GDM (43.2 vs. 11.5%; $P < 0.001$). No associations between 25(OH)D concentrations and GDM were observed in other BMI groups. These findings give an important aspect of the role of maternal body size in the association between vitamin D and GDM in high-risk women.

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Introduction

Gestational diabetes (GDM) refers to hyperglycemia first recognized in pregnancy [1]. Major risk factors for GDM include obesity and a history of GDM [2].

Observational studies have linked low 25-hydroxyvitamin D (25(OH)D) concentrations during pregnancy with a higher risk of GDM [3]. Also, randomized studies have reported improved maternal glucose–insulin metabolism after vitamin D supplementation [4]. However, the evidence for vitamin D-glucose metabolism associations is still contradictory [5].

Obesity increases the risk of both low 25(OH)D concentrations [6] and GDM [1]. In the studies on vitamin D and GDM, body mass index (BMI) has usually been used only for adjustments whereas further examination of the role of BMI is limited.

The objective of the present study was to explore prospectively whether the association of change in maternal 25(OH)D concentrations and GDM is dependent on maternal body size in high-risk women. To our knowledge, no such study has been published.

Table 1 Baseline characteristics according to BMI in the first trimester of pregnancy ($n = 219$ unless otherwise specified)

	BMI (kg/m^2)				
	<25.0 ($n = 43$)	25.0-29.9[a] ($n = 34$)	30.0-34.9 ($n = 84$)	≥35.0 ($n = 58$)	P[b]
Age (years)	33.0 (3.9)	33.2 (3.6)	31.7 (4.7)	31.4 (4.3)	0.052
Gestational age (weeks)	12.7 (1.7)	13.1 (2.1)	13.3 (1.7)	13.4 (2.1)	0.064
Educational attainment (n 216), n (%)					0.027
No education/vocational school	14 (33)	13 (39)	34 (41)	27 (47)	
Vocational degree	11 (26)	7 (21)	27 (33)	19 (33)	
Academic degree	18 (42)	13 (39)	21 (26)	12 (21)	
Previous deliveries, n (%)	43 (100)	32 (94)	42 (50)	24 (41)	<0.001
Prior GDM, n (%)	43 (100)	30 (88)	15 (18)	8 (14)	<0.001
Blood pressure (mmHg) (n 215)					
Systolic	115 (10)	118 (13)	123 (14)	127 (12)	<0.001
Diastolic	72 (8)	73 (7)	79 (9)	81 (8)	<0.001
Total cholesterol (mmol/l) (n 201)	4.79 (0.80)	4.87 (1.06)	4.96 (0.90)	5.01 (0.76)	0.157
HDL cholesterol (mmol/l) (n 201)	1.89 (0.25)	1.68 (0.32)	1.75 (0.33)	1.67 (0.28)	0.002
LDL cholesterol (mmol/l) (n 201)	2.62 (0.68)	2.79 (0.88)	2.82 (0.83)	2.91 (0.58)	0.035
Total triglycerides (mmol/l) (n 200)	1.02 (0.37)	1.30 (0.64)	1.38 (0.51)	1.51 (0.92)	<0.001
Fasting glucose (mmol/l)	4.79 (0.32)	4.97 (0.21)	4.85 (0.24)	4.90 (0.22)	0.559
1-h glucose (mmol/l)	7.18 (1.55)	7.31 (1.53)	6.80 (1.34)	7.09 (1.07)	0.415
2-h glucose (mmol/l)	5.90 (1.25)	5.78 (1.03)	5.76 (1.03)	5.90 (1.04)	0.600
HbA1c (%) (n 190)	5.26 (0.23)	5.24 (0.24)	5.22 (0.32)	5.23 (0.23)	0.662
Fasting insulin (mU/l) (n 200)	5.47 (4.46)	5.79 (2.74)	9.78 (9.41)	10.85 (4.46)	<0.001
HOMA-IR[c] (n 190)	1.19 (0.97)	1.26 (0.67)	2.10 (2.08)	2.38 (1.04)	<0.001
hs-CRP (mg/l) (n 216)	4.09 (4.50)	5.33 (4.79)	6.82 (4.36)	10.26 (5.67)	<0.001
HFII score (n 193)	11.1 (2.7)	10.2 (3.0)	9.9 (2.6)	10.1 (2.9)	0.112
25(OH)D (nmol/l)	74 (23)	73 (32)	64 (24)	57 (22)	<0.001
Physical activity (min/week) (n 200)					0.432
Median	90	85	60	60	
IQR	45, 150	30, 130	30, 120	43, 120	
Current smoking, n (%)	1 (2)	2 (6)	1 (1)	3 (5)	0.723
Vitamin D deficiency (<50 nmol/l), n (%)	5 (12)	9 (26)	26 (31)	25 (43)	0.001
Season of blood collection, n (%)					0.455
Spring	12 (28)	8 (24)	23 (27)	16 (27)	
Summer	9 (21)	11 (32)	18 (21)	8 (14)	
Fall	14 (32)	7 (21)	19 (23)	19 (33)	
Winter	8 (19)	8 (23)	24 (29)	15 (26)	

The data are given as mean (s.d.) for continuous variables and as n (percentages) for categorical variables

GDM gestational diabetes, *HOMA-IR* homeostatic model assessment of insulin resistance, *hs-CRP* high-sensitivity C-reactive protein, *25(OH)D* 25-hydroxyvitamin D, *HbA1c* glycated hemoglobin, *HFII* Healthy Food Intake Index, *IQR* interquartile range

[a]In the BMI group 25.0-29.9 kg/m^2, 12% ($n = 4$) had BMI of ≥30 kg/m^2 before pregnancy but lost weight until the first trimester of pregnancy. Thus, these women were included in the BMI group 25.0–29.9 kg/m^2

[b]P values are for linearity across BMI groups by using ANOVA or Cochran–Armitage test for trend

[c]Calculated as [fasting insulin (mU/l) × fasting glucose (mmol/l))/22.5]

Subjects and methods

The subjects were a part of the Finnish gestational diabetes prevention study (RADIEL), which is a lifestyle intervention study conducted between 2008 and 2014 among high-risk women. The study was performed according to the guidelines laid down in the Declaration of Helsinki. All procedures were approved by the Ethics Committees of Helsinki

University Central Hospital and South-Karelia Central Hospital. All participants provided written informed consent.

The inclusion criteria were age of ≥18 years, and a history of GDM or pre-pregnancy BMI of ≥30 kg/m^2, or both.

Out of the original 357 women, 219 were eligible for the current study.

The criteria for GDM diagnosis was at least one pathological glucose value in a 2-h 75 g oral glucose tolerance test (OGTT); fasting glucose ≥5.3 mmol/l, 1-h glucose ≥10.0 mmol/l, and/or 2-h glucose ≥8.6 mmol/l [7]. The OGTT was conducted in the first (5–20 wk in the current study) and second (22–30 wk) trimester.

Serum 25(OH)D concentrations were measured in the first (7–18 wk) and second (20–27 wk) trimester.

Stata 13.1, StataCorp LP (College Station, TX, USA) was used in the analyses. The women were stratified into groups according to first-trimester BMI; BMI of <25, 25.0–29.9, 30.0–34.9, and ≥35 kg/m^2. Statistical comparison between groups for GDM was made by the analysis of variance (ANOVA). ANOVA and Cochran–Armitage test were used to evaluate statistical significance for hypotheses of linearity. Correlations were calculated between percentage change in 25(OH)D concentrations from the first to the second trimester and area under the curve (AUC) of the diagnostic OGTT in the second trimester. Correlation coefficients were calculated by the Pearson method. The total and incremental AUCs for OGTT (fasting, 1-h, and 2-h glucose values) were determined by the trapezoidal method. Bootstrap-type test was performed if the assumptions were violated (e.g., non-normality). A P value of <0.05 was considered significant.

Adjustments were performed for potential confounding factors; baseline 25(OH)D concentrations, season, intervention group, and change in diet quality, physical activity, and weight from the first to the second trimester.

The prevalence of previous GDM was 100% ($n = 43$) and 88% ($n = 30$) in the BMI groups <25.0 and 25.0–29.9 kg/m^2, respectively. Thus, the adjustments for previous GDM were performed only in the BMI groups 30.0–34.9 and ≥35 kg/m^2. In the BMI group 25.0–29.9 kg/m^2, four women had pre-pregnancy BMI of ≥30 kg/m^2 but lost weight until the first trimester.

More detailed description of the exclusion criteria and data collection is available in the Supplementary Information.

Results

Baseline characteristics are presented in Table 1.

The overall GDM incidence was 17% ($n = 37$). According to BMI, the incidence was 37% ($n = 16$) in the BMI group <25 kg/m^2, 24% ($n = 8$) in the BMI group 25.0-29.9 kg/m^2, 7% ($n = 6$) in the BMI group 30.0-34.9 kg/m^2, and 12% ($n = 7$) in the BMI group ≥35 kg/m^2 ($P < 0.001$).

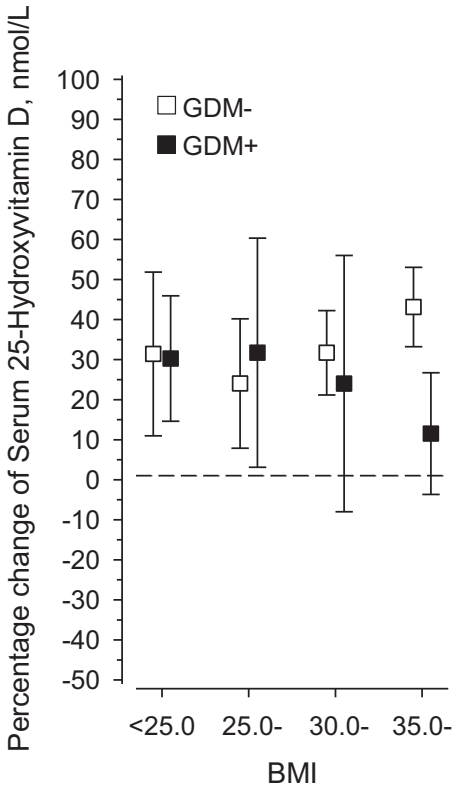

Fig. 1 Percentage change in serum 25(OH)D concentrations from the first to the second trimester in different GDM groups according to first-trimester BMI. The increase in serum 25(OH)D concentrations was significantly higher among women not developing GDM (GDM-) compared to women developing GDM (GDM+) in the BMI group ≥35 kg/m^2 ($P < 0.001$). *GDM* gestational diabetes, *25(OH)D* 25-hydroxyvitamin D

In the BMI group ≥35 kg/m^2, the increase in 25(OH)D concentrations was significantly higher among women not developing GDM compared with women developing GDM (43.2 vs. 11.5%; $P < 0.001$) (Fig. 1). The difference remained after adjustment for the confounders ($P < 0.01$). Similarly, the change in 25(OH)D concentrations was inversely correlated with AUC of the $OGTT_{(0\text{-}2h)}$ in the second trimester only among women in the highest BMI group (Supplementary Fig. S1).

Changes in 25(OH)D concentrations, weight, and lifestyle are available at Supplementary Table S1.

Discussion

These findings suggest that a greater increase in 25(OH)D concentrations is associated with lower GDM risk in pregnant women with BMI of ≥35 kg/m^2 but not among women with lower BMI. The findings were further supported by

that the change in 25(OH)D concentrations was inversely correlated with AUC of the diagnostic OGTT.

The current results are similar to findings from observational studies suggesting that 25(OH)D concentrations may have more influence on glucose–insulin metabolism among overweight and obese individuals compared with normal-weight individuals [8, 9].

Studies on overweight and obese adults have shown improved 25(OH)D concentrations after vitamin D supplementation but no changes in glucose and insulin metabolism [10]. Reasons for this might include too low vitamin D dose or examining the obese and severely obese participants as one group. However, as suggested by the current findings, improved 25(OH)D concentrations may have more beneficial influence in severely obese than in obese individuals.

More adverse metabolic profile in the BMI group ≥35 kg/m^2 compared with other BMI groups may partly explain the current findings. Additionally, the GDM incidence was highest among women with the lowest BMI and metabolic risk status, which most likely results from the inclusion criteria; all women with BMI of <30 kg/m^2 had a history of GDM. Previous GDM increases the risk for future GDM and thus may have attenuated the results among these women.

These findings provide an important aspect of the complex association between body size, 25(OH)D concentrations, and risk of GDM. Large randomized controlled trials are required to conclude if maternal BMI influences the association of vitamin D with GDM in high-risk population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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