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Risk of gestational diabetes mellitus in relation to maternal dietary calcium intake

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Abstract

Objective: The present study sought to examine the association between dietary Ca intake and risk of gestational diabetes mellitus (GDM).

Design: We assessed periconceptional (i.e. before conception and early pregnancy) Ca intake and consumption of foods rich in Ca using an FFQ among 3414 participants in a prospective cohort study. Diagnoses of GDM were abstracted from medical records. We used multivariable generalized linear regression models to derive estimates of relative risk (RR) for GDM and 95 % confidence intervals.

Setting: A prospective cohort of women in Seattle and Tacoma, WA, USA.

Subjects: Women (n 3414).

Results: A total of 169 GDM incident cases were identified in the cohort (4·96 %). Higher dietary Ca intake was inversely, although not statistically significantly, associated with GDM risk. After adjusting for confounders, the RR (95 % CI) for GDM according to successive increasing quartile of Ca intake was 1·00, 0·63 (0·41, 0·98), 0·66 (0·39, 1·11) and 0·57 (0·27, 1·21), respectively, with the lowest quartile as the reference ($P_{trend}=0·131$). Compared with women in the first quartile for Ca intake, women in the higher three quartiles (≥795 *v.* <795 mg/d) had a 42 % (RR = 0·58; 95 % CI 0·38, 0·90; $P=0·015$) lower GDM risk. GDM risk was inversely associated with low-fat dairy ($P_{trend}=0·032$) and whole grains ($P_{trend}=0·019$) consumption.

Conclusions: These findings suggest that higher levels of periconceptional Ca intake, particularly intake of Ca-rich low-fat dairy products and whole grains, are associated with lower GDM risk.

Keywords
Dietary calcium
Gestational diabetes
Low-fat dairy
Whole grains

Ca, the most abundant mineral in the human body, performs a number of basic functions including maintaining bone mass, cell signalling, blood clotting, muscle contraction and insulin secretion, among others[1]. During pregnancy, Ca absorption increases to meet fetal bone mineralization requirements[2]. The RDA of Ca for pregnant women is 1000 mg/d, with a tolerable upper intake level of 2500 mg/d[3]. National dietary surveys in the USA have reported that reproductive-age women do not meet RDA recommendations. Of note, the median Ca intake of African-American and Caucasian women is 467 and 642 mg/d, respectively[4,5]. Dairy products and foods such as milk, yoghurt and cheese provide the majority of Ca (70 %) in the general US diet[6]. Other foods such as some leafy green vegetables, legumes, whole grains and fish provide Ca, but generally in lower amounts per serving than do dairy products[6]. An extensive body of evidence shows that supplemental Ca intake during pregnancy is associated with lower risk of pre-eclampsia[7] and preterm birth[7] as well as reduced risk of long-term maternal morbidities such as excessive bone loss[8]. However, few epidemiological studies have focused on Ca intake from dietary sources and the risk of gestational diabetes mellitus (GDM). Findings from some studies conducted among non-pregnant women[9,10], although not all[11], have suggested that Ca intake is associated with reduced risk of incident type 2 diabetes. Given mounting available epidemiological evidence from studies of non-pregnant women supporting associations between Ca intake and reduced risk of type 2 diabetes[9,10], we hypothesized that higher periconceptional dietary Ca intake may be associated with a reduced risk of GDM. We also hypothesized that consumption of low-fat dairy products, an important source of dietary Ca, may be associated with

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reduced GDM risk. We investigated these hypotheses among a well-characterized prospective cohort of pregnant women.

Methods

Study population

The Omega Study is a prospective cohort study designed to examine the dietary risk factors of adverse pregnancy outcomes. Participants were women attending prenatal care clinics affiliated with the Swedish Medical Center and Tacoma General Hospital in Seattle and Tacoma, WA, USA[12,13]. Eligible women were those who began prenatal care before 20 weeks' gestation, spoke and read English, were aged >18 years, and planned to deliver at either of the two hospitals. During early pregnancy, participants were asked to complete an interviewer-administered questionnaire. Participants also completed a 121-item semi-quantitative FFQ[14]. Pregnancy outcome information was abstracted from medical records. All procedures and study protocols were approved by the institutional review boards of the study hospitals. All participants provided written informed consent.

Analytical population

The analytical study population was derived from participants enrolled in the Omega Study between 1996 and 2008. During this period, 5825 eligible women were approached and 4602 (approximately 79 %) agreed to participate. Women found to have physician-diagnosed pre-gestational diabetes (i.e. type 1, type 2 diabetes) and previous history of GDM (n 48), those with multi-fetal pregnancies (n 136), those with pregnancies lasting <20 weeks' gestation (n 45) and those with iron-deficiency anaemia (n 156) were excluded. Also excluded were women who did not complete the FFQ (n 566), those who reported extreme levels of daily total energy intake (<2092 kJ/d (<500 kcal/d; n 27) or 14 644 kJ/d (>3500 kcal/d; n 52)) and women who moved out of the study area (n 158). A cohort of 3414 women remained for analysis.

Data collection

From structured questionnaire and medical records, we obtained information on covariates including maternal age, educational attainment, height, pre-pregnancy weight, reproductive and medical histories, and medical histories of first-degree family members. We also collected information on maternal smoking during pregnancy. Self-reported pre-pregnancy weight and height were used to calculate pre-pregnancy BMI (= [weight (kg)]/[height (m)]^2). Participants completed a self-administered, validated and semi-quantitative FFQ[14] at a mean gestational age of 15 weeks to assess periconceptional (i.e. 3 months before conception and up to 3 months post conception) diet. The Women's Health Initiative FFQ allows for assessment of intake, portion size and food additives. Participants were provided clear instructions including photographs of portion sizes. This FFQ has documented reliability of accurately recording intake over an extended period of observation[14]. Ca intake from all dietary sources was estimated using food composition tables from the University of Minnesota Nutrition Coordinating Center nutrient database (Minneapolis, MN, USA). We also identified the major sources of dietary Ca in our population originating from high-fat and low-fat dairy products, whole grains, and fish with high Ca content. We calculated whole grains and dairy consumption by adding the daily number of servings of individual items. Total dairy products included whole milk, 2 % milk, skimmed milk, milk or cream in coffee or tea, yoghurt, frozen yoghurt, butter on bread or rolls, and cheeses or cheese spread. Low-fat dairy products included reduced-fat milk (≤2 % fat), reduced-fat yoghurt and reduced-fat frozen yoghurt, and high-fat dairy included all other dairy items. Yoghurt and frozen yoghurt were assumed to be high-fat if women indicated that they rarely used low-fat products. Whole grains included wholegrain bread, brown rice, wheat germ, bran, oat bran, hot breakfast cereal, wholegrain cold cereal and other whole grains. Fish considered high in Ca content according to the US Department of Agriculture were sardines, albacore tuna, rainbow trout, regular canned tuna and shrimp[6]. We considered the following as fatty fish: anchovies, herring (pickled or regular), kipper snacks, salmon (canned, fresh or smoked), sardines, albacore tuna, swordfish, rainbow trout, smelt and mackerel, in accordance with the US Department of Agriculture[6].

Maternal medical records were reviewed to collect detailed clinical information. As part of routine antenatal follow-up of all women at participating clinics, a 50-g, 1-h oral glucose challenge test was administered between 24 and 28 weeks' gestation to screen for GDM. Women who failed the screening test (glucose ≥ 7·8 mmol/l (≥140 mg/dl)) completed a diagnostic 100-g, 3-h oral glucose tolerance test within 2 weeks of the screening test. According to American Diabetes Association 2004 guidelines, women were diagnosed with GDM if two or more 100-g, 3-h oral glucose tolerance test levels exceeded the following criteria: fasting ≥ 5·3 mmol/l (≥95 mg/dl); 1-h ≥ 10·0 mmol/l (≥180 mg/dl); 2-h ≥ 8·6 mmol/l (≥155 mg/dl); 3-h ≥ 7·8 mmol/l (≥140 mg/dl)[15].

Statistical analysis

We classified each woman according to quartiles of maternal daily dietary Ca intake. We examined general characteristics of the study population using means for continuous variables and percentages for categorical variables. ANOVA or the χ^2 test was used to evaluate differences in sociodemographic, reproductive, medical

and dietary characteristics according to quartiles of dietary Ca intake. We calculated Pearson's correlation coefficients to assess the relationship of Ca intake with a number of foods known to be major dietary sources of Ca. To estimate relative risks (RR) and 95 % confidence intervals for GDM, we fitted generalized linear models with a log-link function, Poisson family (a 'log Poisson' regression model) and robust standard errors. This model allows estimation of RR for prospective studies with binary outcome data[16]. To assess confounding, we entered covariates into each model one at a time and compared adjusted and unadjusted RR. Final models included covariates that altered unadjusted RR by at least 10 % and those that were identified *a priori* as potential confounders such as maternal age, race/ethnicity, physical activity, family history of diabetes, red meat intake and sugar-sweetened beverages. Directed acyclic graphs were used to inform our analytical approach to adjusting for confounding.

In multivariable analyses, we evaluated linear trends in GDM risk by treating Ca intake as a continuous variable after assigning a score to each quartile. We explored the possibility of a non-linear relationship between Ca intake and GDM risk by fitting a multivariable logistic regression model that implemented the generalized additive modelling method[17]. We completed a series of stratified analyses to determine whether observed associations between Ca intake and GDM risk were evident and/or modified by other GDM risk factors (e.g. advanced maternal age, pre-pregnancy overweight status, physical inactivity during pregnancy, family history of diabetes, low daily vitamin C, vitamin D, total fibre, Mg and whole grains intakes, as well as high cholesterol, haem Fe and red meat intakes). All analyses were performed using the statistical software package Stata 12.0. All reported P values are two-sided and deemed significant at $\alpha = 0{\cdot}05$.

Results

Overall, the median daily intake of Ca was 1112 mg for women in the study cohort. On the basis of the Institute of Medicine guideline[3], only 58·4 % of the cohort met the daily recommendation for Ca intake (1000 mg/d). Characteristics of the study population according to maternal dietary Ca intake are shown in Table 1. Women with higher Ca intake tended to be white, more highly educated and physically active during pregnancy. Women with a higher Ca intake were less likely to have a family history of diabetes. Higher Ca intake was associated with higher intakes of dairy products (including low-fat milk and low-fat yoghurt), Mg, vitamin C, vitamin D, fruits and vegetables, carbohydrate and total protein. Alcohol and cholesterol intake were inversely associated with Ca intake (Table 1). Pearson's correlation coefficients with daily dietary Ca intake were 0·81 for low-fat dairy ($P < 0{\cdot}0001$), 0·31 for high-fat dairy ($P < 0{\cdot}0001$), 0·23 for whole grains ($P < 0{\cdot}0001$) and 0·10 for fish with high Ca content ($P < 0{\cdot}0001$).

A total of 169 incident GDM cases were identified in the cohort (4·96 %; Table 1). Higher dietary Ca intake was inversely, although not statistically significantly, associated with GDM risk (Table 2). After adjusting for total energy, maternal age, race/ethnicity, educational attainment, cigarette smoking status, pre-pregnancy BMI, prenatal vitamin use, physical activity, family history of diabetes and dietary covariates, including vitamin D and Mg, the RR of GDM was 0·63 (95 % CI 0·41, 0·98), 0·66 (95 % CI 0·39, 1·11) and 0·57 (95 % CI 0·27, 1·21) for quartiles 2, 3 and 4 of daily Ca intake, respectively, when compared with quartile 1, the lowest quartile ($P_{\text{trend}} = 0{\cdot}131$). Additional adjustment for intakes of total carbohydrate, total protein and saturated fat resulted in no appreciable change in estimates (<10 % changes in regression coefficients). When we combined women in the upper three quartiles (≥795 mg/d) of Ca intake and compared them with women in the lowest quartile (<795 mg/d), women consuming ≥795 mg of Ca daily experienced a 42 % reduction in GDM risk as compared with the reference group (RR = 0·58; 95 % CI 0·38, 0·90; $P = 0{\cdot}015$). As shown in the bottom panel of Table 2, we classified participants according to whether their daily Ca intake met the RDA of ≥1000 mg/d (no *v.* yes). Women who consumed ≥1000 mg/d, as compared with those who did not, had a 29 % reduced risk of GDM (adjusted RR = 0·71; 95 % CI 0·47, 1·09; $P = 0{\cdot}116$), although this association was not statistically significant. We explored the possibility of a non-linear relationship between Ca intake and GDM risk using regression procedures based on a generalized additive model. As shown in Fig. 1, the risk of GDM related to lower daily Ca intake levels was pronounced for daily Ca intake below 1200 mg/d. The risk of GDM appeared to level off for Ca intake of ≥1000 mg/d. Given the shape of the relationship of GDM risk with daily Ca intake, and that the risk appeared to be concentrated among women with intake values <1200 mg/d, we conducted a *post hoc* analysis after restricting our analysis to women with intake of <200 mg Ca/d (n 1944). From these analyses, we found that a 200 mg increase in daily Ca intake among women with low intake (<1200 mg/d) was associated with a 22 % reduction in risk of GDM (adjusted RR = 0·78; 95 % CI 0·61, 0·99; $P = 0{\cdot}042$). Additionally, we restricted our analysis to those women who were taking dietary Ca below the RDA (<1000 mg/d) and we found a 24 % reduction in GDM risk associated with a 200 mg increase in daily dietary calcium intake (n 1420; adjusted RR = 0·76; 95 % CI 0·56, 1·04; $P = 0{\cdot}09$).

We next assessed GDM risk in relation to maternal intake of Ca-rich foods (i.e. low-fat dairy products, whole grains, fish with high Ca). As shown in Table 3, higher consumption of low-fat dairy products was associated with a lower risk of GDM. Adjusted RR for GDM were 1·00,

Table 1 Participants' characteristics according to quartiles of dietary calcium intake, Seattle and Tacoma, WA, USA; Omega Study

Characteristic	Cohort (*n* 3414)	Dietary Ca intake (mg/d) Quartile 1 (<795) (*n* 852)	Quartile 2 (795–1111) (*n* 855)	Quartile 3 (1112–1526) (*n* 853)	Quartile 4 (≥1527) (*n* 854)	P_{trend}
Median Ca intake (mg/d)	1112	612	953	1292	1857	
Maternal age (years)	32·8	32·7	32·8	33·0	32·9	0·209
Pre-pregnancy BMI (kg/m^2)	23·5	23·8	23·4	23·1	23·5	0·085
Gestational age at delivery (weeks)	38·9	38·9	38·8	39·2	38·8	0·877
Non-Hispanic white (%)	86·8	76·3	88·4	89·9	92·4	<0·001
Post high-school education (%)*	97·0	95·8	96·3	97·5	98·6	<0·001
Married (%)	92·5	90·7	93·0	93·7	92·5	0·137
Nulliparous (%)	62·4	63·2	59·9	63·0	63·5	0·586
Smoked during pregnancy (%)*	5·4	5·4	6·2	5·2	4·7	0·355
Prenatal vitamin use (%)	97·9	97·2	98·0	97·5	98·7	0·065
Physically inactive during pregnancy (%)*	10·8	12·6	11·4	8·4	10·8	0·082
History of hypertension (%)	4·1	4·7	3·9	2·2	5·5	0·791
Family history of hypertension (%)	48·9	50·9	48·9	48·2	47·8	0·168
Family history of diabetes (%)	13·5	15·9	13·7	12·9	11·7	0·012
Incidence of GDM (%)	4·96	6·8	4·0	4·5	4·6	0·036
Total energy intake (kJ/d)	7209	5017	6640	7791	9397	<0·001
Total energy intake (kcal/d)	1723	1199	1587	1862	2246	<0·001
% Energy from carbohydrate	53·2	52·5	53·1	53·3	53·9	<0·001
% Energy from protein	17·3	16·5	17·0	17·4	18·4	<0·001
% Energy from fat	31·4	32·7	31·9	31·2	29·7	<0·001
% Energy from saturated fat	11·1	11·0	11·3	11·3	11·0	0·808
% Energy from polyunsaturated fat	6·5	7·1	6·6	6·4	5·9	<0·001
% Energy from monounsaturated fat	11·1	11·8	11·3	11·0	10·4	<0·001
% Energy from *n*-3 fatty acids	0·76	0·84	0·78	0·74	0·68	<0·001
Cholesterol (mg/d)†	269	293	280	273	251	<0·001
Alcohol (g/d)†	0·87	1·41	1·01	0·92	0·55	<0·001
Total fibre (g/d)†	21·1	20·9	21·7	21·4	20·7	<0·001
Total Fe (mg/d)†	16·2	14·6	15·5	16·0	17·4	<0·001
Haem Fe (mg/d)†	0·98	1·22	1·08	0·99	0·81	<0·001
Mg (mg/d)†	337	295	318	336	366	<0·001
Vitamin C (mg/d)†	137	114	128	133	153	<0·001
Vitamin D (mg/d)†	6·72	3·13	4·37	6·17	9·87	<0·001
Red meats (servings/d)	0·41	0·34	0·40	0·44	0·48	<0·001
Processed meats (servings/d)	0·22	0·18	0·22	0·24	0·26	<0·001
Fruit and vegetables (servings/d)	4·31	3·18	4·3	4·56	5·37	<0·001
Coffee and tea (servings/d)	0·63	0·47	0·66	0·73	0·67	<0·001
Sugar-sweetened beverages (servings/d)	0·14	0·14	0·14	0·14	0·13	0·594
Low-fat dairy foods (servings/d)	2·07	0·78	1·44	2·19	3·85	<0·001
High-fat dairy foods (servings/d)	0·91	0·54	0·83	1·06	1·23	<0·001
Low-fat/skimmed milk (servings/d)	1·53	0·54	0·96	1·59	3·05	<0·001
Low-fat yoghurt (servings/d)	0·19	0·10	0·18	0·21	0·28	<0·001
Whole grains (servings/d)	0·42	0·26	0·38	0·48	0·55	<0·001
Fatty fish (servings/week)*,‡	0·70	0·56	0·68	0·77	0·77	<0·001
Fish with high Ca content (servings/week)§	1·11	0·89	1·07	1·23	1·24	<0·001

GDM, gestational diabetes mellitus.
Data presented are medians, means or percentages. *P* values derived from ANOVA or χ^2 test.
*Variables with missing data. For education, *n* 3316; for smoking status, *n* 3305; for physical activity, *n* 3202; for fatty fish intake, *n* 3326.
†Energy-adjusted (8368 kJ/d (2000 kcal/d)).
‡Fatty fish: anchovies, herring (pickled or regular), kipper snacks, salmon (canned, fresh or smoked), sardines, albacore tuna, swordfish, rainbow trout, smelt and mackerel.
§Fish with high Ca content: shrimp, regular canned tuna, salmon, sardines, albacore tuna and rainbow trout.

0·89, 0·66 and 0·57 across successive quartiles of low-fat dairy intake, with the first quartile serving as the reference group ($P_{trend} = 0·032$). A statistically significant inverse relationship between whole grains consumption and GDM risk was also observed ($P_{trend} = 0·019$). Adjusted RR of GDM were 1·00 (reference), 0·87, 0·71 and 0·61 for successive increasing quartiles of whole grains intake.

We observed no evidence of an inverse association of GDM risk with increasing intake of fish with high Ca content ($P_{trend} = 0·724$). Finally, we assessed the extent to which, if at all, GDM risk in relation to Ca intake differed according to a number of maternal characteristics. As summarized in the online supplementary material, Supplemental Table 1, observed associations of GDM risk in relation to Ca intake did not differ according to advanced maternal age, pre-pregnancy overweight status, physical inactivity during pregnancy or family history of diabetes. Associations also did not differ according to dietary factors known to be associated GDM including low daily vitamin C, vitamin D, total fibre, Mg and whole grains intakes; as

Table 2 Relative risks (RR) and 95 % confidence intervals of gestational diabetes mellitus (GDM) according to quartiles of calcium intake, Seattle and Tacoma, WA, USA; Omega Study

		No GDM		Energy-adjusted		Adjusted*		Adjusted†	
Dietary Ca (mg/d)	Median	Incidence	%	RR	95 % CI	RR	95 % CI	RR	95 % CI
Quartile 1 (<795)	612	58	6·8	1·00	Referent	1·00	Referent	1·00	Referent
Quartile 2 (795–1111)	953	34	4·0	0·55	0·35, 0·86	0·66	0·43, 1·02	0·63	0·41, 0·98
Quartile 3 (1112–1526)	1292	38	4·5	0·59	0·37, 0·95	0·73	0·44, 1·20	0·66	0·39, 1·11
Quartile 4 (≥1527)	1857	39	4·6	0·57	0·31, 1·04	0·74	0·40, 1·36	0·57	0·27, 1·21
P_{trend}				0·089		0·387		0·131	
Quartile 1 (<795)	612	58	6·8	1·00	Referent	1·00	Referent	1·00	Referent
Quartile 2–4 (≥795)	1292	111	4·3	0·57	0·38, 0·85	0·65	0·43, 0·99	0·58	0·38, 0·90
P				0·006		0·045		0·015	
Less than RDA (<1000 mg/d)	737	82	5·8	1·00	Referent	1·00	Referent	1·00	Referent
Meet RDA (≥1000 mg/d)	1441	87	4·4	0·71	0·49, 1·04	0·82	0·55, 1·22	0·71	0·47, 1·09
P				0·079		0·322		0·116	

*Adjusted for daily energy intake, maternal age, race/ethnicity, educational attainment, cigarette smoking status, pre-pregnancy BMI, prenatal vitamin use, physical activity, family history of diabetes, alcohol, coffee, sugar-sweetened beverages, red and processed meats, fatty fish and total fibre intakes.
†Adjusted for all above with additional adjustments for dietary Mg and vitamin D intakes.

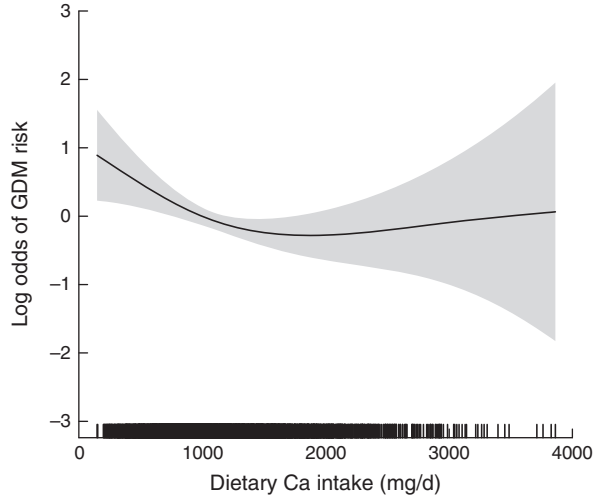

Fig. 1 Relationship between maternal dietary calcium intake in early pregnancy and risk of gestational diabetes mellitus (GDM) (solid line), with 95 % confidence interval (shaded area), Seattle and Tacoma, WA, USA; Omega Study. The vertical bars along the dietary calcium intake axis indicate the distribution of study participants

well as high cholesterol, haem Fe and red meat intakes. Lastly, we completed sensentivity analyses restricted to 3145 of the 3414 participants with complete data for all covariates (i.e. 92·1 % of the study cohort). Estimated RR from these analyses were not materially different from those reported here (data not shown).

Discussion

In the present large cohort of middle-aged women, we found that higher levels of maternal periconceptional dietary Ca intake, particularly intakes of Ca-rich low-fat dairy products and whole grains, are associated with lower GDM risk. Since previous studies focused on dairy foods instead of Ca intake and GDM risk[18,19], the role of Ca cannot be singled out in those studies. To the best of our knowledge, the present study is the first to examine the risk of GDM in relation to maternal dietary Ca intake during the periconceptional period. Our findings are largely consistent with existing literature reporting associations of Ca intake with lower risk of incident type 2 diabetes in non-pregnant women[9,20,21].

The biological mechanisms underlying associations of diabetes risk and dietary Ca might involve regulation of intracellular Ca affecting both insulin sensitivity and insulin release[22,23] as well as appetite regulation and related fat intake[24]. Of note, our results showed lower intakes of total fat and cholesterol with increased Ca intake. Whether dietary Ca intake might modify GDM risk through direct (insulin release) or indirect effects (lower fat intake) should be addressed in future studies. On the other hand, among women with low Ca intake (<1200 mg/d), our results showed a 22 % reduction in GDM risk with an increase of 200 mg/d in dietary Ca intake. Several food sources might provide approximately 200 mg of Ca. For example, 200 ml of skimmed milk, 50 g of natural yogurt, 60 g of Mozzarella cheese, 200 mg of rice pudding, a broccoli rabe or four oranges added to the diet can provide 200 mg of Ca[25]. Larger studies are needed to more formally and precisely assess GDM risk in relation to overall dietary Ca intake and specific Ca-rich food sources.

Dairy products are the main source of Ca in the general US diet[6] and in our study setting. Higher intake of low-fat dairy was significantly associated with lower GDM risk. Our findings are in line with some studies[20,26], but not all[27], reporting risk of type 2 diabetes with intake of low-fat dairy among non-pregnant adults. The evidence regarding GDM risk and low-fat dairy intake remains inconclusive in part because available studies are focused largely on total dairy (high-fat and low-fat) or dietary patterns that include dairy products. For instance, Bao and co-workers reported no statistically significant associations

Table 3 Relative risks (RR) and 95 % confidence intervals of gestational diabetes mellitus (GDM) according to quartiles of intake of low-fat dairy, whole grains and fish with high calcium content, Seattle and Tacoma, WA, USA; Omega Study

	Quartile 1		Quartile 2		Quartile 3		Quartile 4			>1st quartile		
Ca-rich foods	RR	95 % CI	RR	95 % CI	RR	95 % CI	RR	95 % CI	P_{trend}	RR	95 % CI	*P*
Low-fat dairy products (daily servings)		<0·89		0·89–1·67		1·68–2·91		≥2·92			≥0·89	
Cases, *n* and %	52	6·2	45	5·3	32	3·8	40	4·6		117	4·6	
Energy-adjusted	1·00	Ref	0·86	0·58, 1·27	0·61	0·40, 0·95	0·76	0·49, 1·18	0·109	0·75	0·54, 1·05	0·094
Adjusted*	1·00	Ref	0·89	0·60, 1·31	0·66	0·42, 1·04	0·57	0·32, 1·02	0·032	0·77	0·54, 1·11	0·169
Whole grains (daily servings)		<0·08		0·08–0·27		0·28–0·56		≥0·57			≥0·08	
Cases, *n* and %	47	6·3	45	5·6	38	4·2	39	4·1		122	4·6	
Energy-adjusted	1·00	Ref	0·89	0·60, 1·33	0·67	0·44, 1·02	0·64	0·42, 0·99	0·022	0·74	0·53, 1·03	0·072
Adjusted*	1·00	Ref	0·87	0·59, 1·29	0·71	0·46, 1·09	0·61	0·39, 0·95	0·019	0·75	0·53, 1·05	0·093
Fish with high Ca content (weekly servings)†		<0·35		0·35–0·80		0·81–1·52		≥1·53			≥0·35	
Cases, *n* and %	40	5·1	41	5·0	37	4·2	48	5·7		126	5·0	
Energy-adjusted	1·00	Ref	0·98	0·64, 1·49	0·84	0·54, 1·29	1·15	0·76, 1·74	0·669	0·98	0·69, 1·39	0·915
Adjusted*	1·00	Ref	0·93	0·60, 1·42	0·82	0·53, 1·28	0·97	0·60, 1·58	0·724	0·89	0·62, 1·29	0·540

*Adjusted for daily energy intake, maternal age, race/ethnicity, educational attainment, cigarette smoking status, pre-pregnancy BMI, prenatal vitamin use, physical activity, family history of diabetes, alcohol, coffee, sugar-sweetened beverages, red and processed meats, fatty fish, total fibre intakes, dietary Mg and vitamin D intakes.
†Eighty-eight participants (three GDM cases and eighty-five non-cases) with missing information regarding Ca-rich fish intake were excluded from this analysis.

between pre-pregnancy intake of total dairy products (high-fat and low-fat diary) and GDM risk in the Nurses' Health Study II[18]. Pre-pregnancy low-fat dairy and fruit intake pattern was not significantly associated with reduced risk of GDM in Australian women[19]. Our results showed no associations with total dairy intake; however, we noted statistically significant inverse associations of GDM risk with maternal habitual consumption of low-fat dairy and these associations were independent of other GDM risk factors.

Among non-pregnant adults, weight loss and lean tissue maintenance have been associated with higher dairy intake[28] and might help to explain, at least in part, the inverse association between dairy intake and type 2 diabetes risk. However, the physiological and molecular mechanisms underlying the impact of dairy constituents on adiposity in pregnant women are incompletely understood and need further investigation.

In addition to low-fat dairy products, whole grains intake was inversely related with GDM risk. To the best of our knowledge, the present study is the first showing an inverse association between whole grains intake and GDM risk. Radesky and co-workers reported no significant association between whole grains intake in early pregnancy and GDM risk[29]. On the other hand, the DASH (Dietary Approchaes to Stop Hypertension) diet, rich in whole grains and low-fat dairy, had beneficial effects on glucose tolerance and lipid profiles compared with the control diet in GDM patients[30]. Similarly, adherence to the Mediterranean diet, also rich in grains and grain products, has been associated with lower GDM risk[19]. In addition to Ca, other constituents of whole grains including dietary fibres, resistant starch, oligosaccharides, vitamins, antioxidants, trace minerals and phyto-oestrogens may contribute to beneficial effects on glucose metabolism[31].

Previous meta-analyses have pointed out the role of Mg as a confounder of the dietary Ca–type 2 diabetes association[32]. The association between Ca intake and diabetes risk disappeared (RR = 1·04; 95 % CI 0·88, 1·24) after adjustment for Mg intake in the Black Women's Health Study[11]. In the Nurses' Health Study, Mg and vitamin D were the dietary covariates primarily responsible for the attenuation of the association between type 2 diabetes and dietary Ca intake[9]. Contrary to these findings, adjustment for Mg strengthened the inverse association between Ca intake and GDM risk in our study population. We observed no evidence of an association of GDM risk with dietary intake of Mg or vitamin D in our study population (data not shown). Finally, we observed no evidence of effect modification by smoking status, physical activity or chronic hypertension status of associations between maternal dietary Ca intake and GDM risk.

The strengths of our study include its large size, rich covariate data and use of a previously validated FFQ. The major limitation of our study is its observational nature; therefore, residual confounding cannot completely be

ruled out for unmeasured variables. The role of maternal consumption of Ca supplements could not be evaluated in the cohort. Finally, the generalizability of our findings is limited to largely white, well-educated obstetric populations of women who register for prenatal care early in pregnancy and participate in regular annual medical examinations.

Conclusions

The present findings suggest that higher levels of maternal periconceptional Ca intake, particularly intakes of Ca-rich low-fat dairy products and whole grains, are associated with lower GDM risk. If confirmed in other pregnancy cohorts, public health nutrition educational materials directed towards reproductive-aged and pregnant women may further emphasize increased dietary Ca intake from low-fat dairy and whole grains.

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Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S1368980016002974

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