



Original Contribution

Risk of Gestational Diabetes Mellitus in Relation to Maternal Egg and Cholesterol Intake

Chunfang Qiu*, Ihunnaya O. Frederick, Cuilin Zhang, Tanya K. Sorensen, Daniel A. Enquobahrie, and Michelle A. Williams

* Correspondence to Dr. Chunfang Qiu, Center for Perinatal Studies, Swedish Medical Center, 1124 Columbia Street, Suite 750, Seattle, WA 98104 (e-mail: Chun-fang.Qiu@Swedish.org).

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Higher egg and cholesterol intakes are associated with increased risk of type 2 diabetes mellitus. However, their association with gestational diabetes mellitus (GDM) has not been evaluated. The authors assessed such associations in both a prospective cohort study (1996–2008; 3,158 participants) and a case-control study (1998–2002; 185 cases, 411 controls). A food frequency questionnaire was used to assess maternal diet. Multivariable models were used to derive relative risks and 95% confidence intervals. Compared with no egg consumption, adjusted relative risks for GDM were 0.94, 1.01, 1.12, 1.54, and 2.52 for consumption of ≤ 1 , 2–3, 4–6, 7–9, and ≥ 10 eggs/week, respectively (P for trend = 0.008). Women with high egg consumption (≥ 7 /week) had a 1.77-fold increased risk compared with women with lower consumption (95% confidence interval (CI): 1.19, 2.63). The relative risk for the highest quartile of cholesterol intake (≥ 294 mg/day) versus the lowest (< 151 mg/day) was 2.35 (95% CI: 1.35, 4.09). In the case-control study, the adjusted odds ratio for consuming ≥ 7 eggs/week versus < 7 eggs/week was 2.65 (95% CI: 1.48, 4.72), and the odds of GDM increased with increasing cholesterol intake (P for trend = 0.021). In conclusion, high egg and cholesterol intakes before and during pregnancy are associated with increased risk of GDM.

cholesterol; diabetes, gestational; eggs

Abbreviations: CI, confidence interval; FFQ, food frequency questionnaire.

Eggs contain a variety of nutrients, including vitamins, minerals, and cholesterol. A medium-sized egg contains approximately 200 mg of cholesterol, which is an integral part of cell membranes and an important regulator for many hormones (1). While consumption of less than 1 egg daily has not been shown to have a substantial overall impact on the risk of coronary heart disease or stroke among healthy men and women (2, 3), high levels of egg consumption (≥ 1 eggs/day) have been related to an abnormal lipid profile in men and women with type 2 diabetes mellitus (2, 3). High egg consumption has also been associated with increased risk of type 2 diabetes in men and women (4). Additionally, positive associations of cholesterol intake with fasting glucose ($p = 0.16$, $P < 0.01$) (5), incident type 2 diabetes (6), and incident gestational diabetes (7) have been reported.

To the best of our knowledge, no previous study has examined the association between egg consumption and the

incidence of gestational diabetes. Given available experimental and epidemiologic evidence (1–8), we hypothesized that higher preconceptional and early-pregnancy egg consumption may be associated with increased risk of gestational diabetes. We investigated this hypothesis and evaluated the association between dietary cholesterol and gestational diabetes risk in a cohort study of 3,158 pregnant women and in an independent case-control study (185 cases, 411 controls).

MATERIALS AND METHODS

This analysis was based on 2 studies conducted in Washington State (9–11). All procedures were in agreement with the protocols approved by the relevant institutional review boards. All participants provided written informed consent. There was no overlap in participants in the 2 studies. There

were no women with more than 1 pregnancy during the study period.

The Omega Study

Study design and setting. The Omega Study was a prospective cohort study designed to examine dietary risk factors for adverse pregnancy outcomes. Participants were recruited from women obtaining prenatal care at clinics affiliated with Swedish Medical Center and Tacoma General Hospital in Seattle and Tacoma, Washington, respectively (9). Eligible women were those who began receiving prenatal care at <20 weeks' gestation, spoke and read English, were ≥ 18 years old, and planned to deliver at either of the 2 hospitals. During early pregnancy, participants were asked to complete an interviewer-administered questionnaire. Participants also completed a 121-item semiquantitative food frequency questionnaire (FFQ) (12). Information on pregnancy outcome was abstracted from medical records.

Analytical population. The study population was derived from participants enrolled in the study between 1996 and 2008. During this period, 5,063 eligible women were approached and 4,000 (79%) agreed to participate. Fifty-seven women with pregestational diabetes (determined by self-report of physician-diagnosed diabetes), those with multifetal pregnancies ($n = 118$), those with pregnancies lasting <20 weeks ($n = 58$), and those who moved out of the study area ($n = 170$) were excluded. Also excluded were 372 women with incomplete dietary intake information and those who reported extreme levels (13) of daily energy intake (<500 calories/day ($n = 24$) or >3,500 calories/day ($n = 43$)). A cohort of 3,158 women remained for analysis. The incidence of gestational diabetes for the women included in the study (5.0%) was similar to that observed among those excluded (4.9%). The 2 groups were similar with respect to maternal age, race/ethnicity, prepregnancy body mass index, cigarette smoking, and leisure-time physical activity status. However, excluded women were less likely to be nulliparous.

Data collection. We obtained information on several covariates, including maternal age, educational attainment, height, prepregnancy weight, and medical history. We also collected information on maternal smoking status and leisure-time physical activity during pregnancy, as previously described (11). Prepregnancy body mass index was calculated as self-reported prepregnancy weight (kg) divided by the square of height (m^2). We used the FFQ from the Women's Health Initiative Clinical Trial (12) to assess dietary intake during the 3-month period before conception and during the first trimester. Participants were provided with instructions, including photos of portion sizes. Participants were asked to report their frequency of egg consumption (excluding egg substitutes). A medium serving size was defined as 2 medium-sized eggs. The questionnaire did not specifically inquire about eggs used in food preparation. Food composition values were obtained from the University of Minnesota Nutrition Coding Center's nutrient database. Participants completed FFQs at an average of 15.3 weeks' gestation (standard deviation, 3.8).

We reviewed medical records to collect detailed clinical information. In our study settings, according to American

Diabetes Association guidelines (14), pregnant women were screened at 24–28 weeks' gestation by means of a 50-g 1-hour oral glucose challenge test. Those who failed this screening test (≥ 7.8 mmol/L) were then followed up within 1–2 weeks with a 100-g, 3-hour oral glucose tolerance test. We also abstracted laboratory results from participants' 50-g 1-hour glucose challenge test and from the diagnostic 100-g 3-hour oral glucose tolerance test. Women were diagnosed with gestational diabetes if 2 or more glucose concentrations from the 100-g oral glucose tolerance test exceeded American Diabetes Association criteria (14): fasting glucose concentration ≥ 5.3 mmol/L; 1-hour postchallenge glucose concentration ≥ 10.0 mmol/L; 2-hour postchallenge glucose concentration ≥ 8.6 mmol/L; or 3-hour postchallenge glucose concentration ≥ 7.8 mmol/L.

Statistical analyses. We classified each subject according to the following categories of egg consumption: never (0), ≤ 1 , 2–4, 5–6, 7–9, and ≥ 10 eggs/week. We examined the frequency distributions of maternal characteristics and energy-adjusted (15) nutrient intake according to these categories. We fitted generalized linear models, using a log-link function, to derive relative risks and 95% confidence intervals (16). To assess confounding, we entered covariates into each model one at a time and compared adjusted and unadjusted relative risks. Final models included covariates that altered unadjusted relative risks by at least 10% and those that were identified a priori as potential confounders. Since other dietary components are known to play a major role in blood cholesterol physiology and pathophysiology (17), we repeated a series of stratified analyses to determine whether observed associations were modified by other dietary components and other established risk factors for gestational diabetes. We repeated similar analytic procedures to examine associations between cholesterol intake and gestational diabetes risk. In multivariable analyses, we evaluated the linear trends in risk by treating the categories of egg intake (or quartiles of dietary cholesterol) as a continuous variable after assigning a score to each category (18). All analyses were performed using Stata 9.0 (Stata Corporation, College Station, Texas).

The Alpha Study

Study design and population. The Alpha Study, a case-control study (1998–2002), was designed primarily to examine the epidemiology of preeclampsia (10, 11). In addition to preeclamptic women, patients with a diagnosis of gestational diabetes were recruited from hospital labor and delivery wards. Women were classified as having gestational diabetes using 3-hour glucose tolerance test cutpoints according to National Diabetes Data Group criteria (19). Controls were women who remained normotensive and did not develop gestational diabetes. Approximately 83% of 288 eligible gestational diabetes cases ($n = 238$) and 58% of 866 eligible controls ($n = 502$) participated. Reasons for nonparticipation included lack of time, no interest in the study goals, and missed appointments.

Data collection. Data collection occurred during the postpartum hospital stay. Trained interviewers administered a structured questionnaire. Self-reported height and weight

3 months before pregnancy were used to calculate body mass index. The same FFQ and nutrient database used in the Omega Study (12) were used to measure dietary intake during the periconceptional period (3 months prior to pregnancy) and for the duration of pregnancy (10). Medical records were reviewed as described previously (10, 11).

Analytical population and statistical analysis. We excluded 33 cases (13.9%) and 63 controls (12.5%) with missing information on dietary intake. We also excluded 13 cases and 23 controls who reported an extreme daily energy intake (<500 calories/day or >3,500 calories/day), as well as 7 cases and 5 controls with multifetal pregnancies. This resulted in a final analytic population of 185 cases and 411 controls. We examined frequency distributions of maternal characteristics according to case-control status. We used multivariable logistic regression to estimate odds ratios and 95% confidence intervals for gestational diabetes according to egg consumption and cholesterol intake. However, except for the difference in the link function used for multivariable modeling, we employed analytical approaches similar to those described above.

RESULTS

The Omega Study

Consumption of eggs, a major food source of dietary cholesterol, explained 72% of the variability in cholesterol intake in this cohort. Selected maternal characteristics are summarized in Tables 1 and 2. Women who reported frequent egg consumption (≥ 7 eggs/week) tended to be older and nonwhite. Egg consumption was positively associated with intakes of saturated fat, *trans* fat, red and processed meats, cholesterol, fruits, and vegetables (Table 1). Egg consumption was inversely associated with fiber intake (P for trend < 0.05). Cholesterol intake varied substantially in this cohort (Table 2). Women with higher cholesterol intake tended to be older and heavier and to report a higher intake of red and processed meats. Higher cholesterol intake was also positively associated with some healthy dietary habits, including higher intake of fruits and vegetables. Maternal egg consumption was highly correlated with cholesterol intake ($\rho = 0.77$, $P < 0.001$) in this population.

Maternal egg consumption and gestational diabetes risk. After adjustment for total energy, maternal age, race/ethnicity, prepregnancy body mass index, leisure-time physical activity, and intakes of meat, fiber, vitamin C, and saturated fat, the relative risks of gestational diabetes were 0.94 (95% confidence interval (CI): 0.50, 1.77), 1.01 (95% CI: 0.51, 1.98), 1.12 (95% CI: 0.57, 2.20), 1.54 (95% CI: 0.75, 3.18), and 2.52 (95% CI: 1.11, 5.72) for consumption of ≤ 1 , 2–3, 4–6, 7–9, and ≥ 10 eggs/week, respectively (P for trend = 0.008), compared with no egg consumption (Table 3). When we combined the groups consuming <7 eggs/week together as a single reference group, women consuming ≥ 7 eggs/week experienced a 1.77-fold increased risk of gestational diabetes (95% CI: 1.19, 2.63). The associations were not confounded by maternal dietary vitamin E or whole grain intake. Observed associations between gestational diabetes risk and frequent egg consumption (≥ 7

eggs/week) did not differ according to advanced maternal age, race/ethnicity, parity, smoking during pregnancy, family history of diabetes, prepregnancy overweight status (body mass index ≥ 25), or major dietary factors known to be related to glucose homeostasis (e.g., daily fruit, vegetable, cholesterol, and fiber intakes) (data not shown).

Total cholesterol intake and gestational diabetes risk. Dietary cholesterol was positively associated with gestational diabetes risk. Adjusted relative risks of gestational diabetes were 1.00 (reference), 0.83, 1.20, and 2.30 for successive quartiles of cholesterol intake (lowest to highest) (Table 3). Cholesterol intake was strongly correlated with saturated fat intake ($\rho = 0.67$, $P < 0.001$). However, the association of cholesterol intake with gestational diabetes risk did not change substantially after further adjustment for saturated fat intake (adjusted relative risks were 1.00, 0.83, 1.21, and 2.35 for successive quartiles). Results from stratified analyses of associations between gestational diabetes risk and high cholesterol intake (≥ 294 mg/day, the upper quartile) did not reveal evidence of effect modification by covariates such as leisure-time physical activity, family history of type 2 diabetes, and dietary intake of other nutrients.

The Alpha Study

Odds of gestational diabetes in relation to maternal egg intake. Gestational diabetes cases and controls differed in the distributions of several maternal characteristics (Table 4). Egg consumption was highly correlated with cholesterol intake in both cases ($\rho = 0.89$, $P < 0.001$) and controls ($\rho = 0.83$, $P < 0.001$). After adjustment for confounders (Table 5), the odds ratios for gestational diabetes were 0.70 (95% CI: 0.36, 1.37), 0.93 (95% CI: 0.47, 1.85), 1.18 (95% CI: 0.60, 2.31), 2.41 (95% CI: 1.08, 5.40), and 2.76 (95% CI: 1.03, 7.43) for consumption of ≤ 1 , 2–3, 4–6, 7–9, and ≥ 10 eggs/week, respectively (P for trend = 0.005), as compared with no egg consumption. When we combined the <7-eggs/week groups together as a single reference group, women consuming ≥ 7 eggs/week had 2.65-fold increased odds of gestational diabetes (95% CI: 1.48, 4.72). Associations of gestational diabetes risk with frequent egg consumption (≥ 7 eggs/week) did not differ across strata defined by other major nondietary and dietary factors known to be related to glucose homeostasis (data not shown).

Odds of gestational diabetes in relation to maternal total cholesterol intake. Dietary cholesterol was positively associated with the odds of gestational diabetes (P for trend = 0.021). When we used the same cutpoints as were used in the Omega Study, the odds ratios for gestational diabetes were as follows: 1.00 (reference), 1.44 (95% CI: 0.65, 3.17), 1.95 (95% CI: 0.88, 4.34), and 2.94 (95% CI: 1.14, 7.60) for successive categories (Table 5). Associations of gestational diabetes risk with high cholesterol intake (≥ 294 mg/day) did not differ across strata defined by other major nondietary and dietary gestational diabetes risk factors (data not shown).

DISCUSSION

We observed significant and positive associations between maternal egg consumption and the risk of gestational

Table 1. Characteristics of Participants According to Category of Weekly Egg Consumption, Omega Cohort Study, Seattle and Tacoma, Washington, 1996–2008

Characteristic	Entire Cohort (n = 3,158)		Egg Consumption, eggs/week								P for Trend				
			0 (n = 267)		≤1 (n = 1,186)		2–3 (n = 650)		4–6 (n = 631)			7–9 (n = 318)		≥10 (n = 106)	
	Mean	%	Mean	%	Mean	%	Mean	%	Mean	%		Mean	%	Mean	%
Maternal age, years	32.7		32.2		32.3		32.9		33.2		33.2		32.9		<0.001
Prepregnancy body mass index ^a	23.5		23.4		23.4		23.3		23.7		23.3		24.2		0.22
Non-Hispanic white race/ethnicity		87.7		89.5		88.5		87.8		87.0		84.3		58.9	0.03
<12 years of education		3.1		2.6		3.4		2.8		2.5		4.1		3.8	0.74
Not married		10.0		13.9		9.1		8.2		11.1		10.1		15.1	0.53
Nulliparous		62.2		62.9		63.2		57.2		62.8		66.7		63.2	0.57
Smoked during pregnancy		5.4		5.6		5.1		5.1		6.2		4.7		7.5	0.57
Prenatal vitamin use		97.6		97.4		97.9		97.1		97.8		97.5		98.1	0.99
No leisure-time physical activity		12.1		12.0		12.4		14.0		10.5		9.4		16.0	0.45
History of hypertension		4.2		3.8		3.7		4.9		4.9		3.5		4.7	0.50
Family history of hypertension		49.2		53.2		48.5		48.8		51.7		45.3		46.2	0.38
Family history of diabetes		13.5		12.4		13.1		12.0		15.7		13.8		16.0	0.15
Daily dietary intake															
Total energy, kcal	1,717		1,574		1,575		1,720		1,818		2,021		2,123		<0.001
Total fiber, g ^b	20.9		21.6		21.1		20.9		20.7		20.6		19.7		<0.001
Saturated fat, g ^b	25.5		23.9		24.8		25.5		25.9		26.6		28.4		<0.001
Polyunsaturated fat, g ^b	14.4		13.8		14.1		14.5		14.6		14.7		15.6		<0.001
Monounsaturated fat, g ^b	25.0		22.7		23.8		25.0		25.6		26.5		29.4		<0.001
Trans fat, g ^b	2.49		2.30		2.41		2.52		2.52		2.58		2.85		<0.001
Omega-3 fatty acids, g ^b	1.67		1.56		1.64		1.70		1.70		1.69		1.79		<0.001
Cholesterol, mg ^b	271		168		203		244		301		389		570		<0.001
Vitamin C, mg ^b	136		135		136		136		138		136		123		0.71
Vitamin E, mg ^b	15.7		15.8		15.2		15.5		16.0		16.3		16.1		0.06
Fruit, no. of servings	2.47		2.34		2.32		2.45		2.63		2.78		2.70		<0.001
Vegetables, no. of servings	1.97		1.89		1.80		1.99		2.09		2.25		2.38		<0.001
Low-fat dairy foods, no. of servings	2.09		2.10		2.05		2.10		2.04		2.32		1.96		0.32
Whole-grain foods, no. of servings	0.63		0.56		0.54		0.63		0.70		0.80		0.85		<0.001
Red and processed meats, no. of servings	0.66		0.51		0.59		0.71		0.69		0.79		0.83		<0.001

^a Weight (kg)/height (m)².^b Adjusted for energy intake.

Table 2. Characteristics of Participants According to Quartile of Daily Cholesterol Intake, Omega Cohort Study, Seattle and Tacoma, Washington, 1996–2008

Characteristic	Quartile of Dietary Cholesterol Intake, mg/day								P for Trend	
	<151 (n = 792)		151–209 (n = 797)		210–293 (n = 787)		≥294 (n = 782)			
	Mean	%	Mean	%	Mean	%	Mean	%		
Maternal age, years	32.4		32.6		32.8		33.1		<0.001	
Prepregnancy body mass index ^a	23.1		23.1		23.7		23.9		<0.001	
Non-Hispanic white race/ethnicity		87.0		89.3		87.2		87.1	0.72	
<12 years of education		3.3		2.6		3.7		2.8	0.90	
Not married		9.3		8.7		10.4		11.6	0.07	
Nulliparous		66.2		62.5		58.8		61.3	0.02	
Smoked during pregnancy		4.2		5.0		6.4		6.1	0.05	
Prenatal vitamin use		97.9		97.4		97.3		98.0	0.92	
No leisure-time physical activity		11.4		13.8		12.5		10.9	0.59	
History of hypertension		3.9		3.5		4.2		5.2	0.15	
Family history of hypertension		49.2		47.8		50.6		49.1	0.77	
Family history of diabetes		12.9		12.4		13.6		15.1	0.15	
Daily dietary intake										
Total energy, kcal	1,244		1,585		1,844		2,202		<0.001	
Total fiber, g ^b	23.6		22.4		20.7		19.0		<0.001	
Saturated fat, g ^b	21.1		23.4		25.4		28.6		<0.001	
Polyunsaturated fat, g ^b	13.6		14.0		14.5		15.0		<0.001	
Monounsaturated fat, g ^b	21.3		23.0		24.9		27.8		<0.001	
Trans fat, g ^b	2.06		2.28		2.49		2.79		<0.001	
Omega-3 fatty acids, g ^b	1.51		1.60		1.68		1.77		<0.001	
Vitamin C, mg ^b	156		13		137		124		<0.001	
Vitamin E, mg ^b	17.0		16.0		15.6		15.0		<0.001	
Eggs, no.	0.10		0.21		0.37		0.86		<0.001	
Fruit, no. of servings	2.20		2.34		2.57		2.78		<0.001	
Vegetables, no. of servings	1.64		1.91		2.02		2.31		<0.001	
Low-fat dairy foods, no. of servings	1.66		2.04		2.21		2.44		<0.001	
Whole-grain foods, no. of servings	0.49		0.56		0.68		0.79		<0.001	
Red and processed meats, no. of servings	0.33		0.57		0.74		0.98		<0.001	

^a Weight (kg)/height (m)².^b Adjusted for energy intake.

diabetes in both a prospective cohort study and a case-control study. Women with high preconceptional and early-pregnancy egg consumption (≥ 7 eggs/week) experienced a 1.8-fold increased risk of gestational diabetes as compared with women consuming fewer eggs. This association was independent of established risk factors for gestational diabetes. Maternal cholesterol intake was also significantly and positively associated with gestational diabetes risk independently of other sociodemographic, medical, and dietary risk factors for gestational diabetes.

To the best of our knowledge, no previous study has examined possible associations of egg consumption preconception and during early pregnancy with gestational diabetes risk. Findings from the present studies of a positive association of egg consumption with gestational diabetes risk are in line with results from some (4–6), though not all (20–21), previous studies concerning egg consumption

and type 2 diabetes risk among men and nonpregnant women. For instance, Djoussé et al. (4) reported that high levels of egg consumption were associated with increased risks of incident type 2 diabetes in both men (hazard ratio = 1.58, 95% CI: 1.25, 2.01) and women (hazard ratio = 1.77, 95% CI: 1.28, 2.43). Data from animal studies also support positive associations of egg and/or dietary cholesterol intake with glucose metabolism (8). A diet enriched with cholesterol significantly increased fasting plasma cholesterol ($P < 0.01$), total lipid ($P < 0.01$), and glucose ($P < 0.05$) concentrations in study animals (8). However, our findings are not in agreement with results from a randomized trial of 28 overweight men who were placed on a carbohydrate-restricted low-fat diet (20). In that study, participants randomized to a regimen of 3 eggs/day had no differences in fasting glucose concentrations when compared with participants randomized to a no-egg-intake regimen. The null

Table 3. Relative Risk of Gestational Diabetes Mellitus in Relation to Maternal Egg Consumption and Cholesterol Intake, Omega Cohort Study, Seattle and Tacoma, Washington, 1996–2008

	Egg Consumption (Categories), eggs/week																				<i>P</i> for Trend				
	0 ^a (<i>n</i> = 267)				≤1 (<i>n</i> = 1,186)				2–3 (<i>n</i> = 650)				4–6 (<i>n</i> = 631)				7–9 (<i>n</i> = 318)					≥10 (<i>n</i> = 106)			
	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI		No.	%	RR	95% CI
GDM cases	12	4.5			49	4.1			29	4.5			33	5.2			22	6.9			13	12.3			
Energy-adjusted RR			1.00		0.92	0.49, 1.73			1.04	0.53, 2.05			1.26	0.65, 2.45			1.78	0.87, 3.65			3.27	1.47, 7.28		<0.001	
Adjusted RR ^b			1.00		0.94	0.50, 1.77			1.00	0.51, 1.98			1.12	0.57, 2.19			1.55	0.75, 3.18			2.54	1.13, 5.70		0.007	
Adjusted RR ^c			1.00		0.94	0.50, 1.77			1.01	0.51, 1.98			1.12	0.57, 2.20			1.54	0.75, 3.18			2.52	1.11, 5.72		0.008	
	Egg Consumption (Dichotomized), eggs/week																								
	<7 ^a (<i>n</i> = 2,734)										≥7 (<i>n</i> = 424)														
	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	
GDM cases	123	4.5			35	8.3																			
Energy-adjusted RR							1.00					2.04	1.38, 3.02												
Adjusted RR ^b							1.00					1.78	1.21, 2.63												
Adjusted RR ^c							1.00					1.77	1.19, 2.63												
	Quartile of Dietary Cholesterol Intake, mg/day																								
	<151 ^a (<i>n</i> = 792)					151–209 (<i>n</i> = 797)					210–293 (<i>n</i> = 787)					≥294 (<i>n</i> = 782)									
	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	No.	%	RR	95% CI	
GDM cases	38	4.8			26	3.3			35	4.5			59	7.5											
Energy-adjusted RR							0.84	0.50, 1.40				1.33	0.80, 2.19				2.76	1.66, 4.60						<0.001	
Adjusted RR ^b							0.83	0.49, 1.38				1.20	0.72, 2.00				2.30	1.34, 3.96						0.001	
Adjusted RR ^c							0.83	0.49, 1.39				1.21	0.72, 2.03				2.35	1.35, 4.09						0.001	

Abbreviations: CI, confidence interval; GDM, gestational diabetes mellitus; RR, relative risk.

^a Reference category.^b Adjusted for total energy intake, maternal age, race/ethnicity, prepregnancy body mass index, leisure-time physical activity, and intakes of meat, fiber, and vitamin C.^c Additionally adjusted for saturated fat intake.

Table 4. Characteristics of Gestational Diabetes Mellitus Cases and Controls, Alpha Case-Control Study, Seattle and Tacoma, Washington, 1998–2002

Characteristic	Gestational Diabetes Cases (n = 185)			Controls (n = 411)			P Value
	No.	%	Mean (SD)	No.	%	Mean (SD)	
Maternal age, years			32.9 (5.3)			31.5 (5.5)	0.003
Prepregnancy body mass index ^a			28.8 (7.4)			22.9 (4.0)	<0.001
Non-Hispanic white race/ethnicity	117	63.2		312	75.9		0.005
≤12 years of education	29	15.7		53	12.9		0.36
Nulliparous	83	44.9		222	54.0		0.04
Smoked during pregnancy	28	15.1		35	8.5		0.02
Prenatal vitamin use	166	89.7		381	92.7		0.22
No leisure-time physical activity	97	52.4		143	34.8		<0.001
History of hypertension	14	7.6		2	0.5		<0.001
Family history of hypertension	102	55.1		184	44.8		0.02
Family history of diabetes	56	30.3		53	12.9		<0.001
Daily dietary intake							
Total energy, kcal			1,896 (639)			1,977 (664)	0.16
Total fiber, g ^b			17.7 (10.3)			19.5 (14.7)	<0.001
Saturated fat, g ^b			30.4 (13.0)			27.6 (18.5)	<0.001
Polyunsaturated fat, g ^b			15.6 (7.5)			13.9 (10.7)	<0.001
Monounsaturated fat, g ^b			29.3 (11.1)			25.4 (15.7)	<0.001
Trans fat, g ^b			3.21 (1.74)			2.81 (2.47)	<0.001
Omega-3 fatty acids, g ^b			1.87 (0.96)			1.69 (1.32)	<0.001
Cholesterol, mg ^b			350.1 (250.6)			273.9 (356.0)	<0.001
Vitamin C, mg ^b			103.6 (122.6)			133.8 (174.2)	<0.001
Vitamin E, mg ^b			13.6 (7.6)			13.7 (7.5)	0.96
Eggs, no.			0.58 (0.78)			0.35 (0.47)	<0.001
Fruit, no. of servings			1.94 (1.30)			2.71 (1.68)	<0.001
Vegetables, no. of servings			2.02 (1.32)			1.95 (1.38)	0.59
Low-fat dairy foods, no. of servings			2.37 (1.87)			2.63 (1.93)	0.13
Whole-grain foods, no. of servings			0.51 (0.56)			0.52 (0.55)	0.78
Red and processed meats, no. of servings			1.07 (0.72)			0.81 (0.61)	<0.001

Abbreviation: SD, standard deviation.

^a Weight (kg)/height (m)².

^b Adjusted for energy intake.

findings in this randomized trial may be attributable to the characteristics of the study population and to the insulin-resistance-lowering effect of the special carbohydrate-restriction and low-fat diet common to all study participants (22). Larger observational and intervention studies conducted in diverse study populations including reproductive-age and pregnant women will be needed to properly disentangle and quantify the independent effects of the nutritive constituents of eggs (e.g., cholesterol, ω -3 polyunsaturated fatty acids, and lutein (23)) on glucose homeostasis.

We are aware of only 1 prior study that examined possible associations between total cholesterol intake during pregnancy and gestational diabetes risk. González-Clemente et al. (7) evaluated 335 pregnant women who were screened for gestational diabetes and who reported information on dietary intake (including cholesterol) for the previous year.

The authors noted that 41 women with gestational diabetes reported a higher mean cholesterol intake than 294 women without gestational diabetes (145.3 mg/1,000 kcal (standard error, 4.5) vs. 134.5 mg/1,000 kcal (standard error, 1.6); $P = 0.03$). The odds of gestational diabetes were 1.88 for each 50-mg/1,000 kcal increment of cholesterol intake (95% CI: 1.09, 3.23). Results from our studies are consistent with those from other studies that have documented associations of cholesterol intake with incident type 2 diabetes in men and nonpregnant women (6, 24, 25). Feskens et al. (6) reported a positive association of dietary cholesterol with incident type 2 diabetes. This association was also confirmed in the Nurses' Health Study (24) and the Iowa Women's Health Study (25).

By analyzing data from both a cohort study and a case-control study, we were able to replicate study findings across 2 independent study populations. We were also able to

Table 5. Odds Ratios for Gestational Diabetes Mellitus According to Maternal Egg Consumption and Total Cholesterol Intake, Alpha Case-Control Study, Seattle and Tacoma, Washington, 1998–2002

Dietary Factor	Gestational Diabetes Cases (n = 185)		Controls (n = 411)		Energy-Adjusted OR	95% CI	Adjusted OR ^a	95% CI	Adjusted OR ^b	95% CI
	No.	%	No.	%						
Egg consumption (categories), eggs/week										
0 ^c	37	20.0	89	21.7	1.00		1.00		1.00	
<1	31	16.8	103	25.1	0.76	0.43, 1.33	0.71	0.36, 1.38	0.70	0.36, 1.37
2–3	33	17.8	84	20.4	1.05	0.60, 1.86	0.91	0.46, 1.80	0.93	0.47, 1.85
4–6	40	21.6	83	20.2	1.31	0.76, 2.28	1.20	0.62, 2.35	1.18	0.60, 2.31
7–9	27	14.6	32	7.8	2.47	1.27, 4.80	2.59	1.16, 5.76	2.41	1.08, 5.40
≥10	17	9.2	20	4.9	2.62	1.20, 5.73	2.91	1.09, 7.72	2.76	1.03, 7.43
<i>P</i> for trend					<0.001		0.003		0.005	
Egg consumption (dichotomized), eggs/week										
<7 ^c	141	76.2	359	87.3	1.00		1.00		1.00	
≥7	44	23.8	52	12.7	2.46	1.54, 3.91	2.82	1.59, 5.00	2.65	1.48, 4.72
Cholesterol intake, mg/day ^d										
<151 ^c	20	10.8	72	17.5	1.00		1.00		1.00	
151–209	34	18.4	75	18.3	2.39	1.22, 4.67	1.50	0.68, 3.30	1.44	0.65, 3.17
210–293	44	23.8	122	29.7	2.53	1.28, 4.99	2.07	0.93, 4.58	1.95	0.88, 4.34
≥294	87	47.0	142	34.5	6.33	3.01, 13.31	3.43	1.35, 8.71	2.94	1.14, 7.60
<i>P</i> for trend					<0.001		0.007		0.021	

Abbreviations: CI, confidence interval; OR, odds ratio.

^a Adjusted for total energy intake, maternal age, race/ethnicity, prepregnancy body mass index, leisure-time physical activity, smoking during pregnancy, family history of diabetes, and intakes of meat, fiber, and vitamin C.

^b Additionally adjusted for saturated fat intake.

^c Reference category.

^d Cholesterol intake categories were defined on the basis of quartiles from the Omega Study (9).

capitalize on the strengths of each study while minimizing the impact of limitations inherent in each study design. The prospective design of the Omega Study and the exclusion of women with diagnosed pregestational diabetes reduced the potential for bias from recall differences or dietary changes secondary to the disorder. Collection of dietary intake information in early pregnancy, before gestational diabetes was diagnosed, enhanced causal inference given our increased ability to infer the temporal relation of egg and cholesterol intakes with subsequent gestational diabetes risk. Additionally, the high follow-up rate of enrolled Omega Study participants (>95%) minimized possible selection bias. The Alpha Study afforded increased statistical power to examine relations of interest. The low participation rates, particularly among controls, suggest the possibility that our case and control groups may not have been representative of the underlying populations from which they were sampled. However, characteristics of participating control subjects were similar to those of all women delivering at the study hospitals (11). Case and control participants may have also differed in their ability and willingness to report dietary habits. Additionally, because of the cross-sectional design and the fact that Alpha Study participants' dietary reporting period included late pregnancy, we cannot exclude the possibility of reverse causality. The directions and magnitudes of point estimates, however, differed little across the 2 studies. This consistency suggests that potential for bias from participation and recall differences or dietary changes secondary to the disorder are unlikely explanations for the Alpha Study findings.

Several limitations should be considered when interpreting our study results. First, because maternal egg consumption was self-reported, we cannot exclude the possibility of reporting error. However, because dietary intake information was collected prior to gestational diabetes testing and diagnosis in the Omega Study, reporting errors are likely to have resulted in attenuation of observed associations. Second, we did not collect information on whether participants consumed egg yolks or egg whites only. Consequently, we were not able to assess gestational diabetes risk in relation to different patterns of egg consumption. Third, universal glucose tolerance testing in early pregnancy is not part of standard obstetric care; hence, we cannot exclude the possibility that some subjects in our study had undiagnosed pregestational diabetes. However, 95% of Omega Study subjects reported having undergone regular medical examinations within the 24-month period before the index pregnancy, and the cumulative incidence of gestational diabetes in our study cohort was consistent with observations in other settings (14). These observations serve to allay concerns. Fourth, as with all observational studies, although we adjusted for known and suspected confounders, we cannot exclude the possibility of residual confounding from unmeasured covariates such as dietary glycemic index. 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. Their dietary behaviors, including egg consumption, are likely to differ from those of women from other socioeconomic, racial, and ethnic backgrounds.

The mechanisms by which high egg and cholesterol consumption might influence glucose homeostasis and diabetes risks are largely unknown. Investigators have speculated that observed associations may be attributable to the hyperglycemic and hyperinsulinemic influence of diets high in cholesterol and animal fat (13). Others have speculated that oxysterols, a family of 27-carbon cholesterol oxidation derivatives, are potentially involved in the initiation and progression of cardiometabolic disorders, including diabetes (26). Malle et al. (27) found that increased monocyte-derived myeloperoxidase (a heme enzyme secreted by activated phagocytes that generates an array of oxidants proposed to play critical roles in host defense and tissue damage) activity contributes to chronic systemic inflammatory conditions in cholesterol-fed rabbits. Björkbacka et al. (28) also linked elevated serum cholesterol concentrations to activated proinflammatory signaling cascades in animal models. Further, Lewis et al. (29) noted that increased cholesterol intake increases serum levels of amyloid A, a marker of inflammation. Taken together, these observations support the thesis that chronic systematic inflammation may be involved in the pathogenesis of gestational diabetes (30). Adiposity, particularly central adiposity, is an important component in the pathophysiologic milieu of insulin resistance syndrome, hyperglycemia, and hyperinsulinemia. Future studies designed to comprehensively assess genetic and nongenetic factors that account for the large variability in individual responses to dietary cholesterol are warranted (31).

In conclusion, our data suggest that higher egg and cholesterol consumption during the preconceptional and early-pregnancy periods are associated with increased gestational diabetes risk among women without preexisting diabetes. Confirmation of these findings in other populations and further exploration of possible underlying biologic mechanisms for the observed associations are warranted.

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Author affiliations: Center for Perinatal Studies, Swedish Medical Center, Seattle, Washington (Chunfang Qiu, Ihunnaya O. Frederick, Tanya K. Sorensen, Daniel A. Enquobahrie, Michelle A. Williams); Division of Epidemiology, Statistics, and Prevention Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland (Cuilin Zhang); and Department of Epidemiology, School of Public Health, University of Washington, Seattle, Washington (Daniel A. Enquobahrie, Michelle A. Williams).

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