Randomized Controlled Trial Investigating the Effects of a Low–Glycemic Index Diet on Pregnancy Outcomes in Women at High Risk of Gestational Diabetes Mellitus: The GI Baby 3 Study

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OBJECTIVE

Dietary interventions can improve pregnancy outcomes in women with gestational diabetes mellitus (GDM). We compared the effect of a low–glycemic index (GI) versus a conventional high-fiber (HF) diet on pregnancy outcomes, birth weight *z* score, and maternal metabolic profile in women at high risk of GDM.

RESEARCH DESIGN AND METHODS

One hundred thirty-nine women [mean (SD) age 34.7 (0.4) years and prepregnancy BMI 25.2 (0.5) kg/m^2] were randomly assigned to a low-GI (LGI) diet (*n* = 72; target GI ∼50) or a high-fiber, moderate-GI (HF) diet (*n* = 67; target GI ∼60) at 14–20 weeks' gestation. Diet was assessed by 3-day food records and infant body composition by air-displacement plethysmography, and pregnancy outcomes were assessed from medical records.

RESULTS

The LGI group achieved a lower GI than the HF group [mean (SD) 50 (5) vs. 58 (5); *P* < 0.001]. There were no differences in glycosylated hemoglobin, fructosamine, or lipids at 36 weeks or differences in birth weight [LGI 3.4 (0.4) kg vs. HF 3.4 (0.5) kg; *P* = 0.514], birth weight *z* score [LGI 0.31 (0.90) vs. HF 0.24 (1.07); *P* = 0.697], ponderal index [LGI 2.71 (0.22) vs. HF 2.69 (0.23) kg/m^3; *P* = 0.672], birth weight centile [LGI 46.2 (25.4) vs. HF 41.8 (25.6); *P* = 0.330], % fat mass [LGI 10 (4) vs. HF 10 (4); *P* = 0.789], or incidence of GDM.

CONCLUSIONS

In intensively monitored women at risk for GDM, a low-GI diet and a healthy diet produce similar pregnancy outcomes.

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that is diagnosed for the first time in pregnancy (1). Pregnancy-related hormonal changes that reduce insulin sensitivity result in glucose intolerance in women with reduced β-cell reserve or with more marked underlying insulin resistance. Glucose intolerance in pregnancy has implications for both mother and child, including higher rates of preeclampsia, operative deliveries, macrosomia, and birth injury (2).

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Hyperglycemia in pregnancy and neonatal adiposity have also been linked to increased subsequent childhood obesity and type 2 diabetes mellitus (T2DM) in early adulthood (3,4). High maternal glycemia results in increased fetal insulin production, which is considered to be the main driver of macrosomia. How the intrauterine environment confers higher risk has not been established, but data from animal studies suggest that epigenetic processes modulate gene transcription in utero (5).

Current best practice for GDM management consists of maintaining maternal blood glucose levels within the normal pregnancy range by dietary intervention either alone or combined with insulin therapy. Dietary intervention often includes a reduction in carbohydrate quantity or in dietary glycemic index (GI). A low-GI diet produces lower postmeal blood glucose levels in healthy individuals (6,7) and has been shown to reduce the incidence of large-for-gestational-age (LGA) babies in nondiabetic pregnancy (8). Some studies suggest that a low-GI diet improves glucose tolerance in women with GDM (9,10) or with a history of macrosomia (11). A low-GI diet may also reduce maternal weight gain in women with normal glucose tolerance, GDM, or T2DM (11,12) but potentially increases the risk of prematurity (12). In women with GDM, we found no additional beneficial effect of a low-GI diet on neonatal outcomes (13), although the relatively late institution of the intervention at 29 weeks' gestation (the time at which GDM is usually diagnosed) may preclude a clinically important effect on fetal growth rate. A greater effect might be achieved in high-risk patients who adopt the diet earlier in pregnancy.

Our aim therefore was to compare the effect of a low-GI diet with a conventional healthy diet on birth weight *z* score in women at high risk of GDM. Secondary aims were to compare the effects on pregnancy outcomes and maternal metabolic profile. Our hypothesis was that infants born to pregnant women at high risk of GDM who receive an early intervention of low-GI dietary advice will have a lower birth weight *z* score and lower body fat mass than those born to mothers who received advice on a macronutrient-matched high-fiber diet with a moderate GI.

RESEARCH DESIGN AND METHODS

The GI Baby 3 study was a two-arm randomized controlled trial based at the antenatal clinic at the Royal Prince Alfred Hospital, Camperdown, NSW, Australia. Apart from the study dietitians (R.M. and S.O.) who provided dietary education, all study personnel were blinded to dietary assignment. The study was conducted according to the Declaration of Helsinki, and all procedures were approved by the Human Research Ethics Committee of the Sydney South West Area Health Service (Royal Prince Alfred Hospital zone; reference no. HREC/10/RPAH/453).

Subject Recruitment, Randomization, and Stratification

Women >18 years of age between 12 and 20 weeks of gestation and at high risk of GDM with an otherwise healthy single pregnancy were eligible for the study. Women were considered to be at high risk if they had at least one of the following risk factors: age >35 years, first-degree relative with T2DM, prepregnancy BMI ≥30 kg/m^2, past history of GDM or glucose intolerance, history of a previous baby >4,000 g, or belonging to a high-risk ethnic group (Aboriginal or Torres Strait Islander, Polynesian, Middle Eastern, Indian, or Asian). Women who had preexisting diabetes or special dietary requirements (including vegetarianism/veganism) were excluded. Subjects were recruited from the fetal medicine clinic at the time of nuchal scanning. A total of 706 women were approached between January 2011 and October 2012, of whom 304 expressed an interest in participating. Of these, 157 subsequently declined, leaving 147 women who formally consented to commence the study. At study entry, all of the women had a routine early (between 14 and 20 weeks' gestation) 75-g oral glucose tolerance test (OGTT). GDM diagnosis was based on modified Australasian Diabetes in Pregnancy Society 1998 criteria (14): fasting glucose level (BGL) ≥5.5 mmol/L, 1 h ≥10.0 mmol/L, and 2 h ≥8.0 mmol/L. However, if fasting BGL was ≥5.8 mmol/L and 2-h reading was ≥11.1 mmol/L in the initial (<20 week) OGTT, subjects were excluded, as these values were considered likely to represent more significant hyperglycemia requiring more intensive management and monitoring. After the OGTT, computer-generated random numbers, which were unpredictable and concealed from the recruiter, were used to allocate subjects to a low- or moderate-GI diet (1:1 allocation), stratified by BMI (<30 vs. ≥30 kg/m^2). Apart from the additional dietary instruction, participants received routine antenatal and GDM care, as applicable, regardless of their dietary assignment. Subjects who had a normal OGTT at study entry had a second OGTT at 26–28 weeks. In subjects with GDM, insulin treatment was commenced if mean fasting or 1-h postprandial BGL in the preceding week exceeded 5.2 and 7.5 mmol/L, respectively, after eliminating abnormal readings clearly attributable to atypical intake.

At enrollment, demographic information, family history of diabetes, ethnicity, and medical history were recorded. Subjects were weighed at study entry and at every antenatal visit wearing light indoor clothes and without shoes.

Dietary Assessment

Subjects were asked to complete a 3-day food record (including 2 weekdays and 1 weekend day) at baseline and again at 34–36 weeks' gestation. Both 3-day food records were entered into an Australian nutrition analysis software (FoodWorks 7 Professional; Xyris Software, Brisbane, QLD, Australia) based on the Australian food composition database AUSNUT2007 (15). The GI of individual food items was assigned according to a published method (16). Dietary glycemic load (GL) was calculated as sum of (GI × available carbohydrate of each food portion)/100 per day. Dietary GI was calculated as (dietary GL/total daily available carbohydrate) × 100.

Dietary Interventions

Subjects attended a total of five individual dietary consultations with a dietitian at 14–20, 18–24, 22–28, 26–32, and 34–36 weeks of gestation. At study visit 1 (14–20 weeks), subjects were randomized to one of two healthy diets of similar macronutrient composition: protein (15–25% total energy intake [E]), fat (25–30%E), and carbohydrate content (40–45%E). One group was asked to follow a low-GI diet (LGI) (target GI ≤50) and the other group a high-fiber, moderate-GI diet (HF), similar to the Australian population average (target GI 60). Both study diets provided all

the essential nutrients for pregnancy other than iron and iodine, which were supplemented as appropriate.

The baseline 3-day food record provided information on usual dietary intake. At visit 1, this served as the basis of dietary counseling where written information regarding suitable LGI/HF foods and pregnancy nutrition was provided. At mid-study visits (visits 2, 3, and 4), four-stage multiple-pass 24-h recalls were performed to check dietary compliance. Subjects were deemed compliant if their final dietary GI was ≤50 in the LGI group and >50 in the HF group. In the case of noncompliance, suitable alternative foods were encouraged. A selection of recipes was also provided. For improvement of diet adherence and product recognition, subjects were provided with food samples containing key foods for the assigned diet at all five consultations. The content of supplementary baskets has previously been described (13).

Blood Biochemistry and Pregnancy Outcomes

Subjects provided fasting blood samples at study entry [mean (SD) 17.4 (2.0) weeks) and at visit 5 (36 weeks' gestation). Last recorded maternal weight before delivery was obtained from the medical record.

Gestational age was estimated from the date of the last menstrual period and early pregnancy ultrasound. Birth weight, length, head circumference, mode of delivery, neonatal complications, and length of stay in neonatal intensive care unit were obtained from the electronic medical record. The infant's body composition was determined within 48 h of the baby's birth using a Pea Pod (COSMED Asia-Pacific Pty Ltd, Artarmon, NSW, Australia), an air-displacement plethysmograph that uses whole-body densitometry to measure percent fat and fat-free mass in infants. Birth weight *z* score was determined using the World Health Organization anthropometry for personal computers software (version 3.2.2, 2011, World Health Organization, Geneva, Switzerland). Birth weight centile was calculated using a macro program for Microsoft Excel (available from http://www.gestation.net) and was used to categorize the infant as small for gestational age (SGA) (birth weight <10th centile), normal, or LGA (birth weight >90th centile). Ponderal index, an estimate of neonatal adiposity, was calculated as birth weight in kilograms × infant length (m^{-3}). Macrosomia was defined as birth weight >4,000 g.

Power Calculation and Statistical Analysis

Data from an Australian study (8) was used to generate the sample size. We aimed to have 60 women in each group (120 in total) so that we had a statistical power of 80% (two-sided α value of 0.05) to detect a difference in birth weight *z* score of 0.5 (~260 g). To allow loss to follow-up of ~20%, we aimed to enroll ~150 women. A biostatistician blinded to the dietary allocation performed the statistical analysis. The primary analysis included all women who attended at least one dietary education session but excluded eight women as described below. All statistical analyses were performed using SPSS (version 22; IBM Australia, St Leonards, NSW, Australia). Results for continuous data are reported as mean (SD) and categorical data (e.g., emergency cesarean delivery) as a percentage. Pearson χ^2 test was used to test for differences between groups for categorical data, while continuous data were tested using one-way ANOVA. A paired *t* test was used to assess within-group changes in outcomes from baseline to end of intervention.

RESULTS

The flow of participants through the study is shown in the CONSORT diagram (Fig. 1). Of the 147 women recruited, 139 were included in the primary intention-to-treat analysis. Among the eight excluded, one was diagnosed with "overt" diabetes after the early OGTT, two underwent pregnancy termination, one had a twin pregnancy, one had a premature delivery (<37 weeks), and three moved interstate. A further 14 participants withdrew after commencing the study (4 were too busy, 2 were lost to follow-up, 4 did not wish to follow their allocated diet, and 4 gave no reason), leaving 125 participants who completed the study (completers analysis). Baseline characteristics are shown in Table 1. There were no differences between the two diet groups with respect to age, BMI, ethnicity, or level of education. There were no differences in risk factors for GDM, apart from family history of T2DM, which was more common in the LGI group. Most subjects had completed tertiary education (68% in LGI and 80% in HF group). Similar numbers of women were diagnosed with GDM at study entry: 10 in the LGI group and 11 in the HF group.

Table 2 shows the diet analysis. At baseline, the LGI group had a slightly lower dietary GI, but the total carbohydrate intake and GL were not significantly different. By the end of the intervention, there was a significant difference in dietary GI and GL between the two groups ($P < 0.001$). The protein and total fat intake did not change in either group, but energy, saturated fat, and total sugars intake were significantly reduced only in the LGI group.

The biochemical parameters are presented in Table 3. Outcomes were similar in both groups at baseline and at the end of the intervention. HbA_{1c} increased significantly with an increase in plasma C-peptide concentration. There was a tendency for C-reactive protein to decline in the LGI group ($P = 0.051$). While triglycerides and LDL cholesterol increased during pregnancy in both groups, free fatty acids did not change. As expected in pregnancy, iron and vitamin B_{12} levels fell but 25-hydroxyvitamin D increased, as this vitamin was routinely supplemented.

Primary and secondary pregnancy outcomes were similar in both groups (Table 4), including birth weight, birth weight centile, birth weight *z* score, % body fat at birth, and maternal weight gain. There was no difference in SGA, LGA, or macrosomia in the offspring, whether analyzed as intention to treat or among completers only, nor was there any difference in mode of delivery or maternal complications (data not presented). Stratification based on family history of T2DM and the actual GI of the mother's diet, regardless of the group to which they were assigned, did not alter the primary outcomes (data not presented). Admission to neonatal intensive care was higher in the HF ($n = 10$, 15%) compared with the LGI ($n = 4$, 6%) group, but the difference was not statistically significant ($P = 0.067$). In the LGI group, one neonate was admitted with jaundice, one with low oxygen saturation and meconium aspiration, one with bilious vomit, and another with respiratory distress. In the

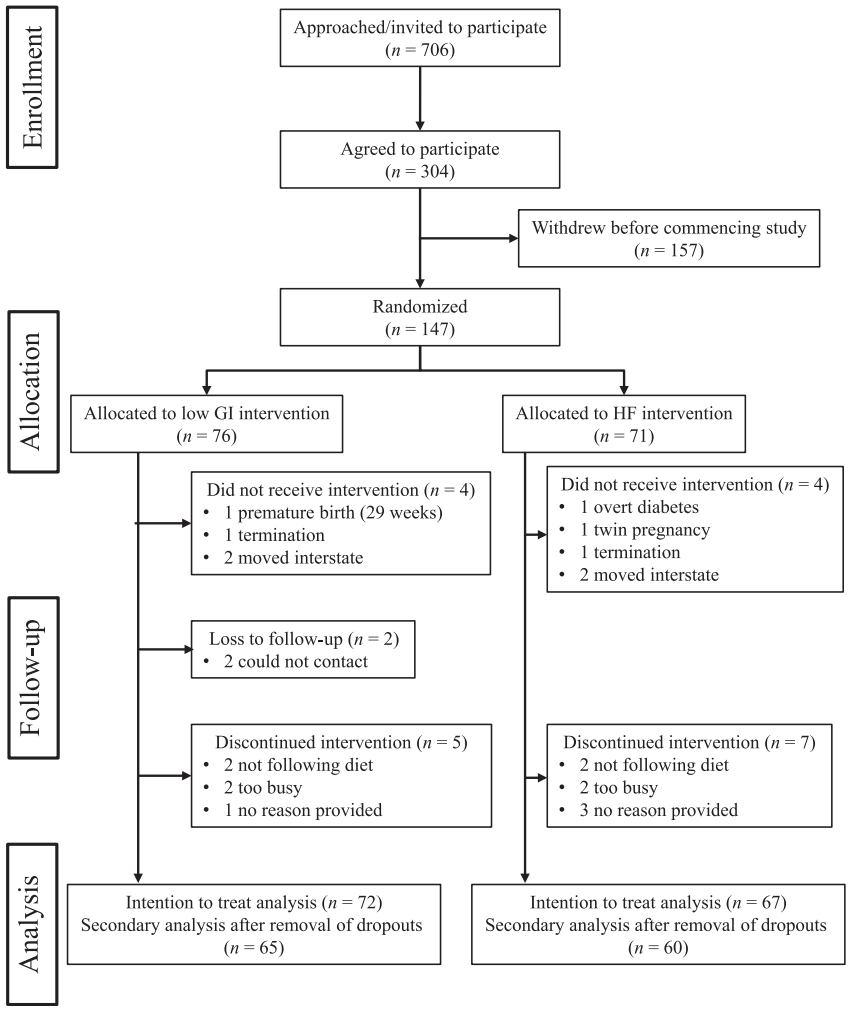

Figure 1—Study flow (CONSORT diagram).

HF group, one neonate was admitted with jaundice; one with jaundice and neutropenia (premature); one with pneumonia and respiratory distress; one with hypothermia, low birth weight, and intrauterine growth retardation; one with hypoglycemia, hypothermia, jaundice, and leuco- and neutrophilia; one with hypoglycemia; one with transient tachypnea; and three were admitted with respiratory distress (one of which was premature).

Ten women (14%) developed GDM before 20 weeks in the LGI group and 11 (16%) in the HF group. Another 14% of women developed GDM by 26–28 weeks in both diet groups (10 in the LGI group and 9 in the HF group) (Table 4). There were no significant differences in GDM diagnosis whether results were examined as intention to treat or completers only. Non-Caucasian women developed GDM earlier, and relatively more women of non-Caucasian ethnicity developed GDM overall. Twenty-one of the 40 women who developed GDM were non-Caucasian (i.e., 53%), whereas this group represented only 40% of the study population. Of the 21 women who had GDM by 20 weeks, 67% were non-Caucasian, and of the further 19 who developed GDM by 28 weeks, 53% were non-Caucasian. Sixteen subjects required insulin treatment in the LGI group and 9 in the HF group ($P = 0.178$). Insulin treatment was commenced at mean (SD) 29 (6) weeks in the LGI group and 25 (5) weeks in the HF group ($P = 0.129$). The maximum insulin dose used was 15.6 (9.9) units in the LGI and 37.9 (27.3) units in the HF group ($P = 0.007$).

CONCLUSIONS

Contrary to our hypothesis, we found no evidence of a difference in pregnancy and neonatal outcomes in women at high risk of GDM who were randomly allocated to follow either a low-GI diet or a conventional healthy diet in the second trimester of pregnancy. The average infant birth weight, birth weight centile, and neonatal percent body fat were in the healthy range in both dietary groups. In particular, the rates of SGA, LGA, and macrosomia were the same in each dietary group and were relatively low for this high-risk cohort.

At study entry, 15% met the diagnostic criteria for GDM and a further 14% developed GDM at the start of the 3rd trimester, with no differences between diet groups. Among those diagnosed with GDM, there was no difference in requirement for insulin therapy commencement, although the women on the LGI diet required a significantly lower dose, and there was a tendency to start insulin later in this group. These findings suggest that the low-GI diet may have had a favorable effect on glycemia. A previous study showed that women with GDM who followed a low-GI diet had a lower need for insulin compared with women on a conventional diet (9), although the baseline BMI of its participants was markedly higher than in our cohort (BMI 32 vs. 25 kg/m^2).

In women with GDM, the rate of macrosomia has been reported to be as high as 22% (2,17), whereas in our study it was 12% overall (11% in those who did not develop GDM, 19% in those who developed GDM before 20 weeks, and 11% in women who developed GDM by 26–28 weeks). Our LGA rates were slightly lower than those reported in a study of women with well-controlled GDM and normal glucose tolerance (18), i.e., 7% in the GDM group and 9% in normal glucose tolerant subjects compared with 5.6% in the LGI group and 6.0 in the HF group in our study. Similarly, the mean SGA rate was only 6.5%, which is lower than expected, and importantly, neither diet increased the rate of SGA (18). The rate of cesarean delivery (28% for our entire cohort) was comparable to the usual rate that has been reported (30% overall and 38% in women with GDM) (19).

There are a number of possible reasons for the lack of an effect of the low-GI diet. These women were predominantly highly educated, with prepregnancy body weight just above the normal range (BMI 25.2 kg/m^2), and from a lower-risk Caucasian population.

Table 1—Subject characteristics

	All subjects (ITT)					Completers only				
Variables	*n*	LGI	*n*	HF	*P*	*n*	LGI	*n*	HF	*P*
Age at study entry (years)	72	35.7 (4.7)	67	34.9 (4.1)	0.282	65	36.0 (4.4)	60	34.7 (4.1)	0.091
Prepregnancy BMI (kg/m^2)	72	25.2 (5.2)	67	25.2 (5.2)	0.946	65	25.1 (5.2)	60	25.2 (5.4)	0.945
Ethnicity (%)	72		66		0.417	65		60		0.275
Asian		22.2		28.8			21.5		31.7	
Caucasian		58.3		59.1			58.5		56.7	
Others		19.4		12.1			20.0		11.7	
Week of gestation at start of intervention	72	17.5 (2.0)	67	17.7 (1.7)	0.377	65	17.5 (2.1)	60	17.8 (1.7)	0.381
GDM diagnosis at study entry (*n*)	72	10	67	11	0.917	65	9	60	11	0.754
Parity	72	0.6 (0.7)	67	0.8 (0.8)	0.071	65	0.6 (0.6)	60	0.8 (0.8)	0.117
Employment	72		66		0.572	65		60		0.529
Full-time		63.9		62.1			61.5		66.7	
Part-time		19.4		25.8			21.5		23.3	
Unemployed/studying/home duties		16.7		12.1			16.9		10.0	
Education	72		66		0.262	65		60		0.321
Secondary		9.7		6.1			7.7		3.3	
Technical college		22.2		13.6			21.5		15.0	
Tertiary/postgraduate		68.1		80.3			70.8		81.7	
GDM risk factors (%)										
Age >35 years	72	63.9	67	53.7	0.224	65	66.2	60	50.0	0.067
Family history of T2DM	72	59.7	67	37.3	0.008	65	58.5	60	38.3	0.024
Previous child >4,000 g	72	6.9	67	9.0	0.661	65	7.7	60	6.7	0.825
Ethnicity*	72	30.6	67	32.8	0.773	65	29.2	60	36.7	0.376
BMI >30 kg/m^2	72	19.4	67	11.9	0.226	65	16.9	60	13.3	0.577
Previous GDM	67	10.4	65	15.4	0.397	61	11.5	58	15.5	0.518
PCOS	65	7.7	63	7.9	0.959	59	3.4	56	7.1	0.36

Data are presented as mean (SD) for continuous variables and percentages for categorical variables. *P* value calculated using one-way ANOVA for continuous variables and Pearson χ^2 for categorical variables. ITT, intention to treat; PCOS, polycystic ovary syndrome. *High-risk ethnicities include Aboriginal or Torres Strait Islander, Polynesian, Middle Eastern, Indian, and Asian.

They may therefore represent a group of well-motivated women who already followed a healthy lifestyle, reflected in their prepregnancy body weight, baseline dietary intake, and willingness to join the study. The antenatal management of all subjects is likely to have been improved by the intensity of the intervention, including an increase in professional contact time. In addition, the conventional healthy diet was high in fiber and had a lower GI than in the control arm of similar studies. Another interpretation of our findings is that a low-GI diet might not convey any benefits to women at high risk of GDM in pregnancy over and above that of a conventional healthy diet. However, a recent meta-analysis of existing dietary studies suggests that a low-GI diet results in less insulin use and lower birth

Table 2—Baseline and end-of-intervention dietary analysis for completers only

	Baseline			End of intervention			Baseline vs. end of intervention	
Variables	LGI	HF	*P*	LGI	HF	*P*	LGI	HF
*n**	65	60	—	63	57	—	63	57
Energy (kJ)	8,720 (1,650)	8,840 (2,050)	0.718	8,040 (1,480)	8,620 (1,660)	0.046	0.004	0.460
Protein (g)	95.7 (24.5)	100.7 (24.8)	0.260	93.2 (21.6)	101.8 (31.1)	0.079	0.530	0.850
Total fat (g)	79.2 (21.1)	80.2 (22.9)	0.794	74.7 (21.4)	79.7 (24.9)	0.242	0.128	0.851
Saturated fat (g)	30.5 (9.9)	30.4 (10.2)	0.981	25.8 (8.9)	29.8 (10.7)	0.026	<0.001	0.718
Total available carbohydrates (g)	234.9 (58.3)	234.6 (69.3)	0.977	205.6 (45.6)	222.4 (52.2)	0.063	<0.001	0.253
Total sugars (g)	101.6 (35.5)	92.7 (37.1)	0.175	91.2 (27.0)	92.7 (36.2)	0.790	0.033	0.863
Starch (g)	131.5 (42.1)	140.4 (53.1)	0.296	112.9 (31.5)	127.9 (34.5)	0.014	0.001	0.007
Dietary fiber (g)	25.8 (8.9)	25.8 (8.4)	0.998	28.0 (8.5)	25.5 (7.9)	0.103	0.033	0.748
GI	55.7 (5.0)	57.7 (5.8)	0.041	50.4 (4.7)	57.7 (5.1)	<0.001	<0.001	0.904
GL	122.2 (32.0)	127.6 (46.1)	0.448	97.1 (25.1)	121.2 (32.4)	<0.001	<0.001	0.412

Data are presented as mean (SD). One-way ANOVA was used to test for difference between groups at baseline and at the end of intervention. Paired-samples *t* test was used to test for difference within group between baseline and end of intervention. *Five participants did not provide food record data at the end of intervention.

Table 3—Biochemical parameters at baseline and end of intervention for completers only

	Baseline					End of intervention					Baseline vs. end of intervention			
	LGI		HF			LGI		HF			LGI		HF	
Variables	*n*	Mean (SD)	*n*	Mean (SD)	*P*	*n*	Mean (SD)	*n*	Mean (SD)	*P*	*n*	*P*	*n*	*P*
HbA_{1c} (%)	65	4.9 (0.3)	58	4.9 (0.3)	0.998	63	5.1 (0.3)	58	5.1 (0.4)	0.869	63	<0.001	56	0.002
HbA_{1c} (mmol/mol)	60	30.2 (3.4)	53	30.4 (3.5)	0.723	60	31.7 (3.7)	58	31.5 (5.2)	0.806	52	0.001	47	0.340
Fructosamine (μmol/L)	39	193.6 (20.0)	35	194.9 (15.4)	0.761	53	178.3 (16.5)	48	183.6 (16.1)	0.109	37	<0.001	35	0.019
Adiponectin (μg/mL)	65	13.7 (6.8)	58	12.8 (6.1)	0.447	62	12.1 (5.7)	59	12.1 (5.7)	0.996	62	0.023	57	0.377
25-(OH)vitamin D (nmol/L)	65	65.1 (20.7)	57	57.5 (17.3)	0.033	62	73.2 (17.1)	59	67.5 (15.2)	0.055	62	0.008	56	<0.001
25-(OH)vitamin D (ng/mL)	65	26.0 (8.3)	57	23.0 (7.0)	0.033	62	29.3 (6.8)	59	27.0 (6.0)	0.055	62	0.008	56	<0.001
C-peptide (nmol/L)	65	431.3 (180.6)	57	497.1 (334.6)	0.172	62	852.5 (462.3)	58	817.0 (560.4)	0.705	62	<0.001	55	<0.001
C-reactive protein (mg/L)	65	4.5 (4.7)	58	6.1 (6.2)	0.121	62	3.4 (2.0)	60	4.8 (5.5)	0.053	62	0.051	58	0.174
Total cholesterol (mmol/L)	65	5.4 (0.9)	57	5.5 (0.9)	0.603	63	6.9 (1.14)	59	7.0 (1.1)	0.596	63	<0.001	56	<0.001
Triglycerides (mmol/L)	65	1.3 (0.5)	57	1.3 (0.4)	0.823	63	2.5 (0.8)	59	2.5 (9.5)	0.748	63	<0.001	56	<0.001
HDL cholesterol (mmol/L)	65	2.1 (0.4)	58	2.2 (0.4)	0.466	63	2.0 (0.4)	59	2.2 (0.5)	0.139	63	0.052	57	0.957
LDL cholesterol (mmol/L)	65	2.7 (0.8)	57	2.7 (0.8)	0.787	63	3.7 (1.1)	57	3.6 (0.8)	0.809	63	<0.001	54	<0.001
Iron (μmol/L)	64	19.0 (5.4)	59	18.7 (5.4)	0.806	60	18.7 (7.3)	59	19.8 (10.0)	0.495	59	0.362	58	0.395
Transferrin (g/L)	65	2.9 (0.4)	59	3.5 (4.2)	0.257	60	4.0 (0.6)	58	4.0 (0.6)	0.775	60	<0.001	57	0.408
Transferrin saturation (%)	64	26.5 (9.0)	59	25.8 (8.8)	0.670	60	19.4 (9.3)	58	20.2 (11.6)	0.676	59	<0.001	57	0.002
Serum ferritin (μg/L)	65	41.3 (35.6)	59	44.9 (31.3)	0.556	60	24.4 (15.9)	58	23.2 (20.8)	0.726	60	<0.001	57	<0.001
Free fatty acids (μmol/L)	65	392.4 (142.6)	57	430.1 (135.4)	0.138	61	400.0 (136.4)	59	405.5 (134.1)	0.824	61	0.721	56	0.408
Vitamin B_{12} (pmol/L)	65	276.3 (107.5)	58	274.4 (109.5)	0.924	61	233.6 (95.8)	59	241.6 (109.3)	0.669	61	<0.001	57	<0.001
Serum folate (nmol/L)	65	40.1 (6.7)	58	39.7 (6.9)	0.732	60	40.7 (6.3)	59	39.4 (7.1)	0.273	60	0.488	57	0.900
Red blood cell folate (nmol/L)	65	1,534.6 (391.6)	58	1,558.8 (299.7)	0.705	59	1,781.5 (287.3)	58	1,712.2 (256.9)	0.172	59	<0.001	57	<0.001

One-way ANOVA was used to test for difference between groups at baseline and at the end of intervention. Paired-samples *t* test was used to test for difference within group between baseline and end of intervention.

Table 4—Pregnancy outcomes

	Intention to treat					Completers only				
	LGI		HF			LGI		HF		
Variables	*n*	Value	*n*	Value	*P*	*n*	Value	*n*	Value	*P*
Gestational age (weeks)	72	39.6 (1.3)	67	39.4 (1.4)	0.590	65	39.6 (1.1)	60	39.4 (1.4)	0.404
Birth weight (g)	72	3,450 (410)	67	3,430 (510)	0.845	65	3,430 (390)	60	3,380 (490)	0.514
Birth weight centile	72	47.4 (25.8)	67	44.8 (26.6)	0.558	65	46.2 (25.4)	60	41.8 (25.6)	0.330
Birth weight *z* score	72	0.31 (0.90)	67	0.24 (1.07)	0.697	65	0.29 (0.83)	60	0.13 (1.05)	0.367
Ponderal index (kg/m^3)	72	27.3 (2.3)	67	27.0 (2.4)	0.444	65	27.1 (2.2)	60	26.9 (2.3)	0.672
% body fat at birth	56	10.2 (4.1)	40	10.0 (3.5)	0.789	56	10.2 (4.1)	40	10.0 (3.5)	0.789
Small for gestational age	72	5.6	67	7.5	0.648	65	6.2	60	8.3	0.638
Large for gestational age	72	5.6	67	6.0	0.916	65	3.1	60	3.2	0.935
Macrosomia	72	9.7	67	14.9	0.349	65	7.7	60	11.7	0.451
Gestational weight gain (kg)	68	11.4 (5.7)	61	11.0 (5.9)	0.687	64	11.0 (5.3)	59	10.7 (5.7)	0.794
Below target		35.3		32.8			37.5		33.9	
Within target		39.7		41.0	0.955		40.6		42.4	0.914
Above target		25.0		26.2			21.9		23.7	
Late (26–28 weeks) GDM diagnosis (%)	72	13.9	67	13.4	0.917	65	13.8	60	15.0	0.754
Women requiring insulin treatment (*n*)	72	16	67	9	0.178	65	14	60	9	0.346
Cesarean delivery	72	30.6	67	23.9	0.378	65	32.3	60	25.0	0.367
Emergency cesarean	72	13.9	67	13.4	0.549	65	13.8	60	15	0.404
Neonatal ICU admission	72	5.6	66	14.9	0.067	65	6.2	59	13.3	0.173

Data are presented as mean (SD) for continuous variables and percentages for categorical variables. *P* value calculated using one-way ANOVA for continuous variables and Pearson χ^2 for categorical variables. ICU, intensive care unit.

weight and concluded that it is currently the most appropriate dietary intervention in GDM (20). The lack of a difference in HbA_{1c} between the interventions is not unexpected, as HbA_{1c} does not provide a good indication of postprandial glycemia. A low-GI diet may elicit other benefits including a reduction in glucose fluctuations and lower inflammatory markers, as evidenced by lower C-reactive protein levels in a study by Wolever et al. (21) and a tendency for this in our study. On the other hand, the fructosamine fell in both groups. While there are few data on fructosamine levels in pregnancy, this parameter represents changes in glycemia over the preceding weeks, rather than months, outside pregnancy. Thus, the fall in fructosamine might reflect the beneficial effects of the intervention more effectively than the HbA_{1c}. It is also possible that dietary intervention initiated in the second trimester is still too late to substantially influence outcomes. In nondiabetic pregnant women, a higher-GI diet that was similar to that of our study (8) was associated with significantly more macrosomia. However, the intervention started earlier, between 12 and 16 weeks.

It is conceivable that the dietary pattern around conception is more important for any effects on metabolic programming than later in the pregnancy. There is increasing evidence that nutrition in the prenatal environment affects epigenetic processes, such as DNA methylation and histone modifications, resulting in modulation of gene transcription, thereby altering the phenotype of the offspring (22). Animal studies, in which dietary manipulations occur from conception, have induced DNA methylation and covalent histone modifications in genes that affect offspring body composition and metabolic phenotype (23,24). In a study in which maternal GI and GL were calculated in early (11 weeks) and late (34 weeks) pregnancy, it was found that only maternal GI and GL in early pregnancy were associated with fat mass at 4 and 6 years of age but not with fat mass at birth (25). A Danish study showed that dietary GI at 30 weeks' gestation was associated with insulin sensitivity and insulin and leptin levels in offspring aged 20 years (26). Thus, the effects of any dietary intervention in pregnancy may not be apparent until sometime after the perinatal period.

The strengths of our study include the randomized design, the diverse ethnicity of the participants, concealment of diet allocation, blinding of investigators, intensity of intervention, measurement of neonatal body composition (not just birth weight), use of medical records for primary and secondary outcomes, and apparent maternal compliance with dietary instruction. Australia is a culturally diverse country, with about one-quarter of the population born overseas and a further 20% of residents having at least one parent born overseas (27). Furthermore, in Australia minority ethnic groups show a higher prevalence of GDM than women of Caucasian origin (28). This is reflected in the current study participants, where ~40% were of non-Caucasian origin, yet this group represented 67% of the women who had GDM by 20 weeks and 53% who were diagnosed with GDM by 28 weeks. However, the study limitations include the fact that those assigned to the LGI diet group not only reduced the GI but also energy, saturated fat, and total sugars. Not all carbohydrate foods were provided (only samples), and there is the possibility that compliance may have been optimized during recording periods. The high level of education and unrepresentative nature of the cohort limit the generalizability of the findings.

In conclusion, we found that a low-GI diet commenced early in the second

trimester in women at high risk of GDM resulted in no apparent advantage over a conventional healthy diet with respect to risk of development of GDM, glycemia, adverse pregnancy outcomes, and neonatal anthropometry. The offspring of both groups had mean birth weight, birth weight centile, and neonatal adiposity within the normal range. Importantly, a low-GI diet did not result in any increased risk of adverse outcomes, and the insulin dose requirement was lower in women who developed GDM. Whether differences may have been seen in a group of more obese or less intensively managed women remains to be determined. Further studies examining the effect of a low-GI diet in women planning pregnancy and of the effects of a low-GI diet in pregnancy on the longer-term metabolic health of the offspring are also recommended.

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Duality of Interest. J.C.Y.L. consults for the Glycemic Index Foundation. J.C.B.-M. is the President of the Glycemic Index Foundation, Director of the University of Sydney Glycemic Index Research Service, and author of popular books about the glycemic index of foods. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. T.P.M., G.P.R., and J.C.B.-M. conceived and conducted the study, interpreted data, and wrote the manuscript. R.M. and S.O. implemented the protocol, instructed the participants, and generated the final data. J.C.Y.L. and P.P. analyzed and interpreted data. G.D. designed and managed the research database. T.P.M., J.H., and G.P.R. oversaw clinical aspects. All authors contributed to the discussion of the manuscript. J.C.B.-M. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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