Short Communication

Effect of a low glycaemic index diet in gestational diabetes mellitus on post-natal outcomes after 3 months of birth: a pilot follow-up study

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Abstract

A low glycaemic index (LGI) diet during pregnancy complicated by gestational diabetes mellitus (GDM) may offer benefits to the mother and infant pair beyond those during pregnancy. We aimed to investigate the effect of an LGI diet during pregnancy complicated with GDM on early post-natal outcomes. Fifty-eight women (age: 23–41 years; mean $\pm$ SD pre-pregnancy body mass index: 24.5 ± 5.6 kg m⁻²) who had GDM and followed either an LGI diet ($n = 33$) or a conventional high-fibre diet (HF; $n = 25$) during pregnancy had a 75-g oral glucose tolerance test and blood lipid tests at 3 months post-partum. Anthropometric assessments were conducted for 55 mother–infant pairs. The glycaemic index of the antenatal diets differed modestly (mean $\pm$ SD: 46.8 ± 5.4 vs. 52.4 ± 4.4 ; $P < 0.001$), but there were no significant differences in any of the post-natal outcomes. In conclusion, an LGI diet during pregnancy complicated by GDM has outcomes similar to those of a conventional healthy diet. Adequately powered studies should explore the potential beneficial effects of LGI diet on risk factors for chronic disease.

Keywords: glycaemic index, OGTT, type 2 diabetes mellitus, post-partum weight loss, gestational diabetes mellitus.

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Introduction

In Australia, almost 1 in 20 pregnant women have gestational diabetes mellitus (GDM) (Templeton & Pieris-Caldwell 2008), and the prevalence is increasing (Anna *et al.* 2008; Moses *et al.* 2011). The main adverse outcome of pregnancy complicated by GDM is excessive fetal growth as a result of chronic maternal hyperglycaemia. Excessive fetal growth leads to increased birthweight, which has been linked with increased risk of common chronic diseases such as type 2 diabetes mellitus, cardiovascular diseases and obesity later in life (Wei *et al.* 2003, 2007; Hillier *et al.* 2007; Wang *et al.* 2007).

GDM is a condition for which dietary intervention is known to improve outcomes (Dornhorst & Frost 2002) because dietary carbohydrate is a major determinant of blood glucose levels (Gannon & Nuttall 2006). Carbohydrate foods with a low glycaemic index (LGI) have been shown to improve postprandial glycaemia in healthy non-pregnant individuals, individuals with type 1 diabetes and women with GDM because they are digested and absorbed slowly, producing a lower rise in postprandial blood glucose levels (Lock *et al.* 1988; Nansel *et al.* 2008; Moses *et al.* 2009; Reynolds *et al.* 2009). An LGI diet has been shown to reduce the need for insulin treatment in GDM (Moses *et al.* 2009; Louie *et al.* 2010), a factor

previously associated with a substantial increased risk of ongoing diabetes post-partum (Chodick *et al.* 2010). In addition, in non-pregnant individuals, an LGI diet has been shown to preserve β -cell function (Wolever *et al.* 2008). Reduced β -cell function may be an important predictor of the risk of post-partum diabetes in mothers who have had GDM (Seghieri *et al.* 2010). No adverse health outcomes have been associated with following an LGI diet in GDM (Louie *et al.* 2011).

Despite the potential benefits of an LGI diet, to our knowledge, there are no studies that have examined the effect of an LGI diet during GDM pregnancy on maternal and infant post-natal outcomes. In the present study, we tested the hypothesis that following an LGI diet during pregnancy will produce better maternal and infant outcomes at 3 months post-partum than a conventional high-fibre, moderate glycaemic index (HF) diet.

Methods and materials

Subjects

This was a follow-up study of a randomised controlled trial investigating the effect of an LGI diet on the outcomes of GDM pregnancies. In brief, 99 women were randomised at 29 weeks gestation to follow either an LGI diet or a macronutrient-matched HF diet, both containing 40–45% energy as carbohydrate, for at least 6 weeks. The main findings of the randomised trial have been reported elsewhere (Louie *et al.* 2011). During the intervention period, dietary compliance was assessed every 2–3 weeks with a multiple pass 24-h recall, and where the subject's diet deviated from the assigned diet, they were encouraged to choose more foods that conformed with their assigned diet. At the end of the intervention (i.e.

36–37 weeks gestation), the subjects also completed a 3-day food record, which showed a six-unit difference in dietary GI between the two groups (47 vs. 53; $P < 0.001$). At the end of the trial, the subjects were invited to participate in this 3-month follow-up study. Seventy-four (out of 99) women consented, and 58 returned for the follow-up (59% of the original cohort). Of these 58 subjects, 43 (74%) were considered to be compliant to their assigned diet during pregnancy.

Determination of maternal glucose homeostasis, insulin sensitivity and metabolic profile

The subjects were asked to return to the hospital in a fasting state approximately 3 months post-partum for a standard 75-g oral glucose tolerance test (OGTT). Blood samples were collected before the subject consumed the 75-g glucose drink. These samples were used to determine the fasting blood glucose and insulin levels, as well as other biochemical parameters. Two additional samples were taken at 1 and 2 h after the start of the glucose drink for the determination of the blood glucose level. Blood glucose results were compared with the World Health Organization's criteria for diagnosis of impaired glucose tolerance and type 2 diabetes mellitus (World Health Organization & International Diabetes Federation 2006). Insulin sensitivity was calculated using the homeostasis model assessment of insulin resistance (HOMA2-IR) model (Wallace *et al.* 2004).

Maternal and infant anthropometry

Of the 58 mother and infant pairs who returned for the follow-up, 55 of them provided maternal and infant anthropometric data. Maternal weight was

Key message

- Following an LGI diet during GDM pregnancy had effects similar to a conventional healthy diet on maternal and infant outcomes at 3 months post-partum.
- There appeared to have no adverse effect at 3 months post-partum for following an LGI diet during GDM pregnancy.
- Following an LGI diet during GDM pregnancy may have beneficial effects on some chronic diseases risk factors.

measured using a Tanita HD-327 scale (Wedderburn, Ingleburn, NSW, Australia) in light clothing with shoes off. Infant weight was measured using a Tanita BD-590 Paediatric scale (Wedderburn) with light clothing. Maternal waist circumference (i.e. the narrowest part of the trunk) and infant supine length were also measured.

Breastfeeding status

Mothers were asked to indicate whether or not their infants were breastfed exclusively. If the infant was fed a formula, the brand name and type of the formula was recorded.

Statistical analyses

All statistical analyses were performed in IBM SPSS version 19 (IBM Australia, St Leonards, NSW, Australia). Outcomes reported as continuous variables were compared between groups using one-way analysis of variance, while categorical outcomes were compared using Pearson's chi-square test when cell size is ≥ 5 , and Fisher's exact test when cell size is < 5 . Analysis of covariance was used to adjust for breastfeeding status and/or infant age in the analyses as appropriate.

Ethical approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Human Research Ethics Committee of the Sydney South West Area Health Service (RPAH Zone). Informed consent was obtained from all subjects in this study.

Results

Maternal antenatal characteristics were similar in the LGI and HF groups (Table 1). Maternal and infant outcomes at 3 months post-partum are summarised in Table 2. There were no significant differences in glucose tolerance, insulin sensitivity or cardiovascular risk factors. However, mothers in the LGI group had lower fasting insulin level (-26% , $P = 0.104$), higher insulin sensitivity ($+30\%$, $P = 0.149$) and high-density lipoprotein-cholesterol ($+14\%$, $P = 0.079$), as well as

greater weight loss (-20% , $P = 0.229$) post-partum than those in the HF group which were all of clinical relevance, although statistical significance was not reached. Infant anthropometry was similar in both groups. The results were similar when the analyses were restricted to those who complied with the study diets during pregnancy (data not shown).

Discussion

In this study, we followed up mother–infant pairs who were randomly assigned to diets of different GI during pregnancies complicated by GDM. At 3 months post-partum, we found no significant differences in either maternal or infant outcomes. However, the study was underpowered to detect small, but clinically relevant differences. Compared with a conventional healthy diet, we found that the LGI group had higher insulin sensitivity, a factor linked to reduced long-term risk of type 2 diabetes, although this did not reach statistical significance.

While the post-partum diet was not formally assessed, mothers were encouraged to continue their assigned diet after delivery. However, it is possible that they reverted to their habitual eating pattern as reported in other studies (Moses *et al.* 2007). In addition, the short length of follow-up in the present study may not have been sufficient to detect an effect of diet on maternal post-natal outcomes. While a small number of women have ongoing diabetes as early as 3 months post-partum (Retnakaran *et al.* 2010), usually diabetes post-GDM takes years to develop (Damm 1998; Chodick *et al.* 2010; Gobl *et al.* 2011). With only 58 subjects, our study was not powered to detect a small difference in the prevalence of diabetes or impaired glucose tolerance. For the differences observed in the present study, 2164 subjects (1082 in each group) and 692 subjects (346 in each group) would be required to achieve 80% statistical power for diabetes prevalence and impaired glucose tolerance, respectively. To detect a clinically meaningful decrease of post-GDM diabetes prevalence from 10% to 5%, 171 women are required in each group. A one-unit difference in maternal body mass index (BMI) at 3 months post-partum could be detected with 182 women in each group. A five-unit decrease in

Table 1. Maternal antenatal characteristics and demographics

	LGI	HF	P-value*
<i>n</i>	33	25	–
Age (years)	34.3 ± 3.6	32.6 ± 4.5	0.129
Pre-pregnancy BMI (kg m ⁻²)	24.4 ± 4.9	24.7 ± 6.0	0.799
Ethnicity (%)			
Asian	60.6	60.0	0.963
Caucasian	33.3	32.0	0.915
Others	6.1	8.0	0.373
Week of gestation at diagnosis	26.0 ± 4.1	26.2 ± 4.1	0.845
Family history of type 2 diabetes (%)			
Maternal	30.3	28.0	0.849
Paternal	24.2	16.0	0.164
Other relatives	27.3	24.0	0.778
Week of gestation at the start of intervention	29.2 ± 4.0	29.7 ± 3.3	0.651
75-g OGTT results during pregnancy (mmol L ⁻¹)			
Fasting blood glucose level	4.6 ± 0.5	4.6 ± 0.5	0.864
1-h blood glucose level	9.4 ± 1.3	9.7 ± 1.5	0.430
2-h blood glucose level	8.5 ± 1.2	8.1 ± 1.2	0.249
Annual household income >\$75 000 (%)	42.4	36.0	0.620
Maternal highest education attained (%)			
Bachelor's degree or above	66.7	70.8	0.743
Diploma or equivalent	20.0	20.8	0.940
Year 12 or below	13.3	8.3	0.561
Nulliparous (%)	60.6	72.0	0.366
Insulin-treated GDM (%)	54.5	60.0	0.678
Dietary glycaemic index at 36 weeks gestation	46.8 ± 5.4	52.4 ± 4.4	<0.001
Total dietary fibre intake at 36 weeks gestation	27.6 ± 7.3	24.7 ± 6.6	0.130

LGI, low glycaemic index; HF, high fibre; BMI, body mass index; OGTT, oral glucose tolerance test; GDM, gestational diabetes mellitus. Values are expressed as mean ± SD for continuous variables, and as percentages for categorical variables. *P-value tested by one-way analysis of variance for continuous variables, and Pearson's chi-square test for categorical variables when cell size is ≥5, and Fisher's exact test when cell size is <5.

infant weight-for-age percentile could be detected at 80% statistical power with 155 infants in each group.

The limitation of a short follow-up also applies to infant outcomes. The ACHOIS study (Gillman *et al.* 2010) team followed up 199 mother and infant pairs in their original randomised controlled trial of the treatment of GDM, and despite a significant reduction in macrosomia at birth, no difference in the BMI of the children at 4–5 years of age was detected. They suggested that the effect of GDM treatment on infant outcomes may not be apparent until later in life (Gillman *et al.* 2010), in which case, longer-term follow-up of the infant–mother pairs would be warranted.

In conclusion, at 3 months post-partum, an LGI diet during pregnancy complicated by GDM had outcomes similar to those of a conventional healthy diet. It does not appear to have adverse effects, and may be

associated with beneficial effects on some risk factors, although larger studies are needed.

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Table 2. Maternal and infant outcomes at 3 months post-partum

	LGI		HF		<i>P</i> -value*
	<i>n</i>	value	<i>n</i>	value	
Maternal outcomes					
75-g OGTT results (mmol L ⁻¹)					
Fasting	33	5.0 (4.8–5.2)	23	4.8 (4.6–4.9)	0.117
1-h	33	8.9 (8.0–9.8)	25	9.1 (8.0–10.1)	0.800
2-h	33	6.9 (6.1–7.7)	25	7.0 (6.3–7.8)	0.764
Glucose tolerance status (%)	33		25		
Normal		72.7		76.0	0.931
IFG/IGT		21.2		16.0	0.237
Type 2 diabetes		6.1		8.0	0.373
Other blood biochemistry					
Insulin (pmol L ⁻¹)	31	39.6 (32.8–46.3)	24	53.8 (35.6–71.9)	0.104
HOMA2-IR (%)	30	0.7 (0.6–0.9)	23	1.0 (0.6–1.3)	0.149
HbA1c (%)	32	5.7 (5.5–5.8)	24	5.6 (5.4–5.7)	0.382
Adiponectin (μmol L ⁻¹)	31	8.9 (7.5–10.2)	19	8.4 (6.7–10.1)	0.661
C-reactive protein (μg L ⁻¹)	32	2.0 (1.3–2.8)	24	3.7 (0.6–6.8)	0.223
C-peptide (μmol L ⁻¹)	30	545.5 (456.3–634.8)	24	646.3 (483.3–809.4)	0.245
Total cholesterol (mmol L ⁻¹)	33	5.1 (4.8–5.4)	25	5.2 (4.8–5.6)	0.758
LDL-cholesterol (mmol L ⁻¹)	32	3.1 (2.8–3.4)	24	3.4 (3.0–3.7)	0.337
HDL-cholesterol (mmol L ⁻¹)	32	1.6 (1.5–1.7)	24	1.4 (1.3–1.5)	0.079
Triglyceride (mmol L ⁻¹)	33	0.9 (0.7–1.0)	25	1.2 (0.7–1.7)	0.185
Free fatty acids (μmol L ⁻¹)	28	616.8 (514.8–718.8)	25	635.6 (515.8–755.4)	0.805
Anthropometry					
Weight (kg) [†]	31	66.2 (62.0–70.3)	21	67.9 (62.9–72.9)	0.736
BMI (kg m ⁻²) [†]	31	25.8 (24.2–27.3)	21	26.3 (24.5–28.2)	0.652
Waist circumference (cm) [†]	31	80.6 (77.9–83.4)	21	80.6 (77.2–83.9)	0.990
Post-partum weight loss (kg) [†]	29	9.1 (7.9–10.4)	23	7.4 (6.0–8.9)	0.892
Post-partum weight loss >10% (%)	29	65.5	23	47.8	0.200
Attained pre-pregnancy weight (%) [‡]	32	25.0	23	21.7	0.244
Infant outcomes					
Weight for age percentile ^{§¶}	31	69.6 (60.5–78.8)	21	68.0 (56.9–79.1)	0.720
Length for age percentile ^{§¶}	31	47.9 (38.6–57.2)	21	48.1 (36.9–59.3)	0.977
Weight for length percentile ^{§¶}	31	72.4 (61.2–83.6)	21	64.6 (51.0–78.1)	0.511
Weight gain per day (g) ^{**}	31	32.6 (29.9–35.4)	21	31.4 (27.5–35.3)	0.527

LDL, low-density lipoprotein; HDL, high-density lipoprotein; LGI, low glycaemic index; HF, high fibre; OGTT, oral glucose tolerance test; HOMA2-IR, homeostasis model assessment of insulin resistance (computer model); BMI, body mass index. Values are expressed as mean (95% confidence intervals) for continuous variables, and as percentages for categorical variables. **P*-value tested by one-way analysis of variance for continuous variables, and Pearson's chi-square test for categorical variables when cell size is ≥5, and Fisher's exact test when cell size is <5.

[†]Analyses adjusted for infant age at measurement and breastfeeding status (exclusive vs. non-exclusive). [‡]Weight at 3 months post-partum no more than 1 kg above pre-pregnancy weight. [§]Percentiles were based on Centers for Disease Control and Prevention growth charts, available from <http://www.cdc.gov/growthcharts/>. [¶]Adjusted for breastfeeding status (exclusive vs. non-exclusive). **Adjusted for breastfeeding status (exclusive vs. non-exclusive) and gender.

Conflicts of interest

JCBM is a co-author of The New Glucose Revolution book series (Hodder and Stoughton, London; Marlowe and Co, NY; Hodder Headline, Sydney; and elsewhere), is the director of a not-for-profit GI-based food endorsement programme in Australia, and manages the University of Sydney GI testing service.

All other authors declare that they have no conflict of interest.

Contributions

All authors were involved in the conception and design of the study, and data interpretation. JCYL collected the data and drafted the manuscript. All

authors were involved in the subsequent edits of the manuscript, and have read and approved the final manuscript.

References

- Anna V., van der Ploeg H.P., Cheung N.W., Huxley R.R. & Bauman A.E. (2008) Sociodemographic correlates of the increasing trend in prevalence of gestational diabetes mellitus in a large population of women between 1995 and 2005. *Diabetes Care* **31**, 2288–2293.
- Chodick G., Elchalal U., Sella T., Heymann A.D., Porath A., Kokia E. *et al.* (2010) The risk of overt diabetes mellitus among women with gestational diabetes: a population-based study. *Diabetic Medicine* **27**, 779–785.
- Damm P. (1998) Gestational diabetes mellitus and subsequent development of overt diabetes mellitus. *Danish Medical Bulletin* **45**, 495–509.
- Dornhorst A. & Frost G. (2002) The principles of dietary management of gestational diabetes: reflection on current evidence. *Journal of Human Nutrition and Dietetics* **15**, 145–156; quiz 157–149.
- Gannon M. & Nuttall F. (2006) Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutrition and Metabolism* **3**, 16.
- Gillman M.W., Oakey H., Baghurst P.A., Volkmer R.E., Robinson J.S. & Crowther C.A. (2010) Effect of treatment of gestational diabetes mellitus on obesity in the next generation. *Diabetes Care* **33**, 964–968.
- Gobl C.S., Bozkurt L., Prikoszovich T., Winzer C., Pacini G. & Kautzky-Willer A. (2011) Early possible risk factors for overt diabetes after gestational diabetes mellitus. *Obstetrics and Gynecology* **118**, 71–78.
- Hillier T.A., Pedula K.L., Schmidt M.M., Mullen J.A., Charles M.A. & Pettitt D.J. (2007) Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care* **30**, 2287–2292.
- Lock D.R., Bar-Eyal A., Voet H. & Madar Z. (1988) Glycemic indices of various foods given to pregnant diabetic subjects. *Obstetrics and Gynecology* **71**, 180–183.
- Louie J.C., Brand-Miller J.C., Markovic T.P., Ross G.P. & Moses R.G. (2010) Glycemic index and pregnancy: a systematic literature review. *Journal of Nutrition and Metabolism* **2010**, 282464.
- Louie J.C.Y., Markovic T.P., Perera N., Foote D., Petocz P., Ross G.P. & Brand-Miller J.C. (2011) A randomized controlled trial investigating the effects of a low glycemic index diet on pregnancy outcomes in gestational diabetes mellitus. *Diabetes Care* **34**, 2341–2346.
- Moses R.G., Luebke M., Petocz P. & Brand-Miller J.C. (2007) Maternal diet and infant size 2 y after the completion of a study of a low-glycemic-index diet in pregnancy. *The American Journal of Clinical Nutrition* **86**, 1806.
- Moses R.G., Barker M., Winter M., Petocz P. & Brand-Miller J.C. (2009) Can a low-glycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. *Diabetes Care* **32**, 996–1000.
- Moses R.G., Morris G.J., Petocz P., San Gil F. & Garg D. (2011) The impact of potential new diagnostic criteria on the prevalence of gestational diabetes mellitus in Australia. *The Medical Journal of Australia* **194**, 338–340.
- Nansel T.R., Gellar L. & McGill A. (2008) Effect of varying glycemic index meals on blood glucose control assessed with continuous glucose monitoring in youth with type 1 diabetes on basal-bolus insulin regimens. *Diabetes Care* **31**, 695–697.
- Retnakaran R., Qi Y., Connelly P.W., Sermer M., Zinman B. & Hanley A.J.G. (2010) Glucose intolerance in pregnancy and postpartum risk of metabolic syndrome in young women. *Journal of Clinical Endocrinology and Metabolism* **95**, 670–677.
- Reynolds R.C., Stockmann K.S., Atkinson F.S., Denyer G.S. & Brand-Miller J.C. (2009) Effect of the glycemic index of carbohydrates on day-long (10 h) profiles of plasma glucose, insulin, cholecystokinin and ghrelin. *European Journal of Clinical Nutrition* **63**, 872–878.
- Seghieri G., Tesi F., De Bellis A., Anichini R., Fabbri G., Seghieri M. *et al.* (2010) Long term predictors of postpartum glucose metabolism in women with gestational diabetes mellitus. *Experimental and Clinical Endocrinology and Diabetes* **118**, 485–489.
- Templeton M. & Pieris-Caldwell I. (2008) *Gestational Diabetes Mellitus in Australia, 2005–06*. The Australian Institute of Health and Welfare: Canberra.
- Wallace T.M., Levy J.C. & Matthews D.R. (2004) Use and abuse of HOMA modeling. *Diabetes Care* **27**, 1487–1495.
- Wang X., Liang L., Junfen F.U. & Lizhong D.U. (2007) Metabolic syndrome in obese children born large for gestational age. *Indian Journal of Pediatrics* **74**, 561–565.
- Wei J.-N., Sung F.-C., Li C.-Y., Chang C.-H., Lin R.-S., Lin C.-C. *et al.* (2003) Low birth weight and high birth weight infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan. *Diabetes Care* **26**, 343–348.
- Wei J.N., Li H.Y., Sung F.C., Lin C.C., Chiang C.C., Li C.Y. *et al.* (2007) Birth weight correlates differently with cardiovascular risk factors in youth. *Obesity (Silver Spring)* **15**, 1609–1616.
- Wolever T., Mehling C., Chiasson J.L., Josse R., Leiter L., Maheux P. *et al.* (2008) Low glycaemic index diet and disposition index in type 2 diabetes (the Canadian trial of Carbohydrates in Diabetes): a randomised controlled trial. *Diabetologia* **51**, 1607–1615.
- World Health Organization & International Diabetes Federation (2006) Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia – Report of a WHO/IDF Consultation. WHO, Geneva, Switzerland.