Excessive Weight Gain Before and During Gestational Diabetes Mellitus Management: What Is the Impact?

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OBJECTIVE

Conventional gestational diabetes mellitus (GDM) management focuses on managing blood glucose in order to prevent adverse outcomes. We hypothesized that excessive weight gain at first presentation with GDM (excessive gestational weight gain [EGWG]) and continued EGWG (cEGWG) after commencing GDM management would increase the risk of adverse outcomes, despite treatment to optimize glycemia.

RESEARCH DESIGN AND METHODS

Data collected prospectively from pregnant women with GDM at a single institution were analyzed. GDM was diagnosed on the basis of Australasian Diabetes in Pregnancy Society 1998 guidelines (1992–2015). EGWG means having exceeded the upper limit of the Institute of Medicine–recommended target ranges for the entire pregnancy, by GDM presentation. The relationship between EGWG and antenatal 75-g oral glucose tolerance test (oGTT) values and adverse outcomes was evaluated. Relationships were examined between cEGWG, insulin requirements, and large-for-gestational-age (LGA) infants.

RESULTS

Of 3,281 pregnant women, 776 (23.6%) had EGWG. Women with EGWG had higher mean fasting plasma glucose (FPG) on oGTT (5.2 mmol/L [95% CI 5.1–5.3] vs. 5.0 mmol/L [95% CI 4.9–5.0]; $P < 0.01$), after adjusting for confounders, and more often received insulin therapy (47.0% vs. 33.6%; $P < 0.0001$), with an adjusted odds ratio (aOR) of 1.4 (95% CI 1.1–1.7; $P < 0.01$). aORs for each 2-kg increment of cEGWG were a 1.3-fold higher use of insulin therapy (95% CI 1.1–1.5; $P < 0.001$), an 8-unit increase in final daily insulin dose (95% CI 5.4–11.0; $P < 0.0001$), and a 1.4-fold increase in the rate of delivery of LGA infants (95% CI 1.2–1.7; $P < 0.0001$).

CONCLUSIONS

The absence of EGWG and restricting cEGWG in GDM have a mitigating effect on oGTT-based FPG, the risk of having an LGA infant, and insulin requirements.

The traditional approach to gestational diabetes mellitus (GDM) management largely focuses on monitoring and treating maternal hyperglycemia. This practice is supported by evidence of fewer adverse maternal and neonatal outcomes with improved glycemic control during pregnancy (1,2). Medical nutrition therapy (MNT) is first-line treatment, and insulin is commenced if MNT is not sufficient to achieve

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glycemic targets. However, some studies have shown that women treated with insulin do not have lower rates of adverse pregnancy outcomes than women treated with MNT (3,4). Although this may be due to differences in prepregnancy BMI, maternal glycemia, or both (3), it is also possible that other clinical nonglycemic variables may contribute. Excessive weight gain before the GDM diagnosis and throughout pregnancy may drive the increasing insulin resistance and further exacerbate maternal hyperglycemia (2,3). Greater fat deposition may reduce the capacity to compensate for the physiological increases in insulin resistance that occur during pregnancy (5). A meta-analysis of over 1 million pregnant women found that gestational weight gain was higher than that specified in Institute of Medicine (IOM) guidelines (6) in 47% of pregnancies (7). Some studies have found that women who have GDM and are obese before pregnancy are even more likely to exceed these targets (8,9). Cundy and Holt (10) reported that "it is often underrecognized that the morbidities attributed to GDM are also strongly associated with maternal obesity and excessive gestational weight gain." However, evidence is limited on whether preventing excessive weight gain before and during GDM management results in improved maternal and neonatal outcomes.

In light of this gap in evidence and the rising global rates of GDM, maternal overweight and obesity, and excessive maternal weight gain, research is needed assessing both the impact of excessive gestational weight gain (EGWG) before GDM diagnosis and EGWG that continues during GDM management (cEGWG).

Therefore, the aim of this study was, first, to determine whether women who were diagnosed with GDM and had EGWG at GDM presentation also had higher rates of adverse outcomes (maternal and neonatal) and higher glucose levels per an antenatal 75-g oral glucose tolerance test (oGTT). EGWG in this study was defined as exceeding the upper limit of an IOM-recommended maternal weight gain target range for the entire pregnancy (6) (based on self-reported prepregnancy weight) by the time of the first presentation to the Diabetes Centre for GDM management. For example, if a patient with a prepregnancy BMI of 28 kg/m^2 first presented to the Diabetes Centre at 30 weeks' gestation having already gained 14 kg, she would be categorized as having EGWG, as the weight gain exceeds the advised maximum weight gain of 11.6 kg for the entire pregnancy for a women with a prepregnancy BMI in the overweight category (25.0–29.9 kg/m^2).

The second aim was to investigate whether cEGWG in women with EGWG was associated with the most pertinent outcomes identified from the first aim: greater likelihood of initiating insulin, a larger mean insulin dose, and having an infant that is large for gestational age (LGA). cEGWG was measured from the first presentation to the Diabetes Centre in order to commence GDM management to the last recorded weight (within 4 weeks of delivery).

RESEARCH DESIGN AND METHODS

The study population comprised women with GDM managed at the Bankstown-Lidcombe Hospital Diabetes Centre. Women were diagnosed according to the Australasian Diabetes in Pregnancy Society 1998 guidelines (11), which have been in use since 1991 (12). These guidelines were fasting plasma glucose (FPG) $\geq$5.5 mmol/L ($\geq$99 mg/dL), 2-h postload glucose $\geq$8.0 mmol/L ($\geq$144 mg/dL) on a 75-g oGTT), or both. A 1-h postload value $\geq$10.0 mmol/L ($\geq$18 mg/dL) on the oGTT was also considered diagnostic for GDM from 2010 onward.

The data analyzed in this study were clinical data collected prospectively as part of routine care for all pregnant women with GDM (1992–2015). The Diabetes Centre at Bankstown-Lidcombe Hospital is situated in a metropolitan region in Sydney, New South Wales (NSW), characterized by ethnic diversity; a significant proportion of the women with GDM within the clinic population have Middle Eastern (26.1%), East and Southeast Asian (35.2%), and South Asian (12.5%) backgrounds.

Clinical care of women with GDM included provision of initial education (group or individual) by a dietitian and diabetes educator. This usually occurred between 26 and 28 weeks' gestation but could take place at any time during the pregnancy. Height was measured with a stadiometer (KaWe wall-mounted height measure, model 44440; Medical World Ltd, West Bromwich, U.K.), and prepregnancy weight was self-reported at the initial education session. Weight was measured at every visit (BWB-600 Digital Patient Medical Scale; Tanita, Tokyo, Japan). After receiving the initial education, for the remainder of the pregnancy women were managed in a multidisciplinary GDM clinic, where their case was reviewed by a diabetes educator and endocrinologist at 1- to 2-week intervals. Each woman received a minimum of one individual dietary review from a dietitian. Blood glucose levels were reviewed at each visit, and insulin therapy commenced and was titrated when MNT did not achieve glycemic targets ($<$5.5 mmol/L [99 mg/dL] fasting glucose and $<$7.0 mmol/L [126 mg/dL] 2-h postprandial glucose) (11). Three or more blood glucose levels above the target at a given time of day over 7 days, after consideration of dietary factors, indicated a need for insulin therapy. The insulins used were the intermediate-acting human NPH insulin protaphane and the rapid-acting analogs insulin aspart (NovoRapid; Novo Nordisk, Baulkham Hills, NSW, Australia) and insulin lispro (Humalog; Eli Lilly, West Ryde, NSW, Australia). Metformin was not used.

Postpartum (8–12 weeks) 75-g oGTT results were assessed by using the following criteria: impaired fasting glycemia was defined as fasting glucose 6.1–6.9 mmol/L (109–125 mg/dL); impaired glucose tolerance was defined as 7.8–11.0 mmol/L 2 h after a 75-g glucose load (140–199 mg/dL); type 2 diabetes was defined as fasting glucose $\geq$7.0 mmol/L (126 mg/dL), glucose $\geq$11.1 mmol/L (200 mg/dL) 2 h after a 75-g oGTT, or both.

The primary outcome of the study was the need for insulin therapy. Insulin therapy was selected as a primary outcome because of the health care resource implications of initiating and titrating insulin, and because of the significantly higher stress and anxiety levels reported in women treated with insulin than in those treated only by managing diet (13).

Gestational age was initially determined from the date of the last menstrual period. However, if an ultrasound indicated a different gestational age, the estimated date of confinement and the gestational age were amended.

The inclusion criterion for aim 1 of this study was a diagnosis of GDM. Exclusion criteria included *1*) the last record of maternal weight dated $>$4 weeks before

delivery, *2*) incomplete weight gain data, and *3*) nonsingleton pregnancies.

The inclusion criterion for aim 2 was weight gain exceeding the IOM-recommended ranges (according to prepregnancy BMI) at GDM presentation (EGWG): ≥18.1 kg for women with a BMI ≤18.5 kg/m^2; ≥16.1 kg for those with a BMI of 18.5–24.9 kg/m^2; ≥11.6 kg for those with a BMI of 25.0–29.9 kg/m^2; or ≥9.1 kg for women with a BMI ≥30.0 kg/m^2. Exclusion criteria were *1*) the last record of maternal weight dated >4 weeks before delivery, *2*) incomplete weight gain data, *3*) nonsingleton pregnancies, and *4*) no EGWG at presentation.

Neonates were categorized on the basis of their birth weight as LGA (>90th percentile) or small for gestational age (SGA) (<10th percentile) by referencing the customized percentile charts described by Gardosi and Francis (14). These charts adjusted for gestational age, infant sex, maternal height, self-reported maternal prepregnancy weight, parity, and ethnicity.

To determine whether EGWG at GDM presentation impacted clinical outcomes, odds ratios (ORs) were calculated for risk of the following outcomes: insulin therapy, early delivery, LGA infant, SGA infant, cesarean delivery, neonatal hypoglycemia, neonatal shoulder dystocia, neonatal jaundice, and maternal abnormal glucose tolerance postpartum. The reference group comprised women who did not have EGWG at GDM presentation. Backward stepwise logistic regression analysis was conducted in order to calculate an adjusted OR (aOR) for each of these adverse outcomes, adjusting for biologically plausible confounders. Potential confounders included in univariate analyses were 75-g oGTT FPG and 2-h postload glucose values, HbA_{1c} at GDM diagnosis, gestational age at diagnosis, gravida, parity, ethnicity (Middle Eastern, European, East/Southeast Asian, South Asian), and vitamin D. Predictors of insulin therapy were then entered into a logistic regression model. The following confounders were found to be independent predictors in the logistic regression analysis and hence were used to calculate aOR: 75-g oGTT FPG; HbA_{1c} at GDM diagnosis; gestational age at diagnosis; parity; and Middle Eastern, European, and Southeast Asian ethnicities. The associated 95% CIs were calculated for each OR and aOR.

Patient characteristics and therapeutic, maternal, and neonatal outcomes were compared between study groups (women with EGWG vs. those with no EGWG at GDM presentation) by using the independent samples *t* test for continuous data and the Pearson χ^2 test for categorical data. The Fisher-Freeman-Halton exact test was used to assess differences in ethnicity. Statistical significance was represented by a *P* value <0.05.

An independent samples *t* test was used to determine whether 75-g oGTT FPG values differed between study groups (women with EGWG vs. those with no EGWG at GDM presentation); this difference was adjusted for in the multivariable analysis by using ANCOVA. In order to calculate adjusted mean 75-g oGTT FPG values, potential confounders were included in univariate analyses. These were the 2-h postload glucose value, HbA_{1c} at GDM diagnosis, gestational age at diagnosis, gravida, parity, ethnicity (Middle Eastern, European, East/Southeast Asian, South Asian), and vitamin D. Independent predictors of mean 75-g oGTT FPG values were then included in the ANCOVA. Backward selection was used to determine the final model.

cEGWG in women with EGWG was assessed incrementally: 0.1–2.0, 2.1–4.0, 4.1–6.0, 6.1–8.0, and >8.0 kg. Women who stopped gaining weight were used as the reference group (≤0 kg). Two-kilogram increments were chosen for practical reasons, as smaller weight changes would be more influenced by factors such as clothing and hydration, rather than changes in adiposity. The reference group (category 1, ≤0 kg) was chosen to assess whether advising women with EGWG to avoid or minimize further weight gain while managing GDM could reduce adverse outcomes and the likelihood of requiring insulin therapy. cEGWG was measured from first presentation at the Diabetes Centre (to commence GDM management) to the last recorded weight (within 4 weeks of delivery).

Logistic regression analyses were performed to determine whether cEGWG was an independent predictor of insulin therapy. Factors considered in the univariate analysis were age, FPG and 2-h postload values on the 75-g oGTT, gestational age at GDM diagnosis, HbA_{1c} at GDM diagnosis, gravida, parity, vitamin D status, and the four main ethnicities in this cohort (Middle Eastern, European, East/Southeast Asian, South Asian). Variables found to be significant predictors of receipt of insulin therapy in the univariate analysis ($P < 0.05$) were initially included in the model. The final model was created by using the backward stepwise selection method.

Further analysis through ANCOVA was also conducted to determine whether cEGWG was an independent predictor of final daily insulin dose. Final insulin dose was defined as the total units per day as of the final clinic visit before delivery (within 4 weeks of delivery, per inclusion criteria for aim 2).

As the primary outcome of this study was insulin treatment, the independent predictors for risk of requiring insulin therapy in the multivariable analysis were used to adjust for the risk of the infant being LGA and the impact on final daily insulin dose.

SPSS Statistics software (version 22.0; IBM, Chicago, IL) was used for all data analyses. Ethical approval for this study was given by the South Western Sydney Local Health District Research and Ethics Committee.

RESULTS

Of 3,343 pregnancies, 3,281 were in women with GDM who met the inclusion criterion for aim 1. A total of 776 women (23.6%) had EGWG—that is, they already exceeded the IOM-recommended maternal weight gain targets for the entire pregnancy at first presentation with GDM (mean ± SD 27.7 ± 4.2 weeks' gestation)—and met the inclusion criterion for aim 2.

Outcomes: Presence Versus Absence of EGWG at First Presentation With GDM

The oGTTs were performed at a median of 28.0 weeks' gestation (interquartile range, 26–30 weeks) for pregnant women with EGWG and 27.0 weeks (interquartile range, 22–29 weeks) for those with no EGWG ($P = 0.201$). Women with EGWG before GDM diagnosis had a clinically and statistically significantly higher FPG than women without EGWG when presenting for the 75-g oGTT—5.4 ± 0.8 mmol/L (97.0 ± 14.4 mg/dL) vs.

5.0 ± 0.7 mmol/L (90.0 ± 13.0 mg/dL) ($P < 0.0001$)—but a significantly lower 2-h postload value (8.6 ± 1.7 mmol/L [155 ± 31 mg/dL] vs. 8.7 ± 1.4 mmol/L [157 ± 25 mg/dL]) ($P < 0.01$). In the ANCOVA, after adjusting for confounders (HbA_{1c} at GDM diagnosis [$P < 0.0001$]; vitamin D [$P < 0.0001$]; and Middle Eastern [$P < 0.0001$], European [$P < 0.0001$], and Southeast Asian [$P < 0.0001$] ethnicities), FPG remained significantly higher: 5.2 mmol/L (95% CI 5.1–5.3) (94 md/dL [95% CI 92–95]) versus 5.0 mmol/L (95% CI 4.9–5.0) (90.0 mg/dL [95% CI 88–90]) ($P < 0.01$). There was no difference in the 2-h postload value.

Table 1 summarizes the characteristics of women with EGWG at presentation to the Diabetes Centre and of those who did not have EGWG. Those with EGWG had significantly higher prepregnancy BMI, older gestational age at diagnosis, higher FPG on the oGTT, and higher HbA_{1c} at GDM presentation.

Women with EGWG at GDM presentation delivered at 39.0 ± 1.2 weeks' gestation; those with no EGWG at GDM presentation delivered at 39.0 ± 1.3 weeks ($P = 0.566$). A 75-g oGTT was completed at a mean ± SD of 9.4 ± 2.1 weeks postpartum among women with EGWG at presentation with GDM ($n = 395$) and at 9.6 ± 2.6 weeks postpartum for women with no EGWG at presentation with GDM ($n = 1,524$) ($P = 0.201$).

As shown in Table 2, insulin therapy and adverse maternal and neonatal outcomes (including LGA, SGA, cesarean delivery, and neonatal hypoglycemia) occurred significantly more frequently among women with EGWG. However, once we adjusted for confounders, only the relationships between EGWG and insulin use, LGA, SGA, and cesarean delivery remained significant.

Outcomes from cEGWG During GDM Management

Figure 1 displays the linear relationship between the percentage of women requiring insulin and incremental cEGWG during GDM treatment. Women who gained no weight or who lost weight during GDM management formed the reference group (mean ± SD weight change was −1.9 ± 1.7 kg). A total of 204 women were in the reference group, and so, by definition, all lost weight (≥0.1 kg; range 0.1–9.7 kg). A total of 120 women were defined as having clinically significant weight loss of ≥1 kg (considering they were weighed while wearing clothing and shoes). However, the majority of women in the reference group ($n = 137$; 67%) lost ≤2 kg, and only 10 women lost what could be perceived as a large amount of weight (≥4.0 kg).

In assessing the relationship between cEGWG and commencement of insulin therapy in the univariate analysis, maternal age, FPG, 2-h postload glucose value (on a 75-g oGTT), HbA_{1c} and gestational age at GDM diagnosis, gravida, parity, cEGWG, and (only) East/Southeast Asian ethnicity were significantly associated with insulin therapy (all $P < 0.05$). When entered into a logistic regression model (backward stepwise method), age ($P < 0.011$), gestational age at GDM diagnosis ($P < 0.0001$), FPG on oGTT ($P < 0.0001$), HbA_{1c} at GDM diagnosis ($P < 0.0001$), and cEGWG ($P < 0.0001$) were independent predictors of insulin therapy, whereas 2-h postload glucose, gravida, parity, and East/Southeast Asian ethnicity were no longer significant.

For every increase in cEGWG category (0.1–2.0, 2.1–4.0, 4.1–6.0, 6.1–8.0, >8.0 kg), there was a 1.39-fold increase in the likelihood of requiring insulin therapy (95% CI 1.24–1.56; $P < 0.0001$). After adjustment for the independent predictors in the logistic regression analysis (age, gestational age at diagnosis, FPG value on a 75-g oGTT, HbA_{1c} at GDM diagnosis), this was slightly attenuated to a 1.32-fold increase in the likelihood of insulin therapy (95% CI 1.14–1.53; $P < 0.001$) for each increase in cEGWG category.

Further, on univariate analysis, for every increase in cEGWG category, there was a 1.36-fold increase in the likelihood of an infant being LGA (95% CI 1.20–1.54 units; $P < 0.0001$). On multivariable logistic regression analysis (again after

Table 1—Baseline characteristics of women with and those without EGWG at presentation for GDM management ($N = 3,281$)

Patient characteristics	EGWG at presentation ($n = 776$)	No EGWG at presentation ($n = 2,505$)	P value*
Age (years)	31.8 ± 5.6	32.3 ± 5.3	
Gravida	3.2 ± 2.1	2.9 ± 1.8	<0.0001
Parity	1.6 ± 1.7	1.3 ± 1.4	<0.0001
Gestational age at diagnosis (weeks)	27.7 ± 4.2	25.2 ± 6.0	<0.0001
Prepregnancy BMI (kg/m^2)	29.2 ± 6.0	25.4 ± 6.3	<0.0001
Weight gain up to presentation (kg)	16.3 ± 5.0	7.7 ± 4.2	0.0001
Total maternal weight gained during gestation (kg)	18.0 ± 5.8	10.3 ± 4.7	0.0001
Ethnicity			<0.0001
Middle Eastern	310 (39.9)	546 (21.8)	
European	232 (29.9)	475 (19.0)	
East/Southeast Asian	99 (12.8)	1,055 (42.1)	
South Asian	71 (9.1)	338 (13.5)	
Other	64 (8.2)	91 (3.7)	
FPG on oGTT (mmol/L [mg/dL])	5.4 ± 0.8 [97.2 ± 14.4]	5.0 ± 0.7 [90.0 ± 12.6]	<0.0001
2-h plasma glucose on oGTT (mmol/L [mg/dL])	8.6 ± 1.7 [154.8 ± 30.6]	8.7 ± 1.4 [156.6 ± 25.2]	<0.010
HbA_{1c} at GDM diagnosis (% [mmol/mol])	5.5 ± 0.7 [37.0 ± 7.7]	5.2 ± 0.5 [33.0 ± 5.5]	<0.0001

Data are n (%) or mean ± SD. *EGWG vs. no EGWG at presentation.

Table 2—Therapeutic and neonatal outcomes in women with and those without EGWG at presentation for GDM management (*N* = 3,281)

Outcomes	EGWG at presentation (*n* = 776 [23.2%])	No EGWG at presentation (*n* = 2,505 [74.9%])	Unadjusted OR (95% CI)	aOR (95% CI)
Therapeutic outcome				
Insulin use	365/776 (47.0)	842/2,505 (33.6)‡	1.754‡ (1.489–2.066)	1.393* (1.132–1.715)
Neonatal outcomes				
LGA infants	169/776 (21.8)	283/2,505 (11.3)‡	2.186‡ (1.771–2.699)	1.645‡ (1.281–2.112)
SGA infant	41/776 (5.3)	215/2,505 (8.6%)‡	0.588* (0.417–0.830)	0.503* (0.369–0.810)
Cesarean delivery	245/772 (31.7)	627/2,501 (25.1)†	1.389† (1.165–1.658)	1.556† (1.206–1.921)
Neonatal hypoglycemia	65/679 (9.6)	133/2,275 (5.8)†	1.705† (1.251–2.324)	1.137 (0.776–1.664)
Shoulder dystocia	5/679 (0.7)	13/2,275 (0.6)	1.291 (0.459–3.634)	2.010 (0.521–7.755)
Jaundice	61/679 (9.0)	242/2,275 (10.6)	0.829 (0.617–1.114)	0.812 (0.73–1.149)
Early delivery	31/776 (4.0)	109/2,502 (4.4)	0.914 (0.608–1.373)	1.096 (0.663–1.813)
Abnormal glucose tolerance postpartum	98/393 (24.9)	428/1,523 (28.1)	0.850 (0.659–1.096)	0.934 (0.686–1.274)

Data are *n*/*N* (%). aORs were adjusted for confounders. Complete data were not available for some variables (*N*). The following confounders were included in univariate analysis: gravida, parity, gestational age at diagnosis, FPG and 2-h postload glucose based on 75-g oGTT, HbA_{1c} at GDM diagnosis, ethnicity (Middle Eastern, European, East/Southeast Asian, South Asian), and vitamin D. In the final model, the following confounders remained significant independent predictors and therefore were used to calculate aOR: gravida; gestational age at diagnosis; FPG per the 75-g oGTT; HbA_{1c} at GDM diagnosis; parity; and Middle Eastern, European, and Southeast Asian ethnicities. *$P < 0.01$, †$P < 0.001$, and ‡$P < 0.0001$, all EGWG vs. no EGWG at presentation.

adjustment for maternal age, FPG on a 75-g oGTT, gestational age at GDM diagnosis, gravida, and HbA_{1c} at GDM diagnosis), for every increase in cEGWG category there was a 1.44-fold increase in the likelihood of an infant being born LGA (95% CI 1.24–1.68 units; $P < 0.0001$).

In terms of insulin dose, for every increase in cEGWG category there was an 11-unit increase in the final daily insulin dose (95% CI 8–15 units; $P < 0.0001$). This remained significant in the multivariable analysis (ANCOVA) after adjustment for the aforementioned confounders: for every increase in weight gain category there was an 8-unit increase in the final daily insulin dose (95% CI 5–11 units; $P < 0.0001$).

There was no significant difference in the rate of infants being SGA between the reference group (women who gained no weight or who lost weight during GDM management; 7.0%) and the women who had cEGWG during GDM treatment (4.6%; $P = 0.192$). There were also no significant differences in rates of infants being SGA across all increments of weight gain during GDM management (95% CI 0.8–1.0; $P = 0.124$).

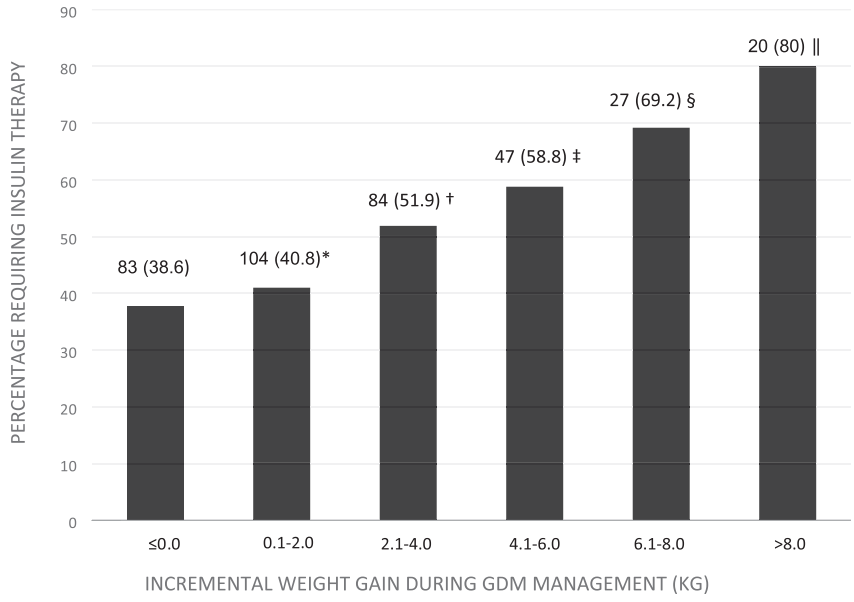

Figure 1—Women with GDM who required insulin, based on the amount of cEGWG. The values above each bar are the specific *n* (%). *NS, †$P < 0.05$, ‡$P < 0.01$, §$P < 0.001$, and ‖$P < 0.0001$, all vs. ≤0 kg cEGWG (reference group).

CONCLUSIONS

This study of prospectively collected clinical data from 3,281 pregnant women with GDM from the Bankstown-Lidcombe Hospital Diabetes Centre identified strong associations between maternal weight gain and a number of clinically important outcomes including higher insulin requirements and the likelihood of delivering an LGA infant.

The percentage of women who exceeded the upper limit of the IOM weight gain targets for the entire pregnancy by the first presentation for GDM management was high at 23.6%. This study is consistent with a systematic review of 23 studies (7), which found that women with EGWG had a significantly higher rate of cesarean delivery, infant birth weight, and rate of delivering an LGA infant. In this study, these higher values occurred despite treatment of hyperglycemia. Although some weight gain during pregnancy is physiological (15), excessive weight gain leads to the deposition of more fat mass in the mother. This greater adiposity is likely to exacerbate insulin resistance as pregnancy progresses, and it may explain many of the associations found in this study. Few women achieve current IOM targets (8–10). However, a recent U.S. study found that only 26.3% of women received advice on gestational

weight gain according to IOM guidelines (16). There seems to be a lack of targeted and tailored maternal weight management interventions of appropriate intensity.

There were significant differences in rates of EGWG between ethnic groups (Table 1). Women from European and Middle Eastern backgrounds were more likely to have EGWG than were women of South and East/Southeast Asian backgrounds. These findings are consistent with those from a systematic review of 23 studies that found significant differences in rates of EGWG between ethnic groups (17). However, evidence seems to be limited regarding the contributing factors. Multifactorial causes likely include differences in socioeconomic characteristics, genetics, and cultural food practices.

With the introduction of the International Association of the Diabetes and Pregnancy Study Groups' diagnostic FPG value (≥5.1 mmol/L [92 mg/dL]) (18), the finding of a relationship between significantly higher FPG on an oGTT and EGWG found in our study is clinically important. Although the relationship between EGWG and risk of GDM has been well documented (19–22), few studies have investigated the relationship between EGWG and specific oGTT values, as has been done in this study. These findings are consistent with those of one recently published study including 451 participants, which also found an association between EGWG and higher FPG on an oGTT (23). Unfortunately, most randomized controlled trials to date have had limited success in reducing EGWG (24,25) and the development of GDM (25,26). Further studies focusing on reducing or preventing early EGWG are still warranted, as this study suggests that pregnancy outcomes could be improved even if GDM still occurs.

Although the reason for the higher FPG value in those with EGWG is unknown, a plausible explanation can be drawn from the shared associations between type 2 diabetes, obesity, and GDM. Impaired fasting glycemia may be related to hepatic insulin resistance (27), to which adiposity seems to contribute significantly (27). Consequently, the effect of insulin on hepatic glucose output may be dampened in the fasting state (28,29).

In this study, for every additional 2 kg of excessive weight gained during GDM management, there was a 32% greater likelihood of insulin being initiated, after adjustment for confounders. Few studies have investigated the impact of cEGWG within GDM management on the need for insulin, medication, or both in addition to MNT. Further, to our knowledge, no other study has assessed the impact of cEGWG incrementally as we have done here. However, several recent studies have found a positive relationship between EGWG (based on differing criteria) and worsening glycemic control, higher medication/insulin use, or both (23,26,30).

This study found that for every additional 2 kg gained, there was a 44% increased likelihood of having an LGA infant. This strong relationship occurred despite intensive monitoring and management of blood glucose levels in order to achieve treatment targets. The link between total excessive maternal weight gain and risk of delivering an LGA infant has been well researched (31–35). However, the impact of cEGWG specifically during GDM management is less well understood. EGWG during GDM management may increase fetal growth because of an associated increase in the amounts of circulating free fatty acids and triglycerides in the mother (36–38).

Clinicians may be concerned about recommending the avoidance of weight gain during GDM management (when IOM targets have already been exceeded) for fear of increasing the rate of delivery of SGA infants. However, the rate of delivery of SGA infants was not significantly higher among those who either lost or maintained weight during GDM management than among those with cEGWG (7.0% vs. 4.6%; $P = 0.192$). Further, rates of having an SGA infant among all the groups in this study were below the expected background risk of 10% (14). However, it would be prudent to promote consumption of a healthy, balanced diet that meets the nutritional requirements of pregnancy in conjunction with providing any gestational weight gain advice and support.

This study has a number of strengths. To our knowledge, it is the first analysis to investigate the impact of early EGWG before GDM diagnosis and of cEGWG during GDM treatment, which involved the same diagnostic criteria and treatment targets through the data collection period. Second, this single-center study had the same leading clinician (J.R.F.) and used the same standardized protocols throughout the data collection period, thereby minimizing clinical variation. Finally, the sample size is large.

This study also has a number of limitations. The findings may not be generalizable to all women with GDM, as this is a cohort of women with various ethnic backgrounds, significant socioeconomic disadvantage, and a high rate of GDM. However, given that GDM is now prevalent worldwide, the range of high-risk ethnic groups represented in this study may make these findings more transferable to a significant proportion of high-risk ethnic groups. Further, the four main ethnic groups represented in our population were entered into the logistic regression model in order to determine independent predictors of insulin therapy. None of the ethnicities confounded the associations found between cEGWG and the likelihood of requiring insulin therapy. Another limitation is the lack of neonatal intensive care data. In addition, the retrospective, observational study design carries several limitations including being unable to attribute causality. Although maternal weight gain was associated with greater insulin requirements, the former may not be causal, particularly given the weight gain–inducing properties of insulin therapy. Also, the possibility of residual confounding cannot be completely excluded and could have influenced the associations we observed. However, the sample size is large, and a number of confounders (including maternal age, gestational age at GDM diagnosis, FPG on the 75-g oGTT, ethnicity, and HbA_{1c} at presentation to the Diabetes Centre) were taken into account in the analysis.

In conclusion, a positive clinical message can be taken from our findings. In those who have already exceeded IOM weight gain targets by the time they present with GDM, these results suggest that the "window of opportunity" has not passed to intervene positively by preventing cEGWG during GDM management. Further, the strengths of the associations observed here suggest a need to provide stronger support for women to achieve healthy maternal weight gain (6) both before and during GDM management, as doing so may have multiple potential benefits. Reducing EGWG may reduce the risk of GDM by

lowering the FPG value on a 75-g oGTT and may decrease insulin requirements and adverse pregnancy outcomes in women with GDM. Reducing both EGWG and cEGWG could reduce rates of delivering LGA infants and the associated complications, as well as related health care expenses. Further, given that commencing and titrating insulin are both costly in terms of time and resources, there is also the potential to conserve clinical time and health care expenditure with lower insulin requirements. Weight management during GDM treatment could also reduce postpartum BMI—a significant benefit in these women, who are at high risk of GDM recurrence (39) and type 2 diabetes (40). All these potential benefits need to be more definitively investigated in well-designed and adequately powered randomized controlled trials.

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