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Original article

The relative importance of gestational weight gain and pre-gestational diabetes on perinatal outcomes: A retrospective cohort study

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ABSTRACT

Aims: The objective of this study is to determine the risks of macrosomia, LGA, and Caesarean section associated with a diagnosis of pre-gestational diabetes or gestational weight gain.
Methods: This is a retrospective cohort study utilizing data from the Perinatal Surveillance Database of Newfoundland & Labrador from 2001 – 2020. Multivariate logistic regression analyses were used to determine odds ratios (OR) associated with GWG and pre-gestational diabetes for the outcomes macrosomia, LGA, and CS, while controlling for other known risk factors.
Results: There were 234 pregnancies complicated by pre-gestational diabetes and 22,048 without diabetes included. There was no significant difference in absolute GWG between groups (15.2 kg vs. 15.5 kg, $p = 0.12$), however more women with pre-gestational diabetes had excessive GWG (85.1% vs. 78.5%, $p = 0.04$). Pre-gestational diabetes was a significant predictor of LGA (OR 5.21, 95% CI 3.96 – 6.87), macrosomia (OR 2.63 95% CI 1.98 – 3.48), and Caesarean section (OR 3.44, 95% CI 2.60 – 4.56). The OR associated with excessive GWG were lower for these same outcomes (LGA OR 2.73, 95% CI 2.40 – 3.11; macrosomia 2.38, 95% CI 2.12 – 2.69; Caesarean section OR 1.29, 95% CI 1.19 – 1.39).
Conclusions: We have identified that pre-gestational diabetes is the most significant risk factor for poor outcomes such as LGA, macrosomia, and Caesarean section, although excessive GWG also plays a role.

1. Introduction

With the increasing incidence of obesity and diabetes in the general population [1], the incidence of pre-gestational diabetes in pregnancy is likewise increasing [2]. This is concerning, given that pregnancies affected by pre-gestational diabetes are at higher risk of stillbirth, congenital malformations, macrosomia (birth weight >4500 g), shoulder dystocia, and the need for Caesarean section [3]. Women with pre-gestational diabetes are advised to maintain control of their blood sugar in order to minimize these complications. Insulin therapy is a mainstay of treatment, as is an appropriate diet and meeting recommended targets for gestational weight gain [3].

In Canada, targets for gestational weight gain are based on the recommendations of the 2009 United States Institute of Medicine report [4]. These target ranges vary based on pre-pregnancy body mass index (BMI, see Table 1), and are based on minimizing poor maternal outcomes (Caesarean delivery and postpartum weight retention), as well as paediatric outcomes (large for gestational age [LGA], small for gestational age [SGA], preterm birth, and childhood obesity) [4]. Some of these sequelae of gestational weight gain above target overlap with those of pre-gestational diabetes. However, these recommendations are based on a general obstetrical population, and do not consider pre-gestational medical conditions such as diabetes mellitus.

There has been a suggestion that decreased targets for GWG amongst women with diabetes can decrease the risk of LGA without increasing the risk of SGA [5,6]. However, if the independent effect of pre-gestational diabetes is greater than the effect of high GWG, then the desired improvement in outcomes may not be realized.

The objective of this study is to determine the risks of macrosomia, LGA, and Caesarean section associated with a diagnosis of pre-gestational diabetes or gestational weight gain. We hypothesized that pre-gestational diabetes and gestational weight gain would have a similar and significant impact (OR >1) on these outcomes.

2. Method

This retrospective cohort study utilized data from the Perinatal Surveillance Database maintained by the Perinatal Program Newfoundland and Labrador (PPNL) from inception (April 2001) to July 2020. This database includes all data collected on perinatal and

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Table 1
Institute of Medicine 2009 recommended gestational weight gain by body mass index.

Body Mass Index (kg/m^2)	IOM 2009 Total Gestational Weight Gain[4]	IOM 2009 Rate of Weight Gain in Second and Third Trimesters
<18.5 (Underweight)	28 – 40 lbs (12.5 – 18 kg)	1 - 1.3 lbs/week (0.44 - 0.58 kg/week)
18.5 – 25	25 – 35 lbs (11.5 – 16 kg)	0.8 – 1 lbs/week (0.35 – 0.50 kg/week)
25.1 – 30 (Overweight)	15 – 25 lbs (7 – 11.5 kg)	0.5 – 0.7 lbs/week (0.23–0.33 kg/week)
> 30 (Obese)	11 – 20 lbs (5 - 9 kg)	0.4 – 0.6 lbs/week (0.17 – 0.27 kg/week)

medical records, including: health care number, age, pre-pregnancy weight, maternal pre-delivery weight, pre-gestational (pre-gestational) diabetes diagnosis, insulin use, smoking in pregnancy, current alcohol use, gestational age at delivery, mode of delivery, birth weight, ICD-10 diagnostic code (e.g. small for gestational age or large for gestational age), and NICU admission. Small for gestational age and large for gestational age are defined as birth weight less than, and greater than the 10th percentile for gestational age, respectively, based on the Kramer 2001 birth weight reference [7]. The unique health care number of the patient was used to link with the electronic health record for last insulin dose before delivery and last HbA1c measured before delivery. Last HbA1c before delivery was used as a surrogate for diabetes control in pregnancy.

Patients with a live singleton pregnancy, with BMI information available and delivering at the provincial tertiary care centre were included in the study. This represents approximately 55% of the province's births. At this centre, obstetricians and family physicians manage pregnancies complicated by diabetes according to national guidelines. Patients with a diagnosis of gestational diabetes in the index pregnancy were excluded.

In this retrospective cohort study, the exposure under investigation was diagnosis of pre-gestational diabetes. The control population included women without a diagnosis of pre-gestational diabetes. Women were then subdivided into a weight gain category: below target as recommended by IOM 2009 guidelines, at target, or above target. The primary outcome was LGA classification. Secondary outcomes included: proportion of macrosomic infants (birth weight >4000 g); proportion of SGA infants; proportion of deliveries by Caesarean section; and proportion of infants admitted to the neonatal intensive care unit. Subgroup analysis by type of diabetes was planned.

SAS software was used for statistical analyses (SAS Institute, Cary, NC, USA). Descriptive analysis was used for demographic and baseline data. Normality was tested using the Kolmogorov-Smirnov test. Differences between groups were assessed using the Mann-Whitney U test for continuous variables and chi-square test for categorical variables. Women were categorized as having gestational weight gain below, at, or above target based on their weekly gestational weight gain in the second and third trimesters and BMI category, according to IOM 2009 recommendations. Weekly gestational weight gain in the second and third trimesters was calculated as: (last weight before delivery minus pre-pregnancy weight) divided by (gestational age at delivery minus 13), which assumes a 0.5–2 kg weight gain in the first trimester [8]. Use of weight gain rate in this fashion controls for gestational age at delivery. Statistical significance was defined by $p<0.05$ or 95% confidence intervals (CI) for odds ratios (OR) not crossing 1.0.

Using both GWG above target and pre-gestational diabetes as predictor variables, multivariate regression analyses were used to determine the association with perinatal outcomes while controlling for age, parity, pre-pregnancy BMI, smoking, and alcohol use. Similar regression analyses were also done for GWG as a continuous variable.

Ethics approval was obtained from the Health Research Ethics Board of Newfoundland & Labrador (# 2018.139).

Table 2
Characteristics of women with pre-gestational diabetes compared to women without diabetes in Newfoundland & Labrador.

	Pre-gestational Diabetes (*N* = 234)	No Diabetes (*N* = 22,048)	p-value
Maternal age (years)	31.1	30.0	0.020[a]
BMI categories, n (%)			<0.0001[b]
Underweight (<18.5)	3 (1.3%)	725 (3.3%)	
Normal weight (18.5 –24.9)	45 (19.2%)	9938 (45.1%)	
Overweight (25 – 29.9)	50 (21.4%)	5896 (26.7%)	
Obese (≥30)	136 (58.1%)	5489 (24.9%)	
Currently smoking, n (%)	35 (15.0%)	2666 (12.1%)	0.18[b]
Alcohol in pregnancy, n (%)	3/231 (1.3%)	202/21,098 (0.9%)	0.83[b]
Gestational age at delivery (weeks)	37.2	39.0	<0.0001[a]
Mean GWG (kg)	15.2	15.5	0.19[a]
GWG Group			0.04[b]
Below Target, n (%)	16 (7.2%)	1499 (7.0%)	
At Target, n (%)	17 (7.7%)	2861 (13.4%)	
Above Target, n (%)	188 (85.1%)	16,719 (78.5%)	

D enominators are different for variables with missing information.
[a]Mann-Whitney U Test; [b]Chi-square test.

3. Results

The dataset provided by the Perinatal Surveillance Database included 43,874 pregnancies. There were 234 women who met the inclusion criteria for the group of interest—that is, singleton pregnancies complicated by pre-gestational diabetes, with known BMI delivering at the Health Sciences Centre. There were 22,048 pregnancies in the control group, that is singleton pregnancies without diabetes and known BMI delivering at the HSC, for a total of 22,282 pregnancies.

Table 2 describes differences between women with and without pre-gestational diabetes. Data were not normally distributed, and Mann-Whitney U tests were therefore used to compare groups for continuous data. Women with pre-gestational diabetes were older by approximately one year. There was a difference in the BMI distribution between groups: there was a higher proportion of obesity amongst women with pre-gestational diabetes (58.1%) compared to women without diabetes (24.9%). There was no difference in current alcohol use or smoking between groups. There was no difference in mean GWG between women with and without pre-gestational diabetes, however there was an increased proportion of women with GWG above target in women with pre-gestational diabetes (85.1% vs. 78.5%, p = 0.04). amongst 234 women with pre-gestational diabetes, 44.9% had type 1 diabetes and 54.7% had type 2 diabetes; type of diabetes was unknown for one individual. The median last recorded insulin dose was 87.9 units/day. The average HbA1c before delivery was 6.4%.

Multivariate logistic regression demonstrates that both GWG above target and a diagnosis of pre-gestational diabetes are significantly associated with LGA, macrosomia, and Caesarean section. (see Table 3), while controlling for confounders. GWG less than current IOM targets was associated with decreased risk of macrosomia, LGA and Caesarean section, but an increased risk of SGA(see Table 4). NICU admission was not associated with either GWG above or less than target (see Tables 3 and 4).

In subgroup analysis by type of diabetes, results were similar (data not shown).

Table 3
Odds ratios (OR) and confidence intervals (CI) for perinatal outcomes associated with excessive gestational weight gain and diagnosis of pre-gestational diabetes.

Outcome	OR for Excessive GWG (95% CI)	OR for pre-gestational diabetes (95% CI)
LGA	2.73 (2.40 - 3.11)	5.21 (3.96 - 6.87)
Macrosomia	2.38 (2.12 - 2.69)	2.63 (1.98 - 3.48)
Caesarean section	1.29 (1.19 - 1.39)	3.44 (2.60 - 4.56)
SGA	0.50 (0.44 - 0.56)	0.61 (0.31 - 1.21)
NICU admission	1.11 (0.98 - 1.26)	6.61 (5.03 - 8.70)

Controlling for parity, BMI, age, smoking, and alcohol use.

Table 4
Odds ratios (OR) and confidence intervals (CI) for perinatal outcomes associated with gestational weight gain below current Institute of Medicine targets.

Outcome	OR for GWG below target (95% CI)
LGA	0.31 (0.25 - 0.38)
Macrosomia	0.32 (0.26 - 0.40)
Caesarean section	0.67 (0.59 - 0.76)
SGA	2.13 (1.79 - 2.53)
NICU admission	0.96 (0.79 - 1.17)

Controlling for pre-gestational diabetes, parity, BMI, age, smoking, and alcohol use.

4. Discussion

In this retrospective cohort study of 22,282 pregnant women in Newfoundland & Labrador, both GWG above target and pre-gestational diabetes were associated with macrosomia, LGA, and delivery by CS. In multivariate logistic regression controlling for maternal age, BMI, parity, smoking, and alcohol use, the odds ratios for LGA and CS outcomes are higher for the pre-gestational diabetes exposure than for excessive gestational weight gain. Previous studies have found that GWG above target in women with any diabetes increases the risk of LGA, macrosomia, and Caesarean section [8–10]. Our study further suggests that the diagnosis of pre-gestational diabetes seems to be the more important predictor for poor outcomes. Although the diagnosis of pre-gestational diabetes is the most important factor in our models of poor perinatal outcomes, excessive GWG remains a potential modifiable risk factor.

Women with pre-gestational diabetes were more likely to have excessive GWG compared to women without diabetes, consistent with a previously described American population [11]. However, there was no difference in the mean GWG between groups. This is likely explained by the BMI differences between groups. Women with pre-gestational diabetes were more likely to be obese, and therefore have stricter GWG targets. Thus, their categorization as having had gestational weight gain above target is due to their BMI.

Some researchers have suggested decreasing targets for GWG for women with diabetes [5]. This group was able to demonstrate a decreased risk for LGA without an increase in SGA, in women with type 2 diabetes who gained ≤5 kg over the course of pregnancy [5]. In our study, although GWG below current targets was associated with decreased risks of LGA, macrosomia, and Caesarean section, there was an increased risk of SGA. Thus, caution must be exercised in recommending decreased weight gain targets. Future studies should focus on evidence-based safe targets for GWG that decrease risks of Caesarean section and macrosomia, without significantly impacting NICU admission or SGA.

This study was adequately powered to assess LGA as the primary outcome using multiple logistic regression. Using the sample size tables of Hsieh[12], when the proportion of LGA is approximately 14%, and the OR for GWG 1.1, a sample size of 12,716 will provide 80% power with alpha 0.05. Our study was able to achieve this sample size.

In considering limitations of the current study, the analyses of women with pre-gestational diabetes alone are likely underpowered, with a total of 234 women with pre-gestational diabetes included over a nearly 19 year span. Although the Perinatal Program Newfoundland & Labrador audits the Perinatal Surveillance Database for accuracy, data may be missing, including pre-pregnancy height and weight, which has a significant impact on the power of analyses.

A strength of this study is the inclusion of women with and without diabetes, as well as the use of multiple logistic regression, which allowed us to determine the independent effects of pre-gestational diabetes and gestational weight gain.

5. Conclusion

In this study, we have identified that both pre-gestational diabetes and gestational weight gain above target are predictors of LGA, macrosomia, and Caesarean section, with diabetes identified as the most significant risk factor. A strategy that focuses on limiting gestational weight gain as well as promoting good glycemic control may be used to improve these outcomes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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