

# Maternal Obesity and the Risk of Placental Vascular Disease

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## Abstract

**Introduction:** While elevated maternal weight in early pregnancy is associated with a higher rate of preeclampsia, the risk of placental abruption and placental infarction is unknown.

**Methods:** We evaluated the risk of placental abruption, placental infarction, and preeclampsia in association with maternal weight quintile at approximately 17 weeks' gestation in 386 323 women with a singleton pregnancy who underwent maternal serum screening in Ontario.

**Results:** After adjusting for age, ethnicity, parity, diabetes mellitus, and tobacco use, the odds ratio (OR) for preeclampsia was 4.1 (95% confidence interval [CI] 3.8–4.4) comparing the highest and lowest weight quintiles. Conversely, there was a lower risk of placental abruption or placental infarction, despite further adjustment for preeclampsia, gestational hypertension and drug dependence (OR 0.81, 95% CI 0.75–0.87).

**Conclusion:** Higher maternal weight in early pregnancy is associated with a higher risk of preeclampsia and a lower risk of placental abruption or placental infarction, a seeming paradox that requires further elucidation.

## Résumé

**Introduction :** Bien qu'un poids maternel élevé aux débuts de la grossesse soit associé à un taux accru de prééclampsie, le risque de décollement placentaire et d'infarctus placentaire est inconnu.

**Méthodes :** Nous avons évalué le risque de décollement placentaire, d'infarctus placentaire et de prééclampsie associé au quintile de poids maternel à environ 17 semaines de gestation chez 386 323 femmes présentant une grossesse monofœtale qui ont subi un dépistage sérique maternel en Ontario.

**Résultats :** À la suite de la neutralisation des effets de l'âge, de l'ethnicité, de la parité, du diabète sucré et du tabagisme, le rapport de cotes (RC) en ce qui concerne la prééclampsie était de 4,1 (intervalle de confiance [IC] à 95 %, 3,8–4,4) comparant les

quintiles du poids le plus élevé et du poids le plus faible. Inversement, nous avons constaté un risque moindre de décollement placentaire ou d'infarctus placentaire, malgré la tenue d'une autre neutralisation qui, celle-là, visait les effets de la prééclampsie, de l'hypertension gestationnelle et de la pharmacodépendance (RC, 0,81; IC à 95 %, 0,75–0,87).

**Conclusion :** La présence d'un poids maternel élevé aux débuts de la grossesse est associée à un risque accru de prééclampsie et à un risque moindre de décollement placentaire ou d'infarctus placentaire, ce qui semble constituer un paradoxe nécessitant de plus amples réflexions.

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## INTRODUCTION

Maternal obesity in pregnancy is associated with a higher risk of adverse maternal and perinatal outcomes,<sup>1,2</sup> which is of concern, given the increasing prevalence of obesity in early pregnancy.<sup>3,4</sup> The risk of preeclampsia–eclampsia (hereafter referred to as “preeclampsia”) rises with increasing maternal pre-pregnancy body mass, insulin resistance, and diabetes mellitus.<sup>5–10</sup> Although preeclampsia is a major risk factor for abruption and infarction of the placenta,<sup>11</sup> little is known about the association between maternal weight in early pregnancy and development of placental abruption or placental infarction. The goal of this study is to further characterize this association.

## METHODS

We performed a retrospective population-based study of all women with a singleton pregnancy who underwent antenatal MSS in Ontario between 1993 and 2000, accounting for about 60% of all pregnancies in Ontario, as described elsewhere.<sup>12</sup> Briefly, the province-wide maternal screening program has been made available since 1993 to all women at 15

**Key Words:** Obesity, pregnancy, preeclampsia, placental abruption, placental infarction, perinatal, cohort study

Competing Interests: None declared.

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**Table 1. Characteristics of participants according to weight quintile, determined at the time of maternal serum screening**

Maternal characteristic	Weight quintile (Q), kg				
	Q1: < 55.4 (n = 77 875)	Q2: 55.4-61.2 (n = 78 157)	Q3: 61.3-67.5 (n = 75 438)	Q4: 67.6-76.6 (n = 77 258)	Q5: > 76.6 (n = 77 595)
Mean (SD) age, years	28.9 (5.2)	29.7 (5.0)	30.0 (4.9)	30.1 (4.8)	29.9 (4.9)
Mean (SD) gestational age at the time of maternal serum screening, weeks	16.7 (1.1)	16.6 (1.1)	16.7 (1.1)	16.7 (1.1)	16.7 (1.1)
Mean (SD) weight at the time of maternal serum screening, kg	50.8 (3.8)	58.6 (1.7)	64.4 (1.7)	71.5 (2.6)	89.3 (12.2)
No. (%) non-caucasian ethnicity	36 957 (49.5)	21 621 (28.6)	16 605 (22.8)	14 768 (19.7)	12 081 (16.0)
Median gravidity	2	2	2	2	2
Median parity	0	0	1	1	1
No. (%) pre-pregnancy diabetes mellitus	139 (0.18)	251 (0.32)	295 (0.39)	418 (0.54)	614 (0.79)
No. (%) gestational diabetes mellitus	1385 (1.8)	1463 (1.9)	1563 (2.1)	2013 (2.6)	3505 (4.5)
No. (%) with gestational hypertension at the index delivery	669 (0.86)	886 (1.1)	1068 (1.4)	1536 (2.0)	3029 (3.9)
No. (%) with hypertension outside of pregnancy, recorded at the index delivery	10 (0.010)	9 (0.010)	19 (0.030)	34 (0.040)	84 (0.11)
No. (%) with tobacco use at the index delivery	184 (0.24)	155 (0.20)	167 (0.22)	191 (0.25)	255 (0.33)
No. (%) with drug dependence at the index delivery	45 (0.060)	47 (0.060)	54 (0.070)	41 (0.050)	34 (0.040)

to 20 weeks' gestation through a physician or midwife. Maternal date of birth, ethnicity, current weight, and presence of pre-pregnancy diabetes are recorded in a standardized fashion on a requisition form at the time of MSS.

Data on obstetrical outcomes for each woman undergoing MSS are linked to the Discharge Abstract Database of the Canadian Institute for Health Information, providing up to eight International Classification of Diseases, Ninth Revision (ICD-9) diagnostic codes for each woman and her fetus/newborn.

Study outcomes included a diagnosis of either placental abruption or placental infarction, according to relevant ICD-9 codes recorded at the delivery hospitalization (Appendix), as well as maternal preeclampsia.

Descriptive variables were computed for each quintile of maternal body weight (Table 1). The association between early maternal weight and each study outcome was analyzed using unconditional logistic regression analysis, expressed as a crude OR and 95% CI, with the lowest weight quintile as the referent. The ORs were also adjusted for those variables listed in the footnotes of Table 2 and the Figure. All

statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary NC), and statistical significance was set at a two-sided *P*-value less than 0.05.

The study research protocol was originally approved through the Ministry of Health and Longterm Care in Ontario, and by the Research Ethics Board of St. Michael's Hospital.

## RESULTS

There were 386 323 singleton pregnancies included within the period of study. Maternal weight was evaluated at an average of 16.7 weeks' gestation (Table 1). While maternal age, gravidity, parity, tobacco use, and drug dependence were similar across weight quintiles, the prevalence of diabetes mellitus and hypertension before and during pregnancy rose with increasing weight (Table 1). There was an inverse relationship between weight quintile and percentage of women of non-white ethnicity.

The rate of preeclampsia increased from 1.6% to 6.0% among those in the lowest and highest weight quintiles, respectively, equivalent to a crude OR of 3.9 (95% CI 3.7–4.2) (Table 2). The adjusted OR for preeclampsia rose significantly with each increasing weight quintile, as demonstrated by non-crossing of the 95% CI, with the exception of quintiles 2 and 3 (Figure).

Placental abruption or placental infarction was diagnosed in 1.7% to 2.0% of women (Table 2). Relative to those in the bottom weight quintile, the associated risk of placental

## ABBREVIATIONS

BMI	body mass index
CI	confidence interval
MSS	maternal serum screening
OR	odds ratio

**Table 2. Risk of preeclampsia, placental abruption, and placental infarction in association with maternal weight quintile, determined at the time of maternal serum screening**

Outcome	Weight quintile (Q), kg	Participants, n	Participants with outcome, n (%)	Odds ratio (95% CI)	
				Crude	Adjusted*
Preeclampsia	Q1: < 55.4	77 875	1239 (1.6)	1.0 (ref)	1.0 (ref)
	Q2: 55.4-61.2	78 157	1553 (2.0)	1.2 (1.2-1.4)	1.3 (1.2-1.4)
	Q3: 61.3-67.5	75 438	1779 (2.4)	1.5 (1.4-1.6)	1.5 (1.4-1.6)
	Q4: 67.6-76.6	77 258	2429 (3.1)	2.0 (1.9-2.2)	2.1 (1.9-2.2)
	Q5: > 76.6	77 595	4615 (6.0)	3.9 (3.7-4.2)	4.1 (3.8-4.4)
Placental abruption or infarction	Q1: < 55.4	77 875	1534 (2.0)	1.0 (ref)	1.0 (ref)
	Q2: 55.4-61.2	78 157	1461 (1.9)	0.95 (0.88-1.0)	0.89 (0.83-0.96)
	Q3: 61.3-67.5	75 438	1389 (1.8)	0.93 (0.87-1.0)	0.86 (0.80-0.93)
	Q4: 67.6-76.6	77 258	1334 (1.7)	0.87 (0.81-0.94)	0.79 (0.73-0.85)
	Q5: > 76.6	77 595	1440 (1.9)	0.94 (0.88-1.0)	0.81 (0.75-0.87)
Placental abruption	Q1: < 55.4	77 875	880 (1.1)	1.0 (ref)	1.0 (ref)
	Q2: 55.4-61.2	78 157	872 (1.1)	0.99 (0.90-1.1)	0.94 (0.85-1.0)
	Q3: 61.3-67.5	75 438	761 (1.0)	0.89 (0.81-0.98)	0.83 (0.75-0.92)
	Q4: 67.6-76.6	77 258	701 (0.91)	0.80 (0.72-0.88)	0.73 (0.66-0.81)
	Q5: > 76.6	77 595	803 (1.0)	0.92 (0.83-1.0)	0.81 (0.73-0.90)
Placental infarction	Q1: < 55.4	77 875	686 (0.88)	1.0 (ref)	1.0 (ref)
	Q2: 55.4-61.2	78 157	621 (0.79)	0.90 (0.81-1.0)	0.84 (0.75-0.94)
	Q3: 61.3-67.5	75 438	652 (0.86)	0.98 (0.88-1.1)	0.90 (0.80-1.0)
	Q4: 67.6-76.6	77 258	655 (0.85)	0.96 (0.86-1.1)	0.85 (0.76-0.96)
	Q5: > 76.6	77 595	680 (0.88)	0.99 (0.89-1.1)	0.82 (0.73-0.92)

\*All models were adjusted for maternal age, non-white ethnicity, parity, pre-pregnancy diabetes mellitus, gestational diabetes mellitus, and tobacco use.

The analyses of placental abruption and/or placental infarction were also adjusted for maternal preeclampsia, gestational hypertension and drug dependence.

abruption or placental infarction was significantly lower for those in all other weight divisions (Table 2, Figure). After adjusting for the variables listed in Table 2, including maternal preeclampsia and gestational hypertension, the OR comparing the highest and lowest weight quintiles was 0.81 (95% CI 0.75–0.87). Similar findings were observed for placental abruption and placental infarction alone (Table 2, Figure).

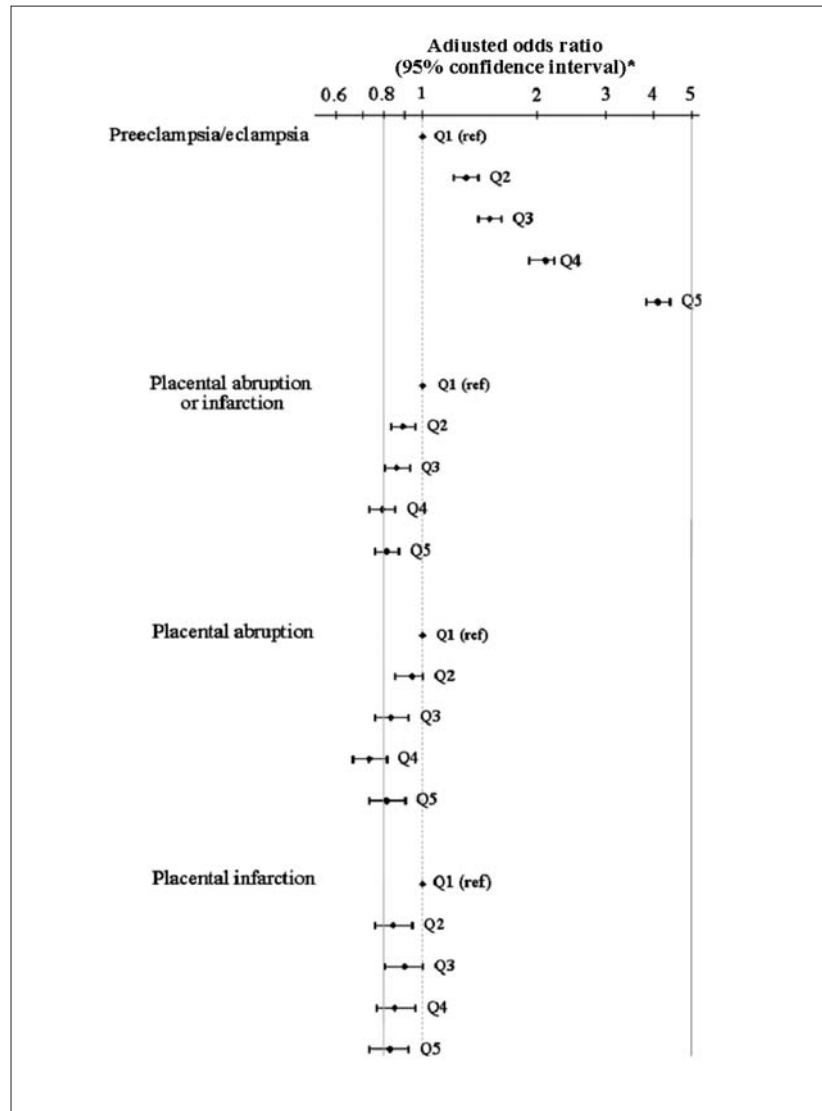
## DISCUSSION

Among more than 385 000 pregnancies, we observed a progressively higher risk of preeclampsia in association with greater maternal weight in early pregnancy. This finding contrasted with a lower associated risk of placental abruption or placental infarction within all higher weight quintiles relative to the lowest weight.

Our study has several limitations. First, poor coding and identification of placental abruption or placental infarction in a database originally designed to focus on congenital and chromosomal anomalies may have occurred. However, the

2% to 3% rate of preeclampsia and the 1% to 2% rate of placental abruption or placental infarction in this database are comparable to other studies.<sup>6,11</sup> Second, the ICD-9 codes used to capture placental abruption or placental infarction at delivery have not been validated. Although the Ontario birth record requires the delivering physician or midwife to describe the gross appearance of the placenta, pathological and microscopic findings are not captured therein. Since a large maternal body habitus may interfere with imaging of the placenta during prenatal ultrasonography,<sup>13</sup> this may have resulted in a lower identification of placental abruption or placental infarction in utero, and consequently lower reporting, in women in the highest weight centile. Small placental abruptions may have been missed by antenatal ultrasonography, since the latter detects retroplacental hematomas of more than 50 mL. Therefore, the reported effect of elevated body weight on the solely clinical diagnosis used herein may differ from true clinical practice. Moreover, women who are obese have higher rates of pre-pregnancy and gestational diabetes

**Risk of preeclampsia and placental abruption or placental infarction in association with maternal weight quintile (Q) in early pregnancy**



\*All models were adjusted for maternal age, non-white ethnicity, parity, pre-pregnancy diabetes mellitus, gestational diabetes mellitus, and tobacco use. The analyses of placental abruption and/or placental infarction were also adjusted for maternal preeclampsia, gestational hypertension and drug dependence.

mellitus, and they are more likely to be delivered earlier by elective Cesarean section.<sup>14</sup> Since we could not capture mode of delivery or gestational age at delivery, it is possible that such women at risk of placental vascular disease may have been delivered earlier or electively by Caesarean section, and thus appeared to be at lower risk of placental abruption otherwise precipitated during labour or by ongoing gestation.<sup>15</sup> However, because we observed a lower risk of placental abruption and placental infarction among women in weight quintiles 2 and 3 (Figure), this is a less plausible explanation.

In this study, maternal weight in early pregnancy was recorded, but BMI was not calculated. When height and

weight were self-reported in other studies, respondents tended to inflate the former and reduce the latter,<sup>16</sup> falsely lowering the reported BMI. Although this may have occurred in our study, we did observe a clear-cut association between maternal weight and preeclampsia risk, which is consistent with many other studies of pre-pregnancy BMI and preeclampsia risk.<sup>6</sup>

The major strength of our study is the inclusion of a large cohort of nearly 400 000 women who delivered within a single province equipped with a universal health care system. The study exposure—early pregnancy body weight—was determined prior to each study outcome, and baseline maternal data were collected in a standardized manner,

enabling us to adjust for several potential confounding variables, including maternal diabetes mellitus.<sup>17</sup>

The mechanisms underlying the group of placental vascular diseases are poorly understood; yet, they may share some risk factors in common with cardiovascular disease.<sup>9</sup> At the same time, smoking, which is an established risk factor for cardiovascular disease, has been found to be associated with a lower risk of preeclampsia<sup>18</sup> and a higher risk of placental abruption or placental infarction.<sup>19</sup> Similarly, our findings suggest that obese women may experience a higher rate of preeclampsia but a lower rate of placental abruption or placental infarction. The underlying reasons for these apparent contradictions require elucidation.

We are unsure whether the observed inverse relationship between higher maternal body weight and placental abruption or placental infarction is real. A prospective study should evaluate the relationship between pre-pregnancy BMI and the risk of preeclampsia, placental abruption and placental infarction. The latter two conditions might be identified not only at delivery, but also by systematic examination of the placenta by antenatal ultrasonography, and pathological assessment post-delivery.

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**Appendix: ICD-9 codes to be used in the current study**

Condition	ICD-9 code(s)*
Preeclampsia or eclampsia	642.4–642.7
Gestational hypertension	642.3, 642.9
Placental abruption	641.2
Placental infarction	656.7
Gestational diabetes mellitus	648.8
Tobacco use	305.1
Drug dependence	304, 648.3

\*Indicates coding International Statistical Classification of Diseases, version 9

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