The Association of Maternal Adult Weight Trajectory with Preeclampsia and Gestational Diabetes Mellitus

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Abstract

Background: Preeclampsia (PE) and gestational diabetes mellitus (GDM) adversely affect pregnancy outcomes and the subsequent health of both mother and infant. It is known that elevated pre-pregnancy body mass index (BMI) is associated with increased risk of these obstetrical complications. However, little is known about the role of adult weight patterns prior to pregnancy.

Methods: Self-reported weight at ages prior to the current pregnancy was recorded in a prospective cohort study of 3567 pregnant women, allowing assessment of longitudinal pre-pregnancy weight trajectories and their association with subsequent PE and GDM in the study pregnancy.

Results: Women who would subsequently experience PE or GDM in the study pregnancy experienced on average almost double the rate of adult weight gain than other women [PE: additional 0.30 kg/year, 95% confidence interval (CI) 0.09, 0.51 and GDM: additional 0.34 kg/year, 95% CI 0.21, 0.48]. Women with mean adult annual weight gain above the 90th percentile (1.4 kg/year) had elevated risk of subsequent PE and GDM independent of their BMI at age 18 and of their obesity status at the time of the study pregnancy. Finite mixture trajectory modelling identified four monotonely ordered, increasing mean weight trajectories. Relative to the second lowest (most common) weight trajectory, women in the highest trajectory were at greater risk of PE [odds ratio (OR) 5.0, 95% CI 2.9, 8.8] and GDM (OR 2.8, 95% CI 1.7, 4.5).

Conclusions: These results indicate that higher adult weight gain trajectories prior to pregnancy may play a role in predisposing women to PE or GDM.

Keywords: preeclampsia, gestational diabetes mellitus, adult weight trajectory.

Hypertensive disorders during pregnancy and gestational diabetes mellitus (GDM) adversely affect maternal, fetal, and neonatal morbidity and mortality.1-3 Women who experience these conditions during pregnancy are at increased risk for diabetes, hypertension, and cardiovascular disease later in life.4-8 Similarly, it has been shown that there are adverse sequelae for their offspring, including diabetes, obesity, and intellectual performance.9-15 The association between prepregnancy weight or body mass index (BMI) and pregnancy outcome has been well established. Prepregnancy BMI has been shown among different populations to be associated with elevated risk of GDM and preeclampsia (PE) during pregnancy.16-20 Furthermore, it has been suggested that higher maternal pre-pregnancy weight is associated with subsequent obesity and cardiovascular disease in the offspring.21,22

Increased risk of PE has been shown in women who had higher adult weight gain23,24 and in women who had experienced weight cycling.23 In a cohort of women aged 25-42 at enrolment, increased risk of GDM was shown to be associated with greater BMI at age 18 and greater weight gain between age 18 and enrolment.25 To date, however, little attention has been paid to the impact on pregnancy outcome of the adult weight trajectory prior to pregnancy.

Chronic hypertension (CH) may play a mediating role in the relationship between weight gain and PE. A number of prospective cohort studies have shown
increased risk of hypertension with increased adult weight gain. In summary, obesity at the time of pregnancy is associated with increased risk of hypertensive disorders and GDM in pregnancy. These conditions are in turn associated with poor infant and maternal health. Using a life course approach, we examined whether the nature of the adult longitudinal weight trajectory of women, prior to pregnancy, has impact on the incidence of PE and GDM.

Methods

Participants: the Omega Study

Participants were drawn from the Omega Study, a prospective cohort study of maternal dietary and other risk factors of PE and GDM. Women participating in the study attended prenatal care clinics affiliated with Swedish Medical Center, Seattle and Tacoma General Hospital, Tacoma, WA. Women eligible for inclusion were those who initiated prenatal care before 20 weeks’ gestation, were at least 18 years of age, could speak and read English, planned to carry the pregnancy to term, and planned to deliver at either of the two study hospitals. Women with pregestational diabetes were excluded from the study.

Between December 1996 and February 2008, 5063 eligible women were approached and 4000 (79%) agreed to participate. Women were included in the study for only one pregnancy. We excluded 42 women with early pregnancy losses, 152 who were lost to follow-up and 239 that did not provide any self-reported weights. Hence, 3567 women remained, including 172 women diagnosed with CH.

Enrolled participants were asked to take part in an hour-long interview in which trained research personnel used a structured questionnaire to elicit information regarding maternal socio-demographic and anthropometric characteristics (including self-reported height), lifestyle habits, and medical and reproductive histories. Self-reported weight prior to the study pregnancy at ages 18, 25, 30, and 35 years (where applicable, e.g. a woman aged 32 could report weight at ages 18, 25, and 30) was also recorded at the interview. Labour and delivery characteristics were ascertained by reviewing participants’ hospital labour and delivery medical records and clinic records after delivery. The procedures used in this study were approved by the Institutional Review Boards of

Swedish Medical Center and Tacoma General Hospital. All participants provided written informed consent. Further details regarding the design, recruitment, and patient characteristics can be found elsewhere.

Outcomes and covariates

PE and CH

The diagnosis of PE was made according to American College of Obstetricians and Gynecologists guidelines. These guidelines defined PE as new onset hypertension with proteinuria in women who are beyond 20 weeks of gestation. Hypertension was defined as sustained blood pressure readings of ≥140/90 mmHg taken ≥6 h apart. Proteinuria was defined as urine protein concentrations of 30 mg/dL on two or more random specimens collected at least 4 h apart. Data on PE status were missing for 41 participants.

CH was determined on the basis of participants’ report of a physician-diagnosed condition. With a view to distinguishing adult weight trajectories in women who had CH by the time of the study pregnancy, we also considered a four-category variable, CHPE, including both CH and subsequent PE (neither, PE only, CH only, and PE and CH, the last group having CH with superimposed PE).

Gestational diabetes

The diagnosis of GDM was made as part of universal screening using the American Diabetes Association 2003 guidelines. All participants were screened at 26–28 weeks gestation using fasting and oral glucose load (50 g) screening tests. Women who had post-load glucose concentrations >140 mg/dL were then followed-up within 1–2 weeks with a 3 h oral glucose (100 g) tolerance test. Women were diagnosed with GDM if two or more of the four diagnostic glucose concentration measurements exceeded the following: fasting > 95 mg/dL; 1 h post-challenge > 180 mg/dL; 2 h post-challenge > 155 mg/dL; 3 h post-challenge > 140 mg/dL. Data on GDM status were missing for 45 participants.

Other covariates

Potential confounders of the association between pregnancy outcome (PE/CHPE, GDM) and adult
weight trajectory considered were education level (post-high school vs. high school or less), parity (nulliparous vs multiparous), maternal age (<25, 25–34, ≥35 years) and smoking history (never, former, current) at the time of the study pregnancy and whether the participant engaged in leisure time physical activity in the week before the interview (yes/no).

**Statistical analysis**

We estimated mean adult longitudinal weight trajectories where weight was regarded as the outcome in a linear model with age (and possibly age squared) and height as independent variables, with interaction between age and CHPE (GDM) status. Robust standard errors were calculated to accommodate the longitudinal records on individual subjects. This approach allows us to estimate the extent to which the average pre-pregnancy adult weight trajectory differs in those with and without subsequent CHPE (GDM).

We next considered a priori adult pre-pregnancy weight trajectory characteristics, without consideration of the pregnancy outcome, defined according to each woman’s BMI at age 18 (the youngest age for which weight was recorded) and her average subsequent annual weight gain prior to the study pregnancy. Women were classified according to whether or not their BMI at age 18 was above the 90th percentile (24.0 kg/m²) and whether or not their subsequent average annual weight gain was greater than the 90th percentile (1.4 kg/year). The association of these trajectory characteristics with PE and GDM in the study pregnancy was assessed in logistic regression analysis. We also considered trajectories defined by annual average weight gain after age 18 and whether or not a woman was obese (BMI ≥30 kg/m²) at the time of the study pregnancy. These analyses excluded 152 women whose only weight record was at age 18.

Finally, finite mixture models were used to parametrically model adult weight trajectories for at most four weight trajectory groups with linear and quadratic terms for the trajectory over age, again without consideration of the pregnancy outcome. Because the distribution of weight was positively skewed, analyses were based on transformed weight (weight^{1.5}) and then back-transformed. The approach is data driven: models with two to four trajectories were considered, and the model with the lowest value of the Bayesian Information Criterion was selected. The associated mean trajectories are determined by maximum likelihood. Each study participant was then assigned to the trajectory for which she had the highest probability of membership, given her observed weights. The association of trajectory membership with subsequent PE and GDM status in the study pregnancy was assessed in logistic regression models with PE (GDM) as the outcome.

The analyses of the association of weight trajectories with subsequent PE and GDM were repeated, including potential confounders. Analyses involving PE were carried out with and without 172 women who had CH. Sensitivity analyses were also considered for a priori weight trajectory groups defined according to 80th (rather than 90th) percentiles for BMI at age 18 and subsequent weight gain; restricting the cohort to nulliparous women only (where the influence on weight of previous pregnancies would not play a role); adjusting for maternal race; and for finite mixture models for trajectories for BMI, rather than weight.

The software packages * stata* version 11 (StataCorp., College Station, TX, USA) and * sas* version 9.2 (SAS Institute, Inc., Cary, NC, USA) were used in the analyses.

**Results**

Table 1 summarises characteristics of the cohort at the time of the study pregnancy, overall, and for those with PE and GDM. Between age 18 and the study pregnancy, women who would experience PE gained, on average, 20.0 kg [standard deviation (SD) 17.7 kg], or 1.5 kg/year, and women who would experience GDM gained, on average, 15.4 kg (SD 15.8 kg), or 1.1 kg/year. Figure 1 summarises weight (kg) at 18, 25, 30, and 35 years, overall, and for those with PE and GDM. Median and interquartile ranges for weights of women who would subsequently experience PE in pregnancy were higher than the rest of the cohort at all ages, whereas for women who would develop GDM, they were higher at older ages.

**Adult pre-pregnancy mean weight trajectories by subsequent CHPE/GDM status**

Linear models were fitted for weight as outcome and with age, CHPE (GDM), and their interactions as primary independent variables, adjusting for height. Quadratic coefficients in age were not statistically significant. Figure 2 illustrates estimated mean weight

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trajectories from age 18 by outcome of the study pregnancy for women of height 1.65 m.

Data on PE during the study pregnancy were available for 3526 women. Of these, 3.7% (n = 129) experienced CH only, 2.2% (n = 79) PE only, and 1.1% (n = 39) experienced both CH and PE. Women who would experience PE, but not CH, had similar mean weight at age 18 as women who would experience neither condition, whereas women who would experience CH were on average heavier at age 18. At age 18, women who would experience CH only were on average 4.4 kg (95% CI 2.8, 5.9) heavier and women who would experience CH and PE were on average 6.1 kg (95% CI 3.4, 8.9) heavier than women who would experience neither condition. Women who would experience neither PE nor CH had mean annual weight increase after age 18 of 0.37 kg/year (95% CI 0.34, 0.40). Mean annual weight change in women with PE but not CH was 0.30 kg/year (95% CI 0.09, 0.51) greater than that for women with neither condition and for women with CH but not PE 0.28 kg/year (95% CI 0.12, 0.44) greater. Women who would experience both CH and PE had a mean annual increase in weight prior to the study pregnancy that was 1.05 kg/year (95% CI 0.74, 1.36) greater than that in women who would experience neither condition. Analysis restricted to women without CH yielded very similar estimates for PE only.

There was no significant difference in mean weight at age 18 in women who would and would not subsequently experience GDM in the study pregnancy. However, average annual weight change after age 18 in women who would experience GDM was 0.34 kg/year (95% CI 0.21, 0.48) greater than the average annual weight gain in women who would not experience GDM (0.37 kg/year, 95% CI 0.34, 0.41).

**A priori-defined weight trajectory groups**

We next considered a priori-defined weight trajectory characteristics, first classifying women according to their BMI at age 18 (relative to 24.0 kg/m², the 90th percentile) and their mean annual weight gain thereafter (relative to 1.4 kg/year, the 90th percentile).
Here, we are considering adult pre-pregnancy weight trajectories ‘anchored’ by BMI at age 18. Records for 3374 women were available for this analysis, which excluded women under age 25 at the time of the study pregnancy who consequently did not have information on weight gain after age 18. Table 2 shows the associations with PE and GDM. Those with higher rate of weight gain prior to the study pregnancy were at greater risk of PE and GDM, independent of their weight at age 18, again indicating that adult weight gain may be associated with PE and GDM. There was no indication of effect modification of the association of adult weight gain with PE and GDM by BMI at age 18 (data not shown).

In secondary analyses, we categorised women according to BMI at age 18 and whether or not they lost weight between age 18 and the study pregnancy. Independent of BMI at age 18, in adjusted analyses,
compared with women who lost weight (14.0% of women), women who gained weight were at greater risk of PE (OR 11.1, 95% CI 2.7, 45.5), and of GDM (OR 3.1, 95% CI 1.6, 5.9). Exploratory nonparametric smoothing indicated that risk of both outcomes increased monotonely as weight gain between age 18 and the study pregnancy increased (data not shown).

We also considered weight trajectory groups anchored at the study pregnancy, classifying women according to their obesity status (BMI ≥ 30 kg/m²) at the time of conception and their obesity status at study pregnancy (women whose median weight was at the 25th, 50th, and 75th percentile for each group).

Table 2. Adjusted odds ratios for preeclampsia and gestational diabetes mellitus, comparing a priori weight trajectory groups

<table>
<thead>
<tr>
<th>Trajectory anchored by BMI at age 18</th>
<th>Preeclampsia</th>
<th>Gestational diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy at age 18&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.5 [0.9, 2.7]</td>
<td>0.9 [0.4, 2.1]</td>
</tr>
<tr>
<td>Weight gainer&lt;sup&gt;c&lt;/sup&gt; after age 18</td>
<td>4.7 [3.0, 7.4]</td>
<td>3.3 [1.8, 6.1]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trajectory anchored by obesity status at study pregnancy</th>
<th>Preeclampsia</th>
<th>Gestational diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gainer&lt;sup&gt;c&lt;/sup&gt; after age 18</td>
<td>2.1 [1.1, 3.7]</td>
<td>1.8 [0.8, 4.0]</td>
</tr>
<tr>
<td>Obese&lt;sup&gt;d&lt;/sup&gt; pre-pregnancy</td>
<td>4.5 [2.5, 7.9]</td>
<td>2.8 [1.3, 6.1]</td>
</tr>
</tbody>
</table>

<sup>a</sup>Adjusted for height, parity, maternal age, smoking, education and leisure time physical activity.
<sup>b</sup>Heavy at age 18 defined as BMI above the 90th percentile (24.0 kg/m²).
<sup>c</sup>Weight gainer defined as average annual weight gain above the 90th percentile (1.4 kg/year).
<sup>d</sup>BMI ≥ 30 kg/m².

Modelling adult pre-pregnancy weight trajectory groups

In finite mixture trajectory modelling, we assume that rather than there being a single common mean trajectory, different members of the population may be associated with different mean trajectories, which may be partitioned into groups. The four fitted weight trajectories (solid lines) are shown in Figure 3. Figure 3 also shows, for each trajectory, observed prepregnancy weight paths (dashed lines) of three study women assigned to that trajectory group (women whose median weight was at the 25th, 50th, and 75th percentile for that group). Of the participants, 12.8% were assigned to trajectory group 1, 46.3% to trajectory group 2, 32.0% to group 3, and 8.9% to group 4. The estimated mean trajectories are all monotone increasing and do not intersect (Figure 3). Trajectory 4, with the highest mean weight at age 18, is also the highest for weight gain.

![Figure 3](image_url)
trajectory with the highest mean weight at age 35. The monotone ordering of the mean trajectory paths means that women on the highest weight trajectory will also likely be those with highest pre-pregnancy weight.

These adult weight trajectories were identified without consideration of the status of the subsequent study pregnancy. The association between trajectory group and PE/GDM status is shown in Table 3, with trajectory group 2 as the reference. Women in the two highest trajectory groups were at significantly greater risk of PE. When women who were diagnosed with CH prior to the study pregnancy were excluded, the association of trajectory group with PE remained but was attenuated. (Of women with CH, 3.5% were in group 1, 29.6% in group 2, 37.8% in group 3, and 29.1% in group 4.) The odds of GDM were significantly higher in trajectory group 4 (highest weight trajectory).

Sensitivity analyses including only primiparous women and adjusting for maternal race yielded similar results for PE and GDM. Analyses considering group-based trajectories for BMI, rather than weight, showed similar associations of increasing trajectory with increased PE and GDM risk (data not shown).

**Comment**

We considered three approaches for assessing the role of adult pre-pregnancy weight trajectory on pregnancy outcome. First, we assessed whether adult weight trajectory differed according to subsequent pregnancy outcome. Women who would subsequently experience PE or GDM in the study pregnancy experienced on average almost double the rate of adult weight gain compared with other women. We then considered characterising adult weight trajectories (either a priori or by finite mixture modelling) independent of study pregnancy outcome and assessing whether those trajectory groups were differentially associated with risk of PE or GDM. Women with mean annual weight gain (from age 18 until the study pregnancy) above the 90th percentile had elevated risk of subsequent PE and GDM relative to other women, independent of their BMI at age 18 and independent of their obesity status at the time of the study pregnancy. Finite mixture longitudinal trajectory modelling identified four monotonely ordered, increasing mean weight trajectories. Relative to the second lowest (most common) weight trajectory, women in the highest trajectory were at elevated risk of subsequent PE and GDM.

These analyses, while consistent with the body of work that indicates that elevated pre-pregnancy weight is associated with increased risk of PE and GDM, add to that knowledge in a number of ways. Women who would experience PE (without CH) or GDM were, on average, of comparable weight at age 18 with those who would not experience these conditions. Women with CH before the study pregnancy were, on average, 5.4 kg heavier at age 18. Women who would experience PE/CH or GDM gained weight at a more rapid rate than other women after age 18, and this was particularly the case for women who would experience both PE and CH.

When mean weight trajectories are parametrically modelled without consideration of subsequent pregnancy outcome, the higher mean weight trajectories are also those with the higher mean pre-pregnancy weight. Hence, it is not clear whether the associated increased risk of PE and GDM reflects the trajectory path itself or the correspondingly high pre-pregnancy

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**Table 3. Adjusted* odds ratios for preeclampsia and gestational diabetes mellitus, comparing modelled weight trajectory groups**

<table>
<thead>
<tr>
<th>Weight trajectory</th>
<th>All women</th>
<th>Excluding chronic hypertension</th>
<th>All women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (Lowest)</td>
<td>450</td>
<td>1.1 [0.5, 2.2]</td>
<td>444</td>
</tr>
<tr>
<td>Group 2</td>
<td>1632</td>
<td>1.0 [Reference]</td>
<td>1583</td>
</tr>
<tr>
<td>Group 3</td>
<td>1130</td>
<td>2.5 [1.5, 4.0]</td>
<td>1066</td>
</tr>
<tr>
<td>Group 4 (Highest)</td>
<td>314</td>
<td>5.0 [2.9, 8.8]</td>
<td>265</td>
</tr>
</tbody>
</table>

*Adjusted for height, parity, maternal age, smoking, education, and leisure time physical activity.
weight. The analyses which consider a priori weight trajectory characteristics throw light on this question as women who have had higher rate of weight gain after age 18 are at greater risk for PE and GDM, independent of their BMI at age 18 and independent of obesity status at the time of the study pregnancy. This is consistent with the observation by Frederick and colleagues,\(^3\) using earlier enrolment for this cohort, that, adjusting for weight at age 18, women who gained more than 10 kg between age 18 and the study pregnancy were at greater risk for PE. Our results are also consistent with the observation that weight gain after age 18 is associated with GDM.\(^5\) Hence, these analyses indicate that adult weight trajectory plays a role in predisposing a woman to PE or GDM, rather than just the endpoint of that trajectory, the pre-pregnancy weight.

Change in pre-pregnancy BMI from first to second pregnancy was recorded and may be regarded as hypothesis generating. Our findings are biologically plausible. While we are not aware of experimental studies linking adult weight gain to insulin resistance and blood pressure control in pregnancy, it is clear that adult weight gain will impact physiological functions, which in turn may plausibly impact the risk of PE or GDM via several biologic pathways. If these findings are independently replicated, greater clarity regarding biological pathways may emerge. These results support targeting of young women towards healthful behavioral changes that lead to weight control during their reproductive years.

Acknowledgements

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References

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