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The Association of Hypertensive Disorders of Pregnancy with Weight Gain over the Subsequent 21 Years: Findings from a Prospective Cohort Study

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ABSTRACT

Obesity is an important risk factor for hypertensive disorders of pregnancy, but most cases of hypertensive disorders of pregnancy occur in women of normal weight. There may be predisposing factors to both hypertensive disorders of pregnancy and obesity. To test this hypothesis, the authors compared changes in body mass index (weight (kg)/height $(m)^2$) over time in women with and without hypertensive disorders of pregnancy. They used data from 3,572 women who received antenatal care at a major public hospital in Brisbane, Australia, between 1981 and 1984 and who were followed up for 21 years. A total of 318 women (8.9%) had experienced hypertensive disorders in the index pregnancy, and 233 of them (73.3%) had a baseline body mass index of $\leq$25 kg/m^2. After the authors adjusted for all potential confounding factors, they found that women with hypertensive disorders of pregnancy gained on average 1.35 kg/m^2 more (95% confidence interval: 0.80 kg/m^2, 1.89 kg/m^2) in body mass index over 21 years than women without hypertensive disorders of pregnancy. The odds of gaining $\geq$5 kg/m^2 were 59% greater for women who experienced hypertensive disorders of pregnancy compared with those who did not (odds ratio = 1.59, 95% confidence interval: 1.24, 2.04). The authors concluded that hypertensive disorders of pregnancy are associated with increased weight gain over 21 years.

body mass index; body weight; hypertension; pre-eclampsia; pregnancy; prospective studies; weight gain; women

Abbreviations: BMI, body mass index; HDP, hypertensive disorders of pregnancy

INTRODUCTION

Obesity is an important risk factor for hypertensive disorders of pregnancy (HDP) (1–3). Maternal obesity is associated with a complex interplay of metabolic abnormalities including hypertension, insulin resistance, hyperlipidemia, hypercoagulability, impaired endothelial function, inflammatory up-regulation (4), and altered adipokine profiles (5), which potentially contribute to the development of preeclampsia (6) and gestational hypertension.

However, many women who develop preeclampsia and gestational hypertension are not overweight or obese (2, 3, 7). Although many women are of normal weight when they develop HDP, we hypothesized that because of underlying predisposing factors, they will have the propensity to gain a greater amount of weight over time compared with women who do not have HDP.

To test this hypothesis, we examined data from a large, prospective birth cohort study involving assessment of mothers 21 years after giving birth. Our study aimed to assess changes in body mass index (BMI; weight (kg)/height $(m)^2$) over time in women with and without HDP.

MATERIALS AND METHODS

We examined the association of HDP with change in BMI from prepregnancy to 21 years after the index pregnancy among 3,572 women who were part of an Australian birth cohort. These women had complete data on HDP at baseline and BMI prepregnancy and at 21 years. Change in BMI was assessed on the basis of two time points: prepregnancy and 21 years after the index pregnancy. This study was approved by the University of Queensland research ethics committee. Written consent was obtained from all participants.

Participants

The Mater-University of Queensland Study of Pregnancy is a prospective cohort study of women and their offspring, who received antenatal care at a major public hospital (Mater Misericordiae Hospital) in South Brisbane, Australia, between 1981 and 1984. The cohort consists of 7,223 women (and their offspring). Each of these women delivered a live singleton baby, who neither died nor was adopted prior to leaving the hospital, and completed both initial phases of data collection. Mothers completed questionnaires at their first antenatal clinic visit and 21 years after the index pregnancy.

Measurements

Maternal height and weight at the first antenatal visit and maternal estimate of prepregnancy weight were obtained at study initiation from obstetric records or maternal questionnaires. Maternal estimates of prepregnancy weight and measured weight at the first antenatal visit were highly correlated (Pearson's correlation coefficient = 0.95). Since weight at the first antenatal visit may be higher (because of the pregnancy) than prepregnancy weight, we did not assess actual level of agreement between self-reported prepregnancy weight and weight at the first antenatal clinic visit. In this study, maternal BMI was derived from self-reported prepregnancy weight and measured height at the first clinic visit, unless this information was not available. For 121 women, data regarding self-reported

prepregnancy weight were not available, so measured height and weight at the first antenatal visit were used. When data on these 121 cases were removed from the analyses, our findings did not substantively differ from those presented here.

At the 21-year follow-up, height and weight were self-reported by 3,525 women, 1,902 of whom also presented for a clinical assessment, including measurement of height and weight. Among these 1,902 women, self-reported BMI and measured BMI were highly correlated (Pearson's correlation coefficient = 0.98). Furthermore, among these women, the mean difference between measured and self-reported BMI was –0.01 kg/m^2 (95 percent confidence interval: –0.06 kg/m^2, 0.04 kg/m^2). The 95 percent level of agreement was from –2.35 kg/m^2 to 2.33 kg/m^2. We compared the mean difference between self-reported and measured BMI in obese and nonobese women and could find no evidence of systematic bias. BMI at 21 years was based on self-report of height and weight. Forty-seven women did not complete the questionnaire but did present for clinical assessment of height and weight, so their BMI was based on measured height and weight.

At both baseline and 21 years, height was measured by using a portable stadiometer, accurate to 1 mm. Weight was determined by using the average of two measurements, with the woman lightly clothed. A scale accurate to 0.2 kg was used.

In accordance with recommended practice (8), we used a priori knowledge to select potential confounding factors rather than allow them to be data driven. Confounding factors were chosen because of their association with both the exposure (HDP) and the outcome (weight change). In this paper, we present a series of models adjusted for these potential confounders even where changes in the point estimates are minimal so that readers can determine the effect of factors that we considered might confound this association. The following paragraphs describe our selected confounders and how they were assessed.

Birth weight (to the nearest gram) and gestational age (completed weeks) were obtained from the obstetric records. A sex and gestational age (per completed weeks), internally standardized, birth-weight *z* score was computed to give a measure of intrauterine growth independent of sex and gestational age. This measure was classified into three categories of low birth weight (birth-weight *z* score ≤–1.3, which represents the 10th percentile or less), normal birth weight (birth-weight *z* score >–1.3 and <1.3), and high birth weight (birth-weight *z* score ≥1.3, which represents the 90th percentile or more). Maternal age at birth, parity (categorized as nulliparous or multiparous), smoking during pregnancy, family income in the year of pregnancy (categorized as low income of <$10,440 (Australian dollars) or not low income), level of education (categorized as completed high school or not completed high school), weight gain in pregnancy (categorized as ≤15 kg and >15 kg), and physical activity (categorized as sedentary or nonsedentary) were obtained from obstetric records and questionnaires at study initiation.

Physical activity (categorized as sedentary or nonsedentary) and smoking status at the 21-year follow-up were obtained from the 21-year self-administered questionnaire. Although physical activity and smoking status 21 years following the index pregnancy could not influence the occurrence of HDP, we considered that these factors would reflect usual adult status for these behaviors and thus provide some indication of prepregnancy levels and as

such would be on a confounding pathway. We did have self-reported smoking data collected during the antenatal period, but, because of the taboo on smoking during pregnancy, these data may be inaccurate. Therefore, we decided that adjusting for both reported smoking during pregnancy and smoking at 21 years would provide a better means of controlling for the potential of prepregnancy smoking to confound any association.

We assessed weight gain during pregnancy and related it to the likelihood of developing HDP. We considered a priori that treating weight gain during pregnancy as a simple confounder in our main analyses was inappropriate since it potentially results in overadjustment. In women with preeclampsia, substantial weight gain in pregnancy may be related to the edema of the condition (as opposed to adiposity), particularly given that edema was used as part of the clinical criteria for preeclampsia at the time. Thus, adjusting for weight gain in pregnancy when examining HDP would be in part adjusting for the condition itself (i.e., overadjustment). However, we explored the relative importance of HDP and weight gain during pregnancy with subsequent weight gain to note from a clinical point of view whether one or both have stronger predictive power.

Definition of HDP

The definition used for HDP at the time of this study (early 1980s) differed from those in common use now. HDP (termed preeclampsia at the time) was defined as a diastolic blood pressure of more than 90 mmHg on at least two occasions beyond 20 weeks' gestation associated with proteinuria and/or excessive fluid retention (defined as generalized edema including the face and hands and excessive weight gain). Proteinuria was diagnosed if the protein reading on dipstick testing (Albustix; Ames Company, Elkhart, Indiana) was at least 2+ on at least two occasions. The diagnosis of preeclampsia was made by consultant obstetricians. Women with hypertension prior to pregnancy, or who were found to have hypertension prior to 20 weeks' gestation, were classified as having essential hypertension and were not considered to have HDP unless they also met the definition as outlined above. According to the currently accepted definitions of the International Society for the Study of Hypertension in Pregnancy (which were introduced in 1986), these women (classified as having preeclampsia at the time) would now be classified as having gestational hypertension, preeclampsia, or preeclampsia superimposed on chronic hypertension (9). Therefore, we refer to these disorders together as HDP in this paper.

Statistical analyses

Student's *t* test was used to compare continuous variables, and chi-squared tests were used to compare categorical variables. Analysis of variance was used to compare the mean change in BMI over 21 years for women whose babies were born in each of the three birth-weight categories. Significance was accepted at the 5 percent level on two-tailed tests for all measures. A series of multiple linear regression models were used to determine the difference between mean change in BMI over 21 years for women with HDP; women without HDP were considered the reference category. A series of multiple logistic regression models were used to assess the association between HDP and an increase in BMI of 5 kg/m^2 or more over 21 years. This value of 5 kg/m^2 was chosen because it represents an increase of at least one BMI category (i.e., it would indicate the equivalent of an increase from normal weight to overweight or overweight to obese). All linear and logistic regression models were conducted for the 3,256 women who had complete data sets for all variables

used in the models. All analyses were undertaken by using Stata version 8.0 software (Stata Corporation, College Station, Texas).

Attrition

Of the 7,223 women eligible for this study, 3,572 (49.4 percent) had information on BMI at both baseline and 21 years. Table 1 provides information regarding characteristics of women included and not included in this study. Women excluded from this study did not have baseline BMI recorded, were not followed up at 21 years, or did not have BMI recorded at the 21-year follow-up. In comparison to excluded women, women included in this study were slightly older, more likely to have HDP, and more likely to be nulliparous, Caucasian, and married and to have completed high school. They were less likely to have a low income and to be sedentary.

TABLE 1. Baseline characteristics of women and their infants included and not included in the Mater-University of Queensland Study of Pregnancy (*n* = 7,223), Brisbane, Australia, 1981–1984

	Included ($n = 3,572$)		Excluded ($n = 3,651$)		*p* value
	No.	%	No.	%	
Age at entry into the study (years)*	25.0 (5.1)		24.1 (5.2)		<0.001
Prepregnancy body mass index (kg/m^2)*	21.9 (3.8)		22.0 (4.1)		0.1
Weight gain during pregnancy (kg)*	14.8 (14.6)		14.9 (14.7)		0.3
Gestational age at delivery (weeks)*	39.4 (1.7)		39.5 (1.7)		0.2
Birth weight (g)*	3,388 (518)		3,382 (523)		0.7
HDP†	318	8.9	270	7.4	0.02
Nulliparous	1,273	35.7	1,126	30.8	<0.001
Completed secondary school‡	2,983	84.1	2,882	79.6	<0.001
Sedentary‡	272	7.7	381	10.7	<0.001
Smoker	1,677	46.9	1,935	53.0	<0.001
Caucasian‡	3,284	94.9	3,519	89.8	<0.001
Married‡	2,850	80.3	2,536	70.2	<0.001
Low income‡	1,023	30.1	1,285	38.4	<0.001

* Values are expressed as mean (standard deviation).
† HDP, hypertensive disorders of pregnancy.
‡ For these characteristics, some data were missing; therefore, percentages do not add to 100.

We used inverse probability weighting with robust estimates for standard errors to account for those women lost to follow-up (10). We explored all sociodemographic, lifestyle, and biologic variables available at baseline. Variables were included in an exploratory logistic regression model to determine whether those subjects remaining in the study significantly differed from those lost to follow-up. Measures that predicted loss to follow-up at 21 years included family income, smoking status, parity, maternal age, physical activity, and HDP. We then estimated inverse probability weighting and applied it to our multivariable models of interest to re-create a sample representative of the original cohort. When weighting adjustments were included in the analyses, results did not change substantively from the unweighted analyses presented in this paper.

RESULTS

Of the 3,572 women included, 318 (8.9 percent) had experienced HDP in the index pregnancy. Table 2 provides information regarding women who did and did not experience HDP. Women who experienced HDP had a higher prepregnancy BMI, had higher rates of overweight or obesity prior to pregnancy, gained more weight during pregnancy, delivered smaller babies at an earlier gestational age, and were more likely to be nulliparous.

TABLE 2. Characteristics of women with and without HDP* (*n* = 3,572), Mater-University of Queensland Study of Pregnancy, Brisbane, Australia, 1981–2005

	No HDP ($n = 3,254$)		HDP ($n = 318$)		*p* value
	No.	%	No.	%	
Age at entry into the study (years)†	25.0 (5.0)		24.5 (5.2)		0.09
Prepregnancy body mass index (kg/m^2)†	21.7 (3.8)		23.2 (4.3)		<0.001
Overweight/obese prepregnancy	467	14.3	85	27.7	<0.001
Weight gain during pregnancy (kg)†	14.6 (5.9)		16.6 (7.2)		<0.001
Change in body mass index over 21 years (kg/m^2)†	5.7 (4.5)		6.8 (5.3)		<0.001
Gestational age at delivery (weeks)†	39.4 (1.6)		38.8 (2.1)		
Birth weight (g)†	3,401 (506)		3,245 (608)		<0.001
Nulliparous	1,088	33.4	186	58.5	<0.001
Completed secondary school‡	2,722	84.2	261	82.8	0.5
Sedentary‡	241	7.5	31	10.0	0.1
Smoker‡	1,538	47.3	139	43.7	0.2
Caucasian‡	2,990	94.8	294	95.1	0.8
Married‡	2,601	80.4	249	78.8	0.5
Low income‡	927	29.9	96	31.6	0.5
Smoker at the 21-year follow-up‡	911	28.0	88	27.7	0.9
Sedentary at the 21-year follow-up‡	239	7.3	31	9.7	0.1

* HDP, hypertensive disorders of pregnancy.
† Values are expressed as mean (standard deviation).
‡ For these characteristics, some data were missing; therefore, percentages do not add to 100.

Of the women who developed HDP, 233 had a baseline BMI of 25 kg/m^2 or less (73.3 percent). Therefore, the majority of women who developed HDP were not overweight or obese prior to pregnancy. Most women gained (rather than lost or maintained) weight over the 21-year follow-up from their index pregnancy: mean change in BMI over the 21 years for all women included in the analysis was an increase of 5.77 kg/m^2 (standard deviation, 4.55 kg/m^2).

Table 3 shows the univariable associations of a variety of characteristics with mean change in BMI over 21 years. Characteristics associated with a greater increase in mean BMI over 21 years included HDP in the index pregnancy, prepregnancy overweight or obesity, low income at baseline, large pregnancy weight gains, and incomplete secondary school education. At

21 years, sedentary lifestyle and nonsmoking were associated with increased mean change in BMI.

Table 4 shows the mean difference in change in BMI between women with HDP and those without HDP after adjusting for potential confounders. As shown in the unadjusted analysis, women with HDP gained on average 1.41 kg/m^2 more (95 percent confidence interval: 0.87 kg/m^2, 1.95 kg/m^2) than women without HDP. The magnitude of this greater increase in BMI for women with HDP did not change substantially with adjustment for any of the potential confounding factors.

TABLE 3. Univariable associations of characteristics with mean change in body mass index (kg/m^2) over 21 years, Mater-University of Queensland Study of Pregnancy, Brisbane, Australia, 1981–2005

	No.	Mean change	95% CI*	*p* value
HDP*				
No	3,254	5.66	5.51, 5.81	
Yes	318	6.85	6.27, 7.44	<0.001
Birth weight category (birth-weight z score)				
Low (≤−1.3)	270	5.69	5.14, 6.25	
Normal (>−1.3 and <1.3)	2,929	5.71	5.55, 5.88	
High (≥1.3)	373	6.25	5.77, 6.72	0.1
Preterm delivery				
No	3,218	5.79	5.63, 5.95	
Yes	354	5.34	5.10, 5.97	0.3
Prepregnancy body mass index (kg/m^2)				
≤25	3,020	5.61	5.46, 5.76	
>25	552	6.60	6.10, 7.10	<0.001
Activity at baseline				
Not sedentary	3,247	5.74	5.59, 5.90	
Sedentary	272	5.99	5.35, 6.63	0.4
Pregnancy smoking status				
Nonsmoker	1,895	5.86	5.66, 6.06	
Smoker	1,677	5.66	5.44, 5.88	0.2
Parity				
Nulliparous	1,274	5.83	5.57, 6.09	
Multiparous	2,298	5.73	5.55, 5.91	0.5
Ethnicity				
Caucasian	3,284	5.77	5.61, 5.93	
Non-Caucasian	178	5.89	5.26, 6.53	0.7
Baseline income (Australian dollars/year)				
≥10,400	2,377	5.63	5.45, 5.80	
<10,400	1,023	6.08	5.78, 6.39	0.006
Pregnancy weight gain (kg)				
≤15	1,692	5.06	4.85, 5.27	
>15	1,880	6.4	6.19, 6.61	<0.001
Secondary education				
Completed secondary school	2,983	5.67	5.52, 6.75	
Did not complete secondary school	565	6.33	5.92, 6.75	0.001
21-Year smoking status				
Nonsmoker	2,573	6.08	5.91, 6.26	
Smoker	999	4.95	4.68, 5.21	<0.001
Activity at 21 years				
Not sedentary	3,302	5.70	5.54, 5.85	
Sedentary	270	6.59	5.99, 7.20	0.002

* CI, confidence interval; HDP, hypertensive disorders of pregnancy.

TABLE 4. Mean increase in body mass index (kg/m^2) over 21 years for women with HDP* compared with women without HDP (*n* = 3,256), Mater-University of Queensland Study of Pregnancy, Brisbane, Australia, 1981–2005

	Mean increase†	95% CI*
Model 1: Unadjusted	1.41	0.87, 1.95
Model 2: Adjusted for baseline income, secondary school completion, and ethnicity	1.40	0.87, 1.95
Model 3: Adjusted for maternal age at birth and parity	1.45	0.90, 1.99
Model 4: Adjusted for birth weight, gestational age, and sex of offspring	1.47	0.92, 2.01
Model 5: Adjusted for maternal smoking during pregnancy, smoking at 21 years, and sedentary lifestyle at 21 years	1.41	0.88, 1.95
Model 6: Adjusted for smoking at 21 years	1.41	0.88, 1.95
Model 6: Adjusted for baseline maternal body mass index	1.28	0.74, 1.82
Model 8: Adjusted for maternal smoking and sedentary lifestyle at 21 years	1.39	0.85, 1.93
Model 7: Adjusted for all of these factors combined	1.35	0.80, 1.89

* HDP, hypertensive disorders of pregnancy; CI, confidence interval.

† Results in this column indicate the mean difference in change in body mass index of women who experienced HDP compared with those who did not; therefore, 0 is the null value (no difference), and a positive result indicates greater weight gain in women with HDP compared with those who did not experience HDP.

Table 5 shows the association between HDP and gains in BMI of 5 kg/m^2 or more over 21 years, adjusting for potential confounding factors. The odds of gaining 5 kg/m^2 or more were 59 percent greater for women with HDP compared with those who had not experienced HDP (odds ratio = 1.59, 95 percent confidence interval: 1.24, 2.04). Again, it was not substantively altered by adjustment for potential confounding factors.

Mean weight gain during pregnancy was 14.78 kg (standard deviation, 6.03). Women with HDP gained on average 2.01 kg (95 percent confidence interval: 1.41 kg, 2.61 kg) more than women without HDP. Weight gain during pregnancy was also associated with greater weight gain during the subsequent follow-up (table 3). When we included excessive weight gain (>15 kg) during pregnancy in the final model of the association of HDP with mean increase in BMI over 21 years, this attenuated to 0.72 kg/m^2 (95 percent confidence interval: 0.18 kg/m^2, 1.26 kg/m^2). The association of excessive weight gain during pregnancy with mean change in BMI over 21 years was 0.19 kg/m^2 (95 percent confidence interval: 0.16 kg/m^2, 0.22 kg/m^2) in this final model with HDP and other covariables included.

TABLE 5. Multivariable odds ratios for an increase in body mass index of at least 5 kg/m^2 over 21 years for women with HDP* compared with those without HDP, Mater-University of Queensland Study of Pregnancy, Brisbane, Australia, 1981–2005

	OR*,†	95% CI*
Model 1: Unadjusted	1.59	1.24, 2.04
Model 2: Adjusted for baseline income, secondary school completion, and ethnicity	1.58	1.24, 2.03
Model 3: Adjusted for maternal age at birth and parity	1.63	1.27, 2.09
Model 4: Adjusted for birth weight, gestational age, and sex of offspring	1.64	1.28, 2.11
Model 5: Adjusted for maternal smoking during pregnancy, smoking at 21 years, and sedentary lifestyle at 21 years	1.60	1.25, 2.05
Model 6: Adjusted for smoking at 21 years	1.61	1.25, 2.06
Model 6: Adjusted for baseline maternal body mass index	1.51	1.18, 1.94
Model 8: Adjusted for maternal smoking and sedentary lifestyle at 21 years	1.59	1.24, 2.04
Model 7: Adjusted for all of these factors combined	1.57	1.22, 2.04

* HDP, hypertensive disorders of pregnancy; OR, odds ratio; CI, confidence interval.

† The odds ratios compare the odds of gaining at least 5 kg/m^2 for women with HDP with those for women who do not experience HDP (the reference category); therefore, a value greater than 1 indicates increased odds of this extent of greater weight gain in women with HDP compared with those without HDP.

DISCUSSION

Implications

This study provides information regarding the relation between change in BMI over 21 years and HDP in a large prospective cohort of women. It confirms our hypothesis that women with HDP gain a greater amount of weight over 21 years than women without HDP.

Women who develop HDP have an increased risk of ischemic heart disease (11–16), hypertension (12, 15), stroke (14, 15), venous thromboembolism (13, 17), and mortality (14, 16, 18) over the long term. Greater weight gain, and the increased risk of overweight and obesity in middle age, is associated with an increased risk of cardiovascular disease, diabetes, cancers, and overall mortality (19–21). There appears to be a linear association between increasing BMI (from 20 kg/m^2) and adverse health outcomes. Compared with women without HDP, women with HDP had a 1.41-kg/m^2 greater mean increase in BMI over 21 years. Although this difference is small, the linear association between BMI and adverse health outcomes suggests that this might be an important pathway to later health problems.

Longer-term follow-up of this study population and other large pregnancy cohorts is required to determine the extent to which greater weight gain in women with HDP mediates associations with disease outcomes. Nonetheless, our work further highlights the potential of the antenatal period for identifying women at future metabolic risk at a time when they might be particularly receptive to initiatives aimed at reducing this risk (22).

The findings from this study also provide some potential insights into the pathogenesis of HDP. The majority of women with HDP in this study were of normal weight at the time of pregnancy but gained a greater amount of weight over 21 years. The factors that contribute to weight gain include excessive caloric intake and inadequate physical activity. However, this is likely to be influenced by a complex interplay between genetic factors, hormones such as insulin and leptin, and central nervous system regulation of energy expenditure, pleasure, and appetite (23, 24). There are a number of plausible explanations for why women with HDP experience increased weight gain compared with women without HDP.

Insulin resistance has been proposed as a key factor in the development of HDP (6, 25). Even in lean, normotensive pregnant women with normal glucose tolerance, insulin resistance at 16–20 weeks' gestation is predictive of subsequent preeclampsia (26). Insulin resistance is strongly associated with obesity, although the nature of this association is complex. In prospective cohort studies, there is evidence that obesity precedes the development of insulin resistance (27). At the same time, insulin resistance and subsequent hyperinsulinemia may have a key role in central nervous system regulation of energy homeostasis, thus driving weight gain (23, 28, 29). It is likely that insulin resistance itself contributes to weight gain.

Thus, the interrelations of and predisposing factors for insulin resistance and obesity are likely to be important in driving the association between HDP and the subsequent increased risk of greater weight gain that we identified in this study. The current Western diet is highly insulinogenic (28), and it is possible that consumption of this diet predisposes to both HDP and long-term weight gain. However, in a large prospective study of nutrient intake, there was no difference in dietary intake between women with and without HDP (30), although that study did not assess glycemic index or the nature of carbohydrates ingested. In our study, we were unable to explore the possible effect of diet on the association between HDP and subsequent weight gain.

Lack of physical activity also contributes to insulin resistance and consequent hyperinsulinemia (24), and some evidence suggests that lack of physical activity might be associated with increased rates of HDP (31–33). Thus, physical inactivity via either an effect on insulin resistance or a more direct effect on HDP and long-term weight gain might explain the associations that we found. Although the association between HDP and subsequent weight gain persisted after adjustment for sedentary lifestyle at the time of pregnancy and at the 21-year follow-up in this study, assessment of activity was relatively crude. Studies with detailed, and preferably objective (such as obtained from accelerometers), measures of physical activity taken at different stages during a woman's life course would provide a better assessment of the role of physical inactivity in linking HDP and subsequent weight gain.

Study strengths and limitations

The major strengths of this study are the prospective collection of obstetric and subsequent data on a general population sample of women. Attrition of the original cohort may have biased our findings because 49.4 percent of the original cohort had been followed and had sufficient information to be included in this study. Loss to follow-up was modestly related to HDP but was not related to prepregnancy BMI or weight gain during pregnancy. The association we found between HDP and increased mean change in BMI over 21 years would be attenuated if, for those lost to follow-up, the association between HDP and change in BMI was either null or opposite that found here (i.e., lower mean change in BMI in women with HDP compared with those without HDP). Although we cannot rule out this possibility, we consider it unlikely. Furthermore, when we used inverse probability weights to reconstruct the distribution of participant characteristics in the original cohort, the results of our analyses were the same as those presented here without these weights, suggesting that our findings were not markedly biased by attrition (10). BMI at both baseline (prepregnancy) and the 21-year follow-up was based on self-reported weight, which may be inaccurate. However, our comparison of self-report with actual measures (at the antenatal clinic for the prepregnancy measure and in a subgroup of more than 1,000 for the 21-year follow-up) suggests that self-report in this study did not importantly bias our findings.

Women with HDP gained on average 2.01 kg more weight during pregnancy than women without HDP. Clinically, we believe that this finding is likely due to edema associated with the preeclamptic syndrome. However, we did not have clinical data to confirm that women with HDP reduced their weight rapidly following delivery. Therefore, we cannot accurately assess the extent to which edema, as opposed to increased adipose tissue, muscle, or other tissue mass, contributed to greater overall pregnancy weight gain. When we included excessive weight gain in our models, the association between HDP and subsequent mean change in BMI was attenuated. We are concerned that doing so represents overadjustment, as outlined in the Materials and Methods section, and consider the final model presented in table 4 to represent our best estimate of the association of HDP with subsequent weight gain. We found that HDP had a relatively stronger association with subsequent weight gain when compared with excessive weight gain in pregnancy.

Conclusion

Our results suggest that women who experience HDP gain greater amounts of weight over time compared with those without HDP. This finding is important because the propensity to gain weight might partly contribute to the excess burden of chronic disease that these women are known to develop. This study contributes to the evidence base for future randomized trials to explore the effect of interventions that minimize weight gain to prevent the development of chronic disease in women identified as at risk during antenatal care.

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