Journal of Developmental Origins of Health and Disease (2013), **4**(1), 42–48.
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doi:10.1017/S2040174412000578

ORIGINAL ARTICLE

Pre-pregnancy maternal overweight and obesity increase the risk for affective disorders in offspring

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Maternal pre-pregnancy obesity has been linked with an increased risk for negative emotionality and inattentiveness in offspring in early childhood. The aim of this study was to examine the association between maternal pre-pregnancy body mass index (BMI) and the development of affective problems (dysthymic disorder, major depressive disorder) throughout childhood and adolescence. In the Western Australian Pregnancy Cohort (Raine) Study, 2900 women provided data on their pre-pregnancy weight, and height measurements were taken at 18 weeks of gestation. BMI was calculated and categorized using standardized methods. Live-born children ($n = 2868$) were followed up at ages 5, 8, 10, 14 and 17 years using the Diagnostic and Statistical Manual of Mental Disorders-oriented scales of the Child Behavior Checklist (CBCL/4–18). Longitudinal models were applied to assess the relationships between maternal pre-pregnancy BMI and affective problems from age 5 through 17. There was a higher risk of affective problems between the ages of 5 and 17 years among children of women who were overweight and obese compared with the offspring of women in the healthy pre-pregnancy weight range (BMI 18.5–24.99) after adjustment for confounders, including paternal BMI. Maternal pre-pregnancy overweight and obesity may be implicated in the development of affective problems, including depression, in their offspring later in life.

Received 7 June 2012; Revised 19 July 2012; Accepted 13 August 2012; First published online 6 September 2012

Key words: depression, mood disorders, obesity, overweight, pre-pregnancy maternal weight

Introduction

Pre-pregnancy overweight and obesity is of increasing global concern for obstetric care providers.[1,2] In addition to the perinatal risks posed to mother and infant, maternal obesity may predispose the offspring to obesity, diabetes and metabolic syndrome later in life.[3] However, until recently very little was known about the relationship between maternal pre-pregnancy overweight and obesity and mental health outcomes for offspring.[4]

Recently, three studies have reported on putative links between the two. The first found that in three cohorts a higher body mass index (BMI) before pregnancy was linked to a greater risk for teacher-rated attention-deficit hyperactivity disorder symptoms in 7- to 12-year-old offspring, including increased inattention and hyperactivity.[5] These authors followed this study with another incorporating symptoms of negative emotionality in the early years, for example sadness, fear and anger.[6] Maternal pre-pregnancy obesity, overweight and underweight were related to both an increased presence of inattention and also higher rates of negative emotionality in children as rated by their teachers.[6] Unfortunately, in the latter study, investigators were unable to examine outcomes past the age of 5 years. In the third study, although some associations between a higher maternal pre-pregnancy BMI and a greater risk for behavioral problems were found, these relationships were no longer significant following adjustment for confounders in children up to the age of 4 years.[7] These authors concluded that there was little evidence for intrauterine effects of a higher pre-pregnancy maternal BMI on child behavior and cognition, but rather the effects observed in previous studies were the result of residual confounding.[7] From these studies, it is uncertain what effect, if any, a higher maternal pre-pregnancy BMI may have on child mental health outcomes, and it is particularly unclear at what age any effects become evident and which specific aspects of mental health may be implicated.

Affective problems, including major depressive disorder and dysthymic disorder (chronic, less severe depression), are among the most common types of mental disorders known to affect both children and adolescents.[8] Although relatively little research has addressed the fetal origins of mental health problems, including depression, new evidence has emerged to suggest that common mental disorders such as depression may be impacted by factors present in fetal life.[9,10] There is also evidence to suggest that obesity and the metabolic syndrome

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https://doi.org/10.1017/S2040174412000578 Published online by Cambridge University Press

are linked to an elevated risk for depression, which points to a possible link to maternal metabolic conditions and *in utero* programming of the fetal brain.[11]

This study aimed to determine the relationship between maternal pre-pregnancy BMI and the development of affective problems, including depression, in a cohort of children followed longitudinally from pregnancy to 17 years, with adjustment for multiple confounding factors including socioeconomic and perinatal factors. We hypothesized that maternal overweight and/or obesity during pregnancy would be associated with an increased likelihood of developing affective problems during childhood and adolescence.

Methods

Participants

This study was conducted using data from the Western Australian Pregnancy Cohort (Raine) Study, a prospective pregnancy cohort study of 2868 live births followed from 1989 to the present day. Complete details of the initial cohort and recruitment procedures are published elsewhere.[12] The study families provided detailed sociodemographic, behavioral and clinical data at subsequent follow-ups. We used data collected during pregnancy at 18 and 34 weeks of gestation and at the 5-, 8-, 10-, 14- and 17-year follow-ups. Informed consent was obtained at the time of enrollment and at every subsequent follow-up, and protocols were approved by the Human Ethics Committees at King Edward Memorial Hospital (KEMH) and Princess Margaret Hospital for Children in Perth, Western Australia. We were able to recruit 90% of those eligible for participation, and the initial sample was representative of the KEMH population.[12] Those who were socially disadvantaged were less likely to remain in the study, but by 14 years the population was similar to the Western Australian population.[13] At the 17-year follow-up, 2352 adolescents and their families were eligible for follow-up (480 had withdrawn, prohibiting further contact, and 36 were deceased). Of those eligible to participate, 414 declined to participate in this follow-up and 184 were unable to be traced, leaving 1754 adolescents and their families who were available to participate in the 17-year follow-up. This represented 75% of those eligible to participate at age 17 and 61% of the original cohort of 2868 live births.

Affective problems

The 118-item Child Behavior Checklist for ages 4–18 (CBCL/4–18) was administered at the 5-, 8-, 10-, 14- and 17-year follow-ups and completed by the primary caregiver.[14] The CBCL demonstrated sensitivity (83% overall) and specificity (67% overall) to a clinical psychiatric diagnosis and good test–retest reliability in a Western Australian clinical calibration.[15] The CBCL/4–18 produces a raw score that was transformed into *T*-scores (standardized by age and sex) for six problems scales using the CBCL Diagnostic and Statistical Manual of Mental Disorders (DSM)-Oriented Scales.[16] The problem scales are considered to map well against the diagnostic criteria of the DSM-IV for affective problems, anxiety problems, somatic problems, attention-deficit/hyperactivity problems, oppositional defiant problems and conduct problems.[17] For this study, the affective problems scale was used, and we applied the recommended clinical cutoff scores (by age and sex) to the *T*-scores to obtain a binary variable indicative of clinically significant affective problems. The term 'clinically significant' refers to maladaptive behavior that falls within a defined clinical range for behavioral problems.[14]

Maternal pre-pregnancy obesity

At 18 weeks of gestation, participants completed a questionnaire that included a request for self-reported weight before pregnancy. Women were asked 'What is your usual weight when you are not pregnant?' and whether they could provide the answer in either stones/pounds or kilograms. If women could not answer this question, their weight at the completion of this questionnaire was used to estimate pre-pregnancy weight. All weights were converted to kilograms. Height measurements were taken at this assessment and used together with the weight (verified by nurses) to calculate BMI before pregnancy using the standard formula [BMI: weight (kg)/height $(m)^2$]. Using the standard cutoffs, we classified BMI measurements into healthy weight, underweight (BMI $<$ 18.5), overweight (BMI $\geqslant$ 25.0) and obese (BMI $\geqslant$ 30.0).[18] In this paper, we refer to 'overweight' as a separate category from 'obese', although we note that by definition obese women are also overweight. Based on World Health Organization principles, we did not separate Asian mothers ($n = 206$) in our classification of BMI categories because of substantial variation in Asian populations.[19] We also calculated paternal BMI using the same formula and cutoffs, based on the father's height and weight measurements collected at enrollment, and this was included in our models as a categorical variable.

Control variables

We adjusted for biological and psychosocial factors from pregnancy, which are known to influence child and adolescent mental health.[10] These factors included maternal age at conception, maternal education, total family income, maternal smoking in pregnancy, maternal alcohol consumption in pregnancy, the presence of the biological father in the family home and the maternal experience of stressful events, measured using a stressful life events scale[20] (all collected at 18 weeks of gestation). We also adjusted for perinatal data including gestational age at birth, maternal gestational diabetes, maternal hypertensive disorders of pregnancy, duration of breastfeeding and birth weight.

Statistical analyses

Frequency data were compared using cross-tabulations for all control variables according to categories of pre-pregnancy

https://doi.org/10.1017/S2040174412000578 Published online by Cambridge University Press

maternal BMI, our predictor variable. We used a logistic regression model to examine whether our predictor variable was associated with clinically meaningful differences in affective problems (i.e. a score above the relevant clinical cut point for age and sex) after establishing that there were no significant (at $P < 0.05$, two-tailed) interactions between maternal pre-pregnancy BMI and the child's age on the outcome of affective problem scores. The model accounted for lack of independence due to repeated observations of the same individuals over time by incorporating generalized estimating equations (GEE).[21] Our model first examined univariate relationships, followed by the inclusion of all potentially confounding variables from pregnancy (paternal BMI, maternal age, maternal education, total family income, maternal smoking, maternal alcohol consumption and the presence of the biological father in the family home), and finally the inclusion of the potentially intermediate variables, which may mediate the relationship between our predictor and outcome variables (maternal experience of stressful events, gestational age, maternal gestational diabetes, maternal hypertensive disorders of pregnancy, duration of breastfeeding and birth weight). This allowed us to examine the effect of partial and full adjustment on our models. IBM SPSS Statistics 19.0 was used for the analyses.

Results

From the 2868 live births in the study, we had data on maternal pre-pregnancy BMI for 2765 mothers (Table 1). Of these women, 1946 (70%) were of healthy weight before pregnancy, 320 were underweight (12%), 319 were overweight (12%) and 180 were obese (7%). Of the children from mothers with valid BMI data who completed the CBCL/4–18, at age 5, 200 (9.4%) were within the clinically significant range for affective problems, with 220 (10.8%) at age 8, 184 (9.3%) at age 10, 119 (6.8%) at age 14 and 103 (7.6%) at age 17 years.

The maternal factors associated with being obese pre-pregnancy included not having finished high school, low income and increased number of cigarettes smoked per day. More than half of all women who were obese before pregnancy had a partner who was either overweight or obese. Overweight and obese women were more likely to develop hypertensive diseases of pregnancy, and their infants were heavier at birth and were breastfed for a shorter duration than the infants of healthy-weight mothers. Being underweight, overweight or obese was associated with an increased likelihood of experiencing three or more stressful life events during pregnancy.

Maternal pre-pregnancy BMI and CBCL/DSM-IV affective problems

We compared pre-pregnancy maternal BMI with affective problem morbidity scores in a logistic regression model (Table 2). We did not observe any significant relationship between pre-pregnancy underweight and risk for affective disorders in children. In the unadjusted, partially adjusted and fully adjusted models, pre-pregnancy obesity was associated with a significantly increased risk of presenting with an affective problem score above the clinical cutoff for morbidity compared with the children of women who were a healthy weight before pregnancy (OR = 1.72, 95% CI = 1.11, 2.67). The children of women who were overweight but not obese were also at a higher risk for affective problems (OR = 1.51, 95% CI = 1.08, 2.12) after adjustment for prenatal and perinatal confounders. Three of the covariates were independently associated with affective problem scores (data not presented). Women who had stayed in high school for longer had children with a lower risk for affective problems (OR = 0.87, 95% CI = 0.77, 0.98), and women who did not live with the biological father of their child during pregnancy (OR = 2.30, 95% CI = 1.42, 3.74) and women who had experienced a higher number of stressful life events during pregnancy (OR = 1.22, 95% CI = 1.15, 1.30) had children with a higher risk for affective problems through to age 17.

Discussion

The key finding of this study was that the offspring of women who were overweight or obese before pregnancy were more likely to have clinically significant affective problems during childhood and adolescence. There were no significant associations evident for women with a BMI in the underweight weight range when analyzed against clinical affective problems. These findings were independent of influences from both within the gestational period and peri- and postnatal mediators, including paternal BMI.

Our results support the recent finding that maternal pre-pregnancy obesity was related to an increased rate of negative emotionality (e.g. sadness, fear and anger) in preschool children.[6] We have extended these findings in examining the effect of pre-pregnancy obesity on outcomes from the age at which the previous study finished (5 years) and following outcomes through to the age of 17 years. In addition, we used maternal reports in which previous studies either relied purely on teachers' reports or found that only teachers' report were significant, rather than maternal ratings of child emotionality.[6] It is known that there can be inconsistency between teacher and parent reports on the CBCL,[22] although the recent study by Brion *et al.*[7] did not find any significant difference between maternal and teacher report in their analysis of the effect of pre-pregnancy BMI on child behavior. Our study is the first, to the best of our knowledge, to examine the effect of pre-pregnancy BMI on child affective problems through to the end of adolescence.

We designed our analytical models so as to be able to ascertain the differences between prenatal confounding and pre- or postnatal factors that may mediate the relationships evident in our study. This was particularly important given the recent conflicting findings as to the role of residual confounding in these observed associations.[4,7] Our adjustment

https://doi.org/10.1017/S2040174412000578 Published online by Cambridge University Press

Table 1. *Cross-tabulations presenting frequency characteristics of sample according to weight category (n = 2765)**

	Maternal pre-pregnancy BMI			
	Healthy weight (*n* = 1946; %)	Underweight (*n* = 320; %)	Overweight (*n* = 319; %)	Obese (*n* = 180; %)
Paternal BMI				
Healthy weight	60.9	66.3	57.7	44.3
Underweight	1.5	1.4	2.3	3.1
Overweight	31.9	28.5	32.5	38.9
Obese	5.7	3.9	7.5	13.7
Maternal age at conception				
<20 years	9.0	16.3	9.7	8.3
20–24.9 years	19.1	28.1	21.9	33.9
25–29.9 years	30.5	32.2	30.4	23.9
30–34.9 years	27.8	16.6	23.2	20.6
35+ years	13.6	6.9	14.7	13.3
Maternal education at pregnancy				
<High school completion	58.2	63.6	67.4	73.9
High school completion	41.8	36.4	32.6	26.1
Father living with family				
Yes	87.8	85.0	86.8	86.7
No	12.2	15.0	13.2	13.3
Maternal ethnicity				
Caucasian	89.1	81.3	88.4	90.6
Asian	7.1	14.7	4.4	2.8
Other	3.8	4.1	7.2	6.7
Low family income in pregnancy				
≤$24,000 per annum	28.0	36.8	41.5	58.1
>$24,000 per annum	72.0	63.2	58.4	41.9
Smoking in pregnancy				
None	75.1	62.5	71.8	72.8
1–5 daily	8.2	12.2	6.9	8.3
6–10 daily	6.4	10.6	6.6	6.7
11–15 daily	5.0	7.8	5.6	5.0
16–20 daily	3.6	3.8	5.0	3.9
21+ daily	1.6	3.1	4.1	3.3
Alcohol in pregnancy (number of drinks)				
None	52.2	59.1	55.8	66.1
≤1/week	23.7	23.0	26.0	17.8
2–6/week	19.6	13.8	15.0	12.2
7–10/week	2.7	2.2	1.6	3.3
11+/week	1.8	1.9	1.6	0.6
Stress events in pregnancy				
None	23.3	19.5	19.5	16.2
1–2 events	41.0	40.1	41.6	38.3
3+ events	35.6	40.4	38.9	45.5
Gender of child				
Male	51.4	48.4	51.4	48.9
Female	48.6	51.6	48.6	51.1
Gestational diabetes				
No	98.7	99.4	96.6	91.6
Yes	1.3	0.6	3.4	8.3
Hypertensive diseases of pregnancy				
None	79.4	86.3	66.8	65.6
Gestational hypertension	18.4	10.6	29.5	27.2
Preeclampsia	2.2	3.1	3.8	7.2
	Healthy weight mean	Underweight mean	Overweight mean	Obese mean
Gestational age				
Weeks	38.83	38.65	38.53	38.77
Birth weight				
Grams	3317.12	3154.80	3363.29	3485.36
Breastfeeding duration				
Months	7.97	6.37	6.89	6.45

BMI, body mass index.

*Missing data excluded from analyses, row percentages presented.

https://doi.org/10.1017/S2040174412000578 Published online by Cambridge University Press

Table 2. *Relationship between maternal pre-pregnancy BMI and CBCL/DSM-IV affective problems*

	Multivariate logistic GEE model – years 5–17 inclusive[a]		
	Unadjusted analysis	Partially adjusted analysis[b]	Fully adjusted analysis[c]
Maternal pre-pregnancy BMI (category)			
Normal weight	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Underweight			
OR	0.84	0.72	0.75
95% CI	(0.60, 1.18)	(0.48, 1.07)	(0.48, 1.17)
P-value	0.324	0.104	0.200
Overweight			
OR	1.26	**1.44***	**1.51***
95% CI	(0.92, 1.71)	(1.03, 2.03)	(1.08, 2.12)
P-value	0.145	0.036	0.017
Obese			
OR	**1.61***	**1.68***	**1.72***
95% CI	(1.12, 2.31)	(1.11, 2.55)	(1.11, 2.67)
P-value	0.010	0.014	0.016

BMI, body mass index; CBCL, Child Behavior Checklist; DSM, diagnostic and statistical manual of mental disorders; GEE, generalized estimating equations; ref. = reference category; OR, odds ratio; CI, confidence interval.

Bold values indicate significance at $^{*}P < 0.05$, $^{**}P < 0.005$.

[a] Obtained with binomial distribution, logit link and auto-regressive working correlation matrix.

[b] Adjusted for paternal BMI, maternal age, maternal education, presence of the biological father in the family home, family income, maternal alcohol consumption and maternal cigarette smoking.

[c] Adjusted for maternal age, maternal education, presence of the biological father in the family home, family income, stress in pregnancy, maternal cigarette smoking, maternal alcohol consumption, gestational age at birth (weeks), birth weight (grams), hypertensive diseases of pregnancy, gestational diabetes and length of breastfeeding.

for paternal BMI at enrollment (18 weeks' gestation) was a particular strength of this study. Although for the most part adjustment did not change whether or not our findings were statistically significant, we did observe some change in the effect sizes in the GEE model (Table 2) when socio-demographic factors, including paternal obesity, were taken into account in the partially adjusted model, but less change in the effect size when perinatal factors were added to the model in the fully adjusted analysis.

Pre-pregnancy obesity has the potential to increase the risk for obstetric complications, and we adjusted for some obstetric complications, although we acknowledge that our list was not exhaustive.[23] We adjusted for the presence of hypertensive diseases of pregnancy, which are linked with both maternal overweight and obesity and the development of behavioral problems in childhood and adolescence.[24] We also adjusted for gestational age and birth weight to ensure that pre-term birth or birth weight were not responsible for the observed effects. Pre-term infants have been found to have more behavioral problems later in life than infants born at full term, including social and attention problems.[25] A large Scandinavian population-based study found that babies who were born pre-term had a one in three chance of developing a behavioral problem by the age of 10 years.[26] Similarly, a number of negative developmental outcomes have been associated with birth weight, including a higher risk for behavioral problems for both low and high birth weight.[27] It was interesting to note that in our analyses adjusting for these factors had only a minor impact on our effect sizes, and thus we suggest that there may be other mechanisms that could explain our results.

A child born to an obese mother is likely to exist within the same 'obesogenic' environment as their mother, and mental health may be influenced by childhood lifestyle factors associated with this environment, for example a lack of physical activity, increased sedentary behaviors and a poor-quality diet.[28] A further explanation for our results may lie with the bidirectional association between obesity and mental illness; however, data on maternal affective disorders were not available for this study. Studies have found that obesity leads to a higher incidence of major depressive disorder, and being obese had a negative impact on the course of mental illness and the response to treatment.[29]

Strengths and limitations

A strength of our study was the use of prospectively collected data over the course of 17 years, from pregnancy to the beginning of adulthood in order to provide the longitudinal

https://doi.org/10.1017/S2040174412000578 Published online by Cambridge University Press

picture that is necessary for research of this nature. We were also able to adjust for a number of potential confounding and mediating variables according to the hypothesis-driven nature of this research in terms of separating those factors that potentially mediate the relationships observed. However, the overweight and obese mothers were of lower education and income status and more likely to smoke, and statistical adjustment for the relatively crude measures of these psychosocial confounders may not be adequate. The use of the CBCL was also a strength, as it is a well-validated and reliable measure of child behavior with good internal consistency in the diagnosis and prediction of behavioral problems.[30] A limitation of the study was the reliance on maternal self-report for pre-pregnancy weight, although in a recent study of women of reproductive age self-report was found to be valid with 84% of women correctly classified into the correct BMI categories.[31] We were also unable to adjust for maternal affective problems either before or during pregnancy because of the data being unavailable and relied on maternal report of life stress instead, which was assessed at 18 and 34 weeks' gestation and verified by the research nurse at the time of collection.

Implications

The public health implications of this study are substantial given the dual burdens of lifestyle-related diseases associated with obesity and depression in Western society.[32] If the relationships are causal, then any intervention that attempted to reduce overweight and obesity in women of reproductive age could potentially have an effect on reducing the rates of depressive symptoms in the population. However, thus far there appears to be a deficiency of effective interventions for maternal obesity both before and during pregnancy.[2] Designing a program to target overweight and obese women before they become pregnant is challenging, as women do not necessarily consult a health professional before conceiving and the idea of postponing a family until they reduce their weight to within the healthy range, a process that may take months or years, is unlikely to appeal.[2] Nevertheless, achieving a normal weight before pregnancy has other benefits, including enhancing fertility and decreasing the risk of many obstetric complications.[2,23]

Conclusion

We have shown that women with a BMI that is classified before pregnancy as overweight or obese are more likely to have children who will develop an affective problem such as depression during childhood and adolescence. We recommend that further research is conducted to delineate the nature of this association in order to more fully inform potential interventions in the pregnancy and pre-pregnancy period.

Acknowledgements

The authors acknowledge the core funding and support of the Raine Medical Research Foundation, The University of Western Australia (UWA), the National Health and Medical Research Council of Australia (NHMRC), the; Telethon Institute for Child Health Research, the; Telstra Foundation, the Western Australian Health Promotion Foundation, the UWA Faculty of Medicine, Dentistry and Health Science, the Women and Infants Research Foundation, Australian Health Management and the National Heart Foundation of Australia/Beyond Blue. Dr Robinson is funded by Australian Rotary Health and Qantas. The authors are extremely grateful to all the families who took part in this study and the Raine Study team, which includes data collectors, cohort managers, data managers, clerical staff, research scientists and volunteers.

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