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Maternal pre-gravid obesity and early childhood respiratory hospitalization: a population-based case-control study

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Abstract

Objectives—Inflammation *in utero* is linked to childhood respiratory and infectious complications. Obesity is an increasingly common chronic inflammatory state, yet little is known about its role in childhood respiratory illness. We sought to examine the association between maternal pre-gravid BMI and early childhood respiratory hospitalization.

Methods—We conducted a population-based case-control study using the Washington State Comprehensive Hospital Abstract Reporting System (CHARS) and linked birth certificate data. Cases were children age 0 to 5 years, born in Washington state, with a respiratory hospitalization between 2003 and 2008. We identified 15,318 cases, frequency matching each case to two controls by birth year (total 31,060 controls). We used logistic regression to estimate the risk (approximated by odds ratios) of early childhood respiratory hospitalization according to maternal pre-gravid body mass index (BMI) category (underweight, normal, overweight, obese), after adjustment for maternal and infant characteristics.

Results—An elevated maternal pre-gravid BMI was associated with increased risk of childhood respiratory hospitalization, with an adjusted odds ratio OR [95% CI] = 1.08 [1.03–1.14] for overweight mothers (BMI 25–29.9 kg/m^2), and OR = 1.29 [1.22–1.36] for obese mothers (BMI ≥ 30 kg/m^2).

Conclusions—An elevated maternal pre-gravid BMI was associated with higher risk of early childhood respiratory hospitalization. Childhood respiratory illness may be an important complication of excess maternal weight that should be shared with expectant mothers.

Keywords

obesity; overweight; mother; infant; child; respiratory tract diseases; asthma; respiratory illness; bronchiolitis

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Conflict of Interest
The authors declare no conflict of interest.

Introduction

Pediatric respiratory illness contributes more to chronic childhood disease burden and health care costs than any other organ or tissue-specific disease (1). Of all pediatric respiratory illnesses, asthma is arguably the most important focus of public health initiatives in developed countries. In the United States, asthma ranks second only to pneumonia as the most common (and potentially preventable) cause of childhood hospitalizations (2). Both asthma prevalence and hospitalizations remain at a historically high level since the 1990s (3–5), causing a disproportionate burden of emergency department visits and hospitalizations in children under 5 years of age (4). According to the U.S. National Health Interview Survey, the number of children suffering from asthma in the past year approximately doubled from 3.6% in 1980 to 7.5% in 1996 (5). During this time, there has been a parallel increase in the proportion of overweight and obese individuals in the U.S. (6, 7) Numerous studies have demonstrated a link between childhood obesity and asthma (8), though establishing the direction of this relationship can be challenging. Hormonal and pro-inflammatory effects, such as elevated TNF-alpha and IL-6 (9, 10), have been proposed as potential mechanisms by which obesity may predispose children to asthma.

There is recent interest regarding whether *in utero* exposure to proinflammatory factors from maternal obesity may also place children at higher risk of respiratory illness. Mirroring the rising trend in childhood obesity, the prevalence of obesity in American women of childbearing age has steadily increased from 15% in 1976 to 31.9% in 2009 (6, 7). The intrauterine environment is increasingly regarded as an important influence on the development of the fetal immune and respiratory systems. I*n utero* exposures to certain inflammatory states (chorioamnionitis, smoking) have been associated with both infant respiratory illness and childhood asthma (11, 12). Data are limited regarding the link between maternal obesity and childhood respiratory illness. Two large population-based studies in Norway and the Netherlands have demonstrated that children of mothers with pre-gravid or gestational obesity are at higher risk of asthma (defined by wheeze, dyspnea, or use of a inhaled corticosteroid) (13, 14). In the United States, studies have reported associations between maternal obesity and recurrent wheeze or parent-reported asthma (15, 16). However, there are no studies to our knowledge that address whether maternal obesity is associated with an increased risk of severe respiratory illness requiring hospitalization (13, 14).

We conducted a population-based case control study in Washington State, U.S., to examine whether maternal pre-gravid obesity is associated with higher risk of childhood hospitalization for respiratory illness including asthma. We hypothesized that children born to mothers with pre-gravid overweight (BMI 25 to 29.9 kg/m^2) or obesity (BMI ≥ 30 kg/m^2) would be at higher risk of respiratory hospitalization during early childhood, compared to children of mothers with normal pre-gravid weight. We also hypothesized that this association may differ depending on the presence or absence of perinatal factors associated with increased risk of childhood respiratory illness, including low birth weight, preterm delivery, and caesarean section (17–19).

Methods

Selection of Cases and Controls

We conducted a population-based case-control study using maternally linked birth certificate data from Washington (WA) State from 2003 to 2008. We identified cases via the Comprehensive Hospital Abstract Report System (CHARS), which includes data on all hospital-born infants in Washington State (only 2.2% of children in WA state are born out-of-hospital) (20). Cases were defined as children age 0 to 5 years who were hospitalized for

a respiratory illness between January 1, 2003 and December 31, 2008. Respiratory illness was defined by ICD-9 admission diagnosis codes, as detailed in a previous study (18). These include ICD-9 codes for asthma (493.0, 493.9, 493.82, 493.1, 493.81), acute bronchitis/bronchiolitis (466 including 4 and 5 digit subclasses), pneumonia/influenza (480–487, including 4 and 5 digit subclasses), bronchitis (490), chronic airways obstruction (496), chronic bronchitis (491, including 4 and 5 digit subclasses), bronchiectasis (494 with all 4 and 5 digit subclasses), respiratory symptoms (786.00, 786.05, 786.07, 786.09, 786.1, 786.2, 786.3, 786.4, 518 with all 4 and 5 subclasses), hypoxemia (799.02), respiratory arrest (799.1), and mechanical ventilation (96.7, including 4 and 5 digit subclasses). Individuals identified from CHARS were retained as cases if they could be linked to the WA State Birth Certificate Database for the years 2003 to 2008. Linkage was performed using date of birth and the first two letters of the first and last names (21).

Controls were randomly selected from the WA State birth certificate database and frequency matched to cases by birth year. This database collects data regarding the mother, father, pregnancy and child at hospitals and birth centers using worksheets completed from medical charts, medical staff, parents, or a combination of these sources. In the case of out-of-hospital births, midwives complete the forms with parental assistance. This study was designed to have sufficient power (>80%) to detect an odds ratio equal to or greater than 1.2 between maternal overweight and obesity and childhood respiratory hospitalization. We estimated that during the study years, there would be approximately 12,600 respiratory hospitalizations (including 1,800 asthma hospitalizations), and that 40% of mothers would be underweight or normal weight, 30% would be overweight and 30% would be obese. Consequently, we matched 2 controls to each case, providing sufficient power (<80%) to examine both respiratory hospitalizations and asthma-specific hospitalizations. Controls were filtered through the WA State Department of Health death file to exclude individuals known to have died before 5 years of age. Only the first hospitalization during the study period for each child was included. The University of Washington Institutional Review Board approved this study.

Exposure: Maternal Anthropometric Measures

Our primary exposure was pre-gravid BMI, which was determined by medical chart review (when available), or alternatively by maternal self-report. We classified maternal pre-gravid BMI into four categories: underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–25 kg/m^2), overweight (BMI 25 to 29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2), as per current guidelines (22). Subjects with missing maternal BMI data were excluded from the analysis.

Additional clinical variables

We obtained data on a host of maternal, obstetric, and perinatal variables that may confound or modify the relationship between maternal BMI and childhood respiratory hospitalization. Maternal-reported birth certificate data included maternal age, race, education, income, smoking, parity, marital status, and plan to breastfeed. We categorized variables as follows: maternal age (<20 years, 20–34 years, 35+ years), maternal race/ethnicity (white, black, Asian, Pacific Islander, Hispanic, Native American), maternal income (by quartile), smoking during pregnancy (yes/no), parity (0, 1, 2, 3+), marital status (married/unmarried), and plan to breastfeed at the time of delivery (yes/no). The only record of family history of asthma available in CHARS was a history of maternal asthma hospitalization, defined by ICD-9 code before or at the time of hospitalization for delivery. Infant and perinatal characteristics obtained from birth certificates included: child's sex, delivery year (2003–2008), gestational age (weeks), birth weight (grams), and delivery mode (caesarean-section or vaginal).

Statistical Analysis

All statistical analyses were performed using STATA 11.0 (StataCorp, College Station, TX). We used logistic regression with robust standard errors to calculate crude odds ratios (OR) of the risk of childhood respiratory hospitalization for maternal overweight and obesity compared to maternal normal weight. We first modeled our exposures of maternal overweight and obesity using dummy variables for each maternal BMI category, and then as a grouped linear variable to evaluate whether there was a linear trend in hospitalization risk with increasing maternal BMI category. Analyses included multivariable adjustment for pre-determined potential confounders that have been associated with both maternal obesity and childhood respiratory illness, including maternal characteristics (age, income, race, education, smoking, parity, marital status, history of asthma hospitalization, and plan to breastfeed) and child characteristics (sex and birth year, included because cases and controls were frequency matched by birth year).

Three perinatal factors (low birth weight, preterm delivery, and caesarean section) have been previously associated with an increased risk of childhood respiratory hospitalization and may also be more common in children born to obese mothers (17–19). We did not adjust for these factors because we hypothesized that they were part of the causal pathway of interest. That is, maternal obesity may cause children to be born at low birth weight or premature (through growth retardation, or preeclampsia requiring early delivery) with abnormally developed lungs that are more susceptible to respiratory illness. Instead of adjusting for these factors, we chose to perform stratified analyses to assess whether the association between maternal obesity and childhood respiratory hospitalization differed by their presence or absence, hypothesizing that .we may find stronger associations in children with preterm delivery, low birth weight, or those requiring C-section. For stratified analyses, we grouped children according to the following categories: 1) gestational age: preterm (<37 weeks), term (37 – 41.9 weeks), and post term (42+ weeks), 2) birth weight: low birth weight (<2500 g), normal birth weight (2500 – 3999 g), and macrosomia (>=4000g), and delivery method (caesarean section versus vaginal).

Sensitivity Analyses

We performed several secondary analyses using modified exposure and outcome variables. To explore whether maternal obesity was specifically associated with risk of childhood asthma, we performed a subgroup analysis restricting our outcome to respiratory hospitalization with a diagnosis of asthma, defined by ICD-9 codes (Table 1). To examine whether the timing of excess weight is an important factor in childhood respiratory hospitalization, we repeated our regression analysis using secondary exposure variables of maternal BMI at delivery and gestational weight gain. We categorized gestational weight gain into three categories based on maternal pre-gravid BMI: excessive (greater than the recommended values), appropriate (within recommended values), or inadequate (below recommended values). Appropriate pregnancy weight gain was defined by the Institute of Medicine 2009 guidelines: 28 to 40 pounds for underweight, 25 to 35 pounds for normal weight, 15 to 25 pounds for overweight, and 11 to 20 pounds for obese women, respectively (23).

Results

From 2003 to 2008, there were 510,858 live births (mean 85,143 births/yr) in WA State (24). From 2003 to 2008, we identified 18,411 children 0 to 5 years of age with a respiratory hospitalization through CHARS that had WA State Birth Certificate records documenting birth in WA State, after excluding duplicate linkages. Two controls were selected for every case, for a total of 55,233 subjects. We excluded subjects with missing maternal BMI or

other model covariates (5407 cases and 8937 controls, 26.0% of entire cohort). Our final analysis cohort included 13,004 cases and 27,885 controls.

Maternal and Delivery Characteristics

Cases were more likely to be male, earlier gestational age, delivered by C-section, and have lower birth weight compared to controls (Table 1). Mothers of cases were younger with lower average annual incomes compared to mothers of controls. Mothers of cases were more likely to be unmarried, multiparous, non-white, have a history of asthma hospitalization, and to have smoked during pregnancy.

Primary Outcome: Childhood Respiratory Hospitalization

The majority (71%) of respiratory hospitalizations occurred in children less than 1 year of age, 25% in children aged 1 to <3 years, and only 4% in children aged 3 to 5 years. Children of overweight and obese mothers had a 1.08-fold (95% CI 1.03–1.14) and 1.29-fold (95% CI 1.22–1.36) increased risk of respiratory hospitalization compared to children of normal weight mothers, after adjustment for confounding factors (Table 2). The association between maternal obesity and childhood respiratory risk differed minimally by birth weight, gestational age, and mode of delivery (Table 3). The odds ratios for respiratory hospitalization associated with maternal obesity were 1.35, 1.30, and 1.17 in low birth weight, normal birth weight, and macrosomic babies. Although the association between maternal obesity and childhood respiratory hospitalization was slightly stronger among children born post-term (OR=1.72) than for preterm (OR=1.32) or term (OR=1.28) births, the finding in post-term births was not statistically significant, due at least in part to small sample size (n=433, 1.0% of cohort).

Sensitivity Analyses

A total of 2,896 children (18.9% of cases) were hospitalized specifically for asthma. We observed a similar association between increasing maternal pre-gravid BMI and childhood asthma hospitalization risk (adjusted OR for maternal obesity = 1.36 [1.23 – 1.49]; P for trend <0.001).

BMI at delivery and gestational weight gain were missing in approximately 3% and 4% of birth certificate records, respectively. Higher maternal BMI at delivery was associated with a similar but attenuated risk of respiratory hospitalization compared to maternal pre-gravid BMI (with an adjusted OR [95% CI] = 0.95 [0.88 – 1.03] for overweight mothers and OR = 1.05 [0.98 – 1.14] for obese mothers; P for trend = 0.03). Conversely, we found that excessive gestational weight gain was associated with a lower risk of respiratory hospitalization (adjusted OR [95% CI] = 0.92 [0.88 – 0.97]; P for trend < 0.001) despite adjustment for maternal pre-gravid BMI and exclusion of women with pre-gravid BMI ≥ 25 kg/m^2 from the analysis. Exploratory analyses suggested that our findings may be explained by differences in preterm delivery, which occurred most frequently among mothers with inadequate weight gain (13%) and least often in those with excessive weight gain (6%). Excessive maternal weight gain was not significantly associated with childhood respiratory hospitalization risk after adjustment for gestational age (P=0.73, results not shown).

At the request of reviewers, we repeated our primary analysis with additional adjustment for maternal diabetes (both pre-existing and gestational), which may serve as a causal mediator between maternal obesity and childhood respiratory risk. Our results were unchanged, suggesting that maternal diabetes is not responsible for the observed association.

Discussion

We found that children born to mothers with pre-gravid overweight or obesity had a higher risk of hospitalization for respiratory illness including asthma in the first 5 years of life, after adjusting for important confounders including sociodemographic characteristics, maternal smoking, and maternal asthma hospitalization. In analyses using alternative measures of maternal obesity, BMI category at delivery exhibited a weaker association with childhood respiratory hospitalization risk than pre-gravid BMI category, while excessive gestational weight gain was associated with a decreased risk. This latter result did not appear to be explained by confounding from pre-gravid weight, but rather by an inverse relationship between gestational weight gain and gestational age.

Our results highlight the importance of careful choice of exposure measurement to study the relationship between maternal obesity and childhood outcomes. We found that obesity prior to pregnancy was a stronger risk factor for childhood respiratory hospitalization than obesity at delivery. This is consistent with the hypothesis that a chronic inflammatory milieu may contribute to poor lung development *in utero*. BMI at delivery may misclassify many women of normal pre-gravid weight as overweight or obese (in our study, 84% of pre-gravid normal weight women met overweight/obese criteria at delivery), biasing risk estimates towards the null. Furthermore, excessive gestational weight gain was inversely associated with the risk of childhood respiratory hospitalization in our study. Our results are consistent with recently published data that this association is mediated by gestational age and the fact that inadequate weight gain is disproportionately associated with perinatal complications, including preterm delivery (25). Gestational weight gain is likely an inappropriate measure of maternal obesity because it reflects factors besides adiposity, including socioeconomic status and access to medical care (26).

Several prior studies have evaluated the relationship between maternal obesity and childhood respiratory illness. A population-based cohort study from Norway found that children born to mothers with a pre-gravid BMI ≥ 30 had a 3.3% higher attributable risk of wheeze compared to those born to normal weight mothers (13); this association was not explained by perinatal complications (low birth weight, preterm birth) or by maternal asthma or smoking. This study was limited by a subjective outcome (wheeze by maternal report), short follow-up (age 6 –18 months), as well as a 66% non-response rate (13). A U.S. birth cohort study of 1,971 children similarly found an increased odds of asthma by age 3 years among children of obese mothers. As in our study, the association was attenuated but remained significant after adjusting for factors including maternal asthma and smoking (OR =1.34; 95% CI: 1.03 – 1.76) (16). A more recent Netherlands birth cohort study of 3,963 children assessed parent-reported asthma at 8 years of age, stratifying by asthma predisposition (history of asthma in either parent) and adjusting for the child's current weight. Maternal obesity was associated with an increased risk of asthma only among children with an asthmatic parent, and the risk was of borderline significance after adjusting for the child's birth weight and current weight (OR = 1.01 – 1.10) (14). While our study was unable to rigorously assess the contributions of family history and childhood obesity due to lack of these variables in our dataset, these factors may have a role in childhood respiratory hospitalization that merits examination in future studies.

Maternal obesity may contribute to childhood respiratory complications through gestational exposure to a chronic inflammatory state, thus altering lung development. Adipose tissue produces a number of pro-inflammatory cytokines and hormones, collectively known as adipokines, such as tumor necrosis factor (TNF)-α, interleukins-6, 8, 10, 1-β and leptin (27). There is increasing evidence that inflammation *in utero* is a potent modulator of lung development, leading to disruption of alveolarization and microvascular development (28).

Pregnant obese women exhibit higher levels of proinflammatory factors (including IL-6 and C-reactive protein) and a heightened placental inflammatory response compared to pregnant women of normal weight (29). Placentae of obese women also exhibit alterations in immune cell populations compared to placentae of non-obese women, which may have implications for childhood susceptibility to infection (29, 30). Further characterization of the immunologic profile of maternal obesity and its correlation with markers of fetal lung development may help to identify mechanisms linking maternal obesity to childhood respiratory outcomes.

Our study is the largest population-based study to date examining the risk of childhood respiratory illness and maternal obesity. However, several limitations should be noted. Our matching of hospital-born cases to controls from the WA State birth certificate database creates the potential for selection bias, as children born outside the hospital system may differ in ways that affect the risk of respiratory hospitalization. We suspect that any such bias would be relatively small, since out-of-hospital births represent a small minority (2.2%) of all births in WA State (20). Second, our study carries limitations inherent to the use of administrative data collected for other purposes, including: inability to determine how individual subjects' data were collected, missing data, and potential confounding by unmeasured factors. Pre-gravid maternal weight was obtained from birth certificate data, reflecting a combination of medical chart data and maternal self-report (which is often underestimated). Without access to the primary data, we cannot determine how a specific woman's weight was recorded or whether reporting accuracy differed depending on birth location. Maternal BMI data were absent in 16% of our cohort. It is unclear in which direction this may have biased our results, as patients with missing data had a combination of characteristics that could place them at either increased (black race, C-section, lower birth weight) or decreased risk (higher education, higher income, and lower maternal smoking prevalence) for respiratory hospitalization (Supplemental Table E1). Third, we cannot exclude the potential for residual bias from factors that were recorded in a limited fashion (family asthma history) or not available (social support, adequacy of prenatal care, nutrition, duration of breastfeeding, smoking exposure, childhood obesity). We also cannot account for hospitalizations that may have occurred outside WA State.

Lastly, there are limitations due to our use of ICD-9 codes to detect severe respiratory illness meriting hospitalization. The decision to admit a child depends not only on illness severity but also potentially on unmeasured social factors. Pertinent to our secondary analysis of asthma-specific hospitalizations is the fact that the majority of our cases were children less than 3 years of age. Distinguishing asthma from infectious illness is particularly challenging in this age group. We expect that misclassification of infectious hospitalizations as asthma hospitalizations (and vice versa) would be unrelated to maternal BMI (non-differential bias), and therefore its effect would be to produce an underestimation of the true risk of asthma hospitalization associated with maternal obesity.

In conclusion, we found a significant association between maternal obesity and early childhood respiratory hospitalization. The association between maternal obesity and childhood respiratory hospitalization risk appeared to be irrespective of the presence or absence of common perinatal complications. Our study adds to the growing body of data showing that maternal obesity is associated with increased risks to offspring in the perinatal period and beyond. Knowledge that excess weight poses risks to future offspring may help to motivate women of childbearing age to develop healthier lifestyles and may be an important extension of public health strategies to improve the long-term health of mothers and their children. Future studies following children to older ages when asthma can be more accurately diagnosed, and in-depth examinations of the fetal milieu during pregnancy in

mothers with pre-gravid obesity, may lend further insight into the mechanisms linking maternal obesity and childhood respiratory illness.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Maternal and infant characteristics of cases and control subjects

Maternal characteristics	**Cases (n = 13,004)**	**Controls (n = 27,885)**
Pre-gravid BMI, *kg/m²*, mean (SD)	27.2 (6.8)	26.1 (6.2)
BMI at delivery, *kg/m²*, mean (SD)	32.1 (6.5)	31.3 (5.9)
Gestational weight gain, *kg*, mean (SD)	13.2 (7.4)	14.1 (7.2)
Age, *years*, mean (SD)	26.7 (6.2)	27.8 (6.0)
Race/ethnicity, n (%)		
White	9,097 (69.9)	21,036 (75.5)
Black	564 (4.3)	1,119 (4.0)
Asian/Pacific Islander	927 (7.1)	2,550 (9.1)
Hispanic	1,805 (13.9)	2,629 (9.4)
Native American	611 (4.7)	551 (2.0)
Education, *years*, n (%)		
< 12	3,723 (28.6)	4,954 (17.8)
12	3,486 (26.8)	6,584 (23.6)
13+	5,795 (44.6)	16,347 (58.6)
Average annual income, *dollars* *, mean (SD)	43,072 (15,440)	46,990 (16,275)
Married, n (%)	5,494 (42.3)	8,311 (29.8)
Smoked during pregnancy, n (%)	2,256 (17.4)	3,042 (10.9)
History of asthma hospitalization, n (%)	511 (3.9)	617 (2.2)
History of diabetes, n (%)		
Established	113 (0.9)	173 (0.6)
Gestational	778 (6.0)	1,411 (5.1)
Parity, n (%)		
0	4,297 (33.0)	11,657 (41.8)
1	4,179 (32.1)	8,874 (31.8)
2+	4,528 (34.8)	7,354 (26.4)
Plan to breastfeed, n (%)	10,972 (84.4)	25,215 (90.4)
Infant Characteristics		
Male sex, n (%)	7.622 (58.6)	14,238 (51.1)
C-section delivery, n (%)	3,931 (30.2)	7,148 (25.6)
Gestational age at birth, *weeks,* mean (SD)	38.2 (2.5)	38.9 (1.6)
Birth weight, *grams*, mean (SD)	3,261 (671)	3,432 (524)

* all P<0.01. Comparisons made using student's t test for continuous and chi square test for categorical variables.

Table 2

Adjusted odds ratios for early childhood respiratory hospitalization as a function of maternal pre-gravid BMI category

	Cases n (%)	Controls n (%)	OR (95% CI) [a]
Underweight	374 (2.9)	920 (3.3)	0.92 (0.81 – 1.05)
Normal	5,586 (42.9)	13,754 (49.3)	Ref
Overweight	3,383 (26.0)	7,103 (25.5)	1.08 (1.03 – 1.14)
Obese	3,661 (28.2)	6,108 (21.9)	1.29 (1.22 – 1.36)
P for trend			<0.001

[a]Adjusted for maternal age, maternal race, average income category (quartiles), maternal education level, marital status, smoking during pregnancy, parity, child's birth year, child's sex, maternal plan to breastfeed, maternal history of asthma hospitalization

Table 3

Adjusted odds ratio for early childhood respiratory hospitalization by maternal pre-gravid BMI category, stratified by birth weight, gestational age, and mode of delivery

	Cases n (%)	Controls n (%)	Adjusted OR (95% CI) [a]
Birth weight			
Low birth weight			
Underweight	57 (4.3)	68 (6.7)	0.67 (0.46 – 0.98)
Normal	639 (48.1)	536 (52.0)	Ref
Overweight	310 (23.3)	229 (22.2)	1.11 (0.90 – 1.38)
Obese	323 (24.3)	197 (19.1)	1.35 (1.09 – 1.68)
P for trend			0.001
Normal			
Underweight	302 (2.9)	803 (3.4)	0.93 (0.81 – 1.07)
Normal	4,507 (43.6)	11,938 (50.8)	Ref
Overweight	2,705 (26.1)	5,924 (25.2)	1.10 (1.04 – 1.17)
Obese	2,829 (27.4)	4,839 (20.6)	1.33 (1.26 – 1.42)
P for trend			<0.001
Macrosomia			
Underweight	13 (1.0)	47 (1.4)	0.78 (0.42 – 1.48)
Normal	423 (32.9)	1,265 (38.0)	Ref
Overweight	357 (27.7)	944 (28.4)	1.03 (0.87 – 1.22)
Obese	494 (38.4)	1,070 (32.2)	1.17 (0.99 – 1.38)
P for trend			0.44
Gestational age			
Preterm			
Underweight	86 (3.3)	89 (4.5)	0.66 (0.46 – 0.96)
Normal	1,126 (43.5)	930 (46.9)	Ref
Overweight	655 (25.3)	494 (24.9)	1.08 (0.91 – 1.28)
Obese	722 (27.9)	469 (23.7)	1.32 (1.11 – 1.57)
P for trend			<0.001
Term			
Underweight	313 (2.8)	840 (3.2)	0.95 (0.83 – 1.09)
Normal	4,707 (42.7)	12,816 (49.4)	Ref
Overweight	2,891 (26.2)	6,614 (25.5)	1.09 (1.03 – 1.15)
Obese	3,111 (28.3)	5,687 (21.9)	1.28 (1.21 – 1.35)
P for trend			<0.001
Post-term			
Underweight	4 (3.3)	8 (2.6)	1.51 (0.47 – 4.87)
Normal	54 (44.7)	157 (50.3)	Ref
Overweight	24 (19.8)	87 (27.9)	0.76 (0.43 – 1.36)
Obese	39 (32.2)	60 (19.2)	1.72 (0.96 – 3.09)
P for trend			0.18

	Cases n (%)	Controls n (%)	Adjusted OR (95% CI) [a]
Mode of delivery			
C-section			
Underweight	109 (2.2)	196 (2.5)	0.84 (0.64 – 1.10)
Normal	1,726 (35.8)	3,260 (40.6)	Ref
Overweight	1,306 (27.1)	2,148 (26.8)	1.07 (0.96 – 1.18)
Obese	1,681 (34.9)	2,417 (30.1)	1.17 (1.06 – 1.29)
P for trend			<0.001
Vaginal			
Underweight	337 (3.2)	823 (3.6)	0.96 (0.83 – 1.10)
Normal	4,814 (45.9)	11,941 (51.8)	Ref
Overweight	2,696 (25.7)	5,802 (25.2)	1.06 (0.99 – 1.13)
Obese	2,649 (25.2)	4,473 (19.4)	1.27 (1.19 – 1.36)
P for trend			<0.001

[a]Adjusted for maternal age, maternal race, average income category, maternal education level, marital status, smoking during pregnancy, parity, child's birth year, child's sex, breastfeeding, maternal history of asthma hospitalization