Maternal Diagnosis of Obesity and Risk of Cerebral Palsy in the Child

Mary D. Crisham Janik, BA[1], Thomas B. Newman, MD, MPH[2,3], Yvonne W. Cheng, MD, PhD[4], Guibo Xing, PhD[5], William M. Gilbert, MD[6], and Yvonne W. Wu, MD, MPH[1,3]

Objective To examine the association between maternal hospital diagnoses of obesity and risk of cerebral palsy (CP) in the child.

Study design For all California hospital births from 1991-2001, we linked infant and maternal hospitalization discharge abstracts to California Department of Developmental Services records of children receiving services for CP. We identified maternal hospital discharge diagnoses of obesity (*International Classification of Diseases, 9th edition* 646.1, 278.00, or 278.01) and morbid obesity (*International Classification of Diseases, 9th edition* 278.01), and performed logistic regression to explore the relationship between maternal obesity diagnoses and CP.

Results Among 6.2 million births, 67 200 (1.1%) mothers were diagnosed with obesity, and 7878 (0.1%) with morbid obesity; 8798 (0.14%) children had CP. A maternal diagnosis of obesity (relative risk [RR] 1.30, 95% CI 1.09-1.55) or morbid obesity (RR 2.70, 95% CI 1.89-3.86) was associated with increased risk of CP. In multivariable analysis adjusting for maternal race, age, education, prenatal care, insurance status, and infant sex, both obesity (OR 1.27, 95% CI 1.06-1.52) and morbid obesity (OR 2.56, 95% CI 1.79-3.66) remained independently associated with CP. On stratified analyses, the association of obesity (RR 1.72, 95% CI 1.25-2.35) or morbid obesity (RR 3.79, 95% CI 2.35-6.10) with CP was only significant among women who were hospitalized prior to the birth admission. Adjusting for potential comorbidities and complications of obesity did not eliminate this association.

Conclusions Maternal obesity may confer an increased risk of CP in some cases. Further studies are needed to confirm this finding. *(J Pediatr 2013;163:1307-12)*.

C erebral palsy (CP) refers to a heterogeneous group of disorders of the development of movement and posture caused by nonprogressive lesions occurring in the developing fetal or infant brain.[1] It is one of the most common motor disabilities in childhood, occurring in 2 to 4 per 1000 live births.[2] Etiologic studies have largely focused on the role of perinatal factors, such as chorioamnionitis and hypoxic-ischemic encephalopathy. However, it is estimated that brain injury occurring during the perinatal and postnatal periods accounts for the minority of cases of CP.[3,4] Moreover, despite improvements in perinatal care in recent decades, most studies have failed to demonstrate any significant decline in the prevalence of CP.[5,6,7] These findings suggest that prenatal factors, including maternal conditions that are present before the onset of labor, may contribute to the pathogenesis of CP in a significant proportion of cases.

The obesity epidemic is a critical public health issue in the US.[8] Among women of childbearing age (20 to 44), nearly one-half are overweight or obese.[9] Maternal obesity is associated with adverse outcomes in both mother and child, including gestational diabetes, preeclampsia, increased rates of cesarean delivery, stillbirth, birth defects, and neonatal encephalopathy.[10,11,12] A growing literature suggests that maternal obesity also detrimentally affects the fetal brain.[13,14] Furthermore, obesity induces a chronic inflammatory state, and maternal inflammatory conditions such as chorioamnionitis are known to contribute to CP.[15,16]

Studies addressing maternal obesity and CP have produced conflicting results. In Australia, one study found a 3.5-fold increased risk of CP among term infants born to obese mothers,[17] whereas two others reported no significant association.[18,19] A recent study in Sweden reported a marginally significant association between increased maternal weight at 34 weeks and CP (OR 1.02 per kg, 95% CI 1.00-1.03).[20] In a large California population, we sought to determine whether a maternal hospital diagnosis of obesity during pregnancy is associated with increased risk of moderate to severe CP in the child.

CP	Cerebral palsy
CRP	C-reactive protein
DDS	Department of Developmental Services
ICD-9	*International Classification of Diseases 9th edition*
IL	Interleukin
OSHPD	Office of Statewide Health Planning and Development
RR	Relative risk

Methods

We conducted a population-based study of all infants born in California hospitals during the 11-year period from January 1, 1991-December 31, 2001. Data were retrieved from 3 statewide sources: (1) the Office of Statewide Health Planning and Development (OSHPD) Patient Discharge Abstracts; (2) the Department of Health Services Linked Vital Statistics Birth and Infant Death file; and (3) the California Department of Developmental Services (DDS). Linkage of these 3 sources was performed using probabilistic record linkage technique with 98% linkage accuracy.[21] All study procedures were approved by the California Protection of Human Subjects Committee and by the institutional review boards at the California OSHPD, the University of California, San Francisco and the University of California, Davis.

The California OSHPD maintains a database of discharge abstracts for all admissions to nonfederal hospitals, representing 96% (571 of 594) of all hospitals in the state. According to the 1991-1998 California natality figures from the Centers for Disease Control and Prevention, 96.7% of all live births in California were recorded in the OSHPD hospital discharge dataset. Maternal hospitalization discharge diagnoses from 1 year before delivery through the birth hospitalization are included, as are infant discharge diagnoses from the birth hospitalization. Each record contains information regarding a single mother–infant pair. Therefore, individual women who gave birth to more than 1 child during this time period are represented more than once in the study population.

From the linked California Department of Health Services' Vital Statistics Birth files, we extracted maternal and infant sociodemographic characteristics, including maternal age at delivery, race, ethnicity, education, level of prenatal care and parity; multiple gestation; and infant sex, birth weight, and gestational age. We determined the source of payment for the birth hospitalization as an indicator of socioeconomic status; women who were publicly insured or uninsured were categorized as having low insurance status, whereas women with private or managed care insurance were categorized as having high insurance status.

The California DDS sponsors a statewide program that provides occupational and physical therapy and social services for residents of the state who have a substantive disability related to CP, regardless of income. CP is defined as a nonprogressive lesion or disorder in the brain occurring during intrauterine life or the perinatal period and characterized by paralysis, spasticity, or abnormal control of movement or posture that is manifest before 2 years of age. Each year, individuals who receive services from the DDS receive a comprehensive evaluation by a staff physician who records data regarding medical diagnoses including CP. We identified study subjects who qualified for DDS services for CP before November 30, 2006. Thus, all children in our study were at least 5 years old at the time of CP ascertainment.

We excluded children with known postnatal causes of CP, including child abuse (n = 272), motor vehicle and other injuries (n = 213), and near drowning (n = 72).

We searched the OSHPD database for maternal hospitalization records that contained the following discharge diagnoses related to obesity, as coded by the *International Classification of Diseases, 9th Revision* (ICD-9): obesity of pregnancy (646.1), unspecified obesity (278.0), and morbid obesity (278.01). We categorized maternal obesity diagnoses into 2 separate time periods: (1) "prenatal," indicating diagnoses made during a maternal hospitalization in the 12 months prior to the birth hospitalization; and (2) "perinatal," indicating diagnoses made during the birth hospitalization. We calculated bivariate relative risks (RRs) and 95% CI to compare CP rates in children of women with and without obesity diagnoses.

We used logistic regression to calculate OR and 95% CI to determine whether CP prevalence in children of women with and without obesity diagnoses remained statistically different after adjusting for the following sociodemographic risk factors: maternal race, age, educational attainment, prenatal care, insurance status, and infant sex. We considered 2 sets of maternal obesity diagnoses in our multivariate analysis: a specific diagnosis of morbid obesity, or any diagnosis of obesity including morbid obesity, unspecified obesity, or obesity of pregnancy. All OR closely approximate the RR given the low prevalence of CP. Analyses were performed using Stata statistical package (v. 12.0; Stata Corporation, College Station, Texas).

In order to investigate factors that might mediate the association between maternal obesity and CP, we identified maternal and infant complications that were associated with both maternal obesity and CP and adjusted for these potential mediators in a logistic regression model. We analyzed the following discharge diagnoses: pregestational diabetes (ICD-9 648.0), gestational diabetes (648.8), preeclampsia (642.4-5 and 642.7), eclampsia (642.6), hypertension (ICD-9 401-405), hypertension of pregnancy (ICD-9 642), chorioamnionitis (658.4), any perinatal infection (646.6, 647.9, 659.3, and 670), placental abruption (641.2), obstructed labor (660.0-9), cord prolapse (663.0), uterine rupture (665.1), medical induction of labor (73.4), surgical induction of labor (73.1), prematurity (765), birth defects (740-759), birth trauma (767), severe birth asphyxia (768.5), and any birth asphyxia (768.5-9). Parity, instrumental delivery, artificial rupture of membranes, and other factors that were not significantly associated with both maternal obesity and CP were not included in the model. Birth weight was not included because it was collinear with prematurity.

Results

Among 6 221 001 infants born in California hospitals between 1991 and 2001, we identified 8397 cases of CP. Population prevalence of CP was 1.4 per 1000 live births. Among