OBSTETRICS

How big is too big? The perinatal consequences of fetal macrosomia

Xun Zhang, PhD, Adriana Decker, MD, Robert W. Platt, PhD, Michael S. Kramer, MD

OBJECTIVE: The objective of the study was to examine the birthweight at which risks of perinatal death, neonatal morbidity, and cesarean delivery begin to rise and the causes and timing (antenatal, early or late neonatal, or postneonatal) of these risks.

STUDY DESIGN: This was a cohort study based on 1999-2001 US-linked stillbirth, live birth, and infant death records. Singletons weighing 2500 g or larger born to white non-Hispanic mothers at 37-44 weeks of gestation were selected (n = 5,983,409).

RESULTS: Infants with birthweights from 4000 to 4499 g were not at increased risk of mortality or morbidity vs those at 3500-3999 g, whereas those 4500-4999 g had significantly increased risks of stillbirth, neonatal mortality (especially because of birth asphyxia), birth injury, neonatal asphyxia, meconium aspiration, and cesarean delivery. Births at 5000 g or larger had even higher risks, including risk of sudden infant death syndrome.

CONCLUSION: Birthweight greater than 4500 g, and especially greater than 5000 g, is associated with increased risks of perinatal and infant mortality and morbidity.

Key words: birth asphyxia, birth injury, macrosomia, stillbirth, sudden infant death syndrome

Cite this article as: Zhang X, Decker A, Platt RW, et al. How big is too big? The perinatal consequences of fetal macrosomia. Am J Obstet Gynecol 2008;198: 517.e1-517.e6.

From the early 1980s to the late 1990s, increases in mean birthweight, mean birthweight for gestational age, and the proportion of large-for-gestational-age (LGA; weight greater than the 90th percentile for gestational age) infants were described in several countries, including Canada,[1] the United States,[2] the United Kingdom,[3,4] and Norway.[5] This trend was shown to be attributable to increases in maternal height, body mass, gestational weight gain, and diabetes; reduced maternal cigarette smoking; and changes in sociodemographic factors.[6] Recent data from the United States, however, show a decline in macrosomia since the late 1990s.[7]

No general consensus exists on the definition of fetal macrosomia; authors have variably defined it as a birthweight greater than 4000, greater than 4500, or greater than 5000 g, regardless of gestational age, or as LGA.[8,9] The birth prevalence of fetal macrosomia varies from 0.5% to 15%, depending on definition. The American College of Obstetricians and Gynecologists defines macrosomia as a birthweight greater than 4500 g, irrespective of gestational age.[10] Maternal complications of fetal macrosomia include prolonged labor, cesarean delivery, postpartum hemorrhage, infection, third- and fourth-degree lacerations, thromboembolic events, and anesthetic accidents.[8,11,12]

Fetal macrosomia has also been associated with higher perinatal mortality[9,13] and neonatal morbidity.[9,11,12] The birthweight-specific infant mortality curve has a well-described inverted-J shape, with a decline in mortality with increasing birthweight until a point at which the slope reverses (ie, increased mortality with rising birthweight).[14,15] The causes and timing (antenatal, early or late neonatal, or postneonatal) of the increased mortality are not fully understood, nor has the birthweight at which the risks begin to rise been clearly identified using data reflecting recent trends in birthweight and obstetric practice. This study attempts to fill these gaps.[11,12]

Materials and Methods

We carried out a population-based, retrospective cohort study using US linked stillbirth–live birth–infant death files for the years 1999, 2000, and 2001. These files are compiled by the US National Center for Health Statistics (NCHS) and include information from the death certificate linked to information from the birth certificate for each infant born in the United States who dies before his or her first birthday. This information is provided to NCHS by the states under the Vital Statistics Cooperative Program. The data are coded according to uniform coding specifications, have passed rigid quality control standards, have been edited and reviewed, and are the basis for official US birth and death statistics.

The primary measure used to assess the gestational age of the newborn is the

From the Departments of Pediatrics (Drs Zhang, Platt, and Kramer) and Epidemiology and Biostatistics (Drs Decker, Platt, and Kramer), McGill University Faculty of Medicine, Montreal, QC, Canada.

Received July 6, 2007; revised Oct. 11, 2007; accepted Dec. 10, 2007.

Reprints not available from the authors.

This study was supported by a grant from the Canadian Institutes of Health Research. R.W.P. is a Monat-McPherson Career Investigator of McGill University and a career investigator (chercheur-boursier) of the Fonds de la recherche en santé du Québec.

0002-9378/$34.00

doi: 10.1016/j.ajog.2007.12.005

See Journal Club, page 603

interval between the first day of the mother's last menstrual period (LMP) and the date of birth. If the length of gestation is not consistent with birthweight (normal-weight births of apparently short gestations and very low birthweight births reported to be full term), the clinical estimate of gestation is used instead. The clinical estimate is also used if the LMP date is not reported. The clinical estimate of gestation is recorded as a separate item on the US birth certificate, but no instructions (prior to the 2003 revision) are provided to specify the basis of the estimate. California does not report the clinical estimate. Gestational age is based on the clinical estimate of gestation for only a small percentage of births (about 5%), most of which (about 97%) are due to missing LMP.[16-18]

The main outcomes studied were fetal death, infant death (including neonatal and postneonatal mortality), and cause-specific mortality during each period. The NCHS does not collect data on causes of stillbirth. For infant mortality, we used International Classification of Diseases-10 codes to categorize underlying causes of death according to the categories recommended by the International Collaborative Effort (ICE) on Perinatal and Infant Mortality: immaturity-related conditions, congenital anomalies, asphyxia-related conditions, sudden infant death syndrome (SIDS), infectious diseases, and external causes.[19] Multiple causes are converted to a single underlying cause of death by Automated Classification of Medical Entities, a computer software package developed by the NCHS that uses World Health Organization rules to select the underlying cause. Neonatal morbidity outcomes studied include Apgar score of less than 4 at 5 minutes, receipt of mechanical ventilation, neonatal seizures, birth injury, and meconium aspiration syndrome.

Birth injury was defined as any impairment of the infant's body function or structure because of adverse influences that occurred at birth.[16-18] Nebraska and Texas did not report birth injury, New York City did not report assisted ventilation, and New Mexico did not report congenital anomalies.[16-18] Finally, we also examined associations with instrumental (forceps or vacuum) vaginal or cesarean delivery.

Maternal risk factors in the linked data included maternal age, parity, marital status, education, diabetes, and cigarette smoking during pregnancy. Maternal age was defined as completed years at time of delivery and classified into 3 categories: younger than 20 years, 20-34 years, and 35 years or older. Missing information on maternal age or marital status was imputed by NCHS; these data items were missing for less than 0.1% of births.[16-18] Missing maternal age was imputed according to the age of mother from the previous birth record of the same race and birth order (based on both fetal deaths and live births). Missing marital status was imputed as "married." Parity was defined as the number of live births before the index pregnancy and dichotomized as primiparous vs multiparous. Maternal education was defined as the number of years of school completed and grouped into 5 categories: 0-8 years, 9-11 years, 12 years, 13-15 years, and 16 years or more. Diabetes includes juvenile-onset, adult-onset, and gestational diabetes. Maternal smoking was recorded as the average number of cigarettes per day during pregnancy and dichotomized for our analysis as any or none. Method of delivery was classified as noninstrumental vaginal, instrumental vaginal, or cesarean.

Because plurality and maternal ethnicity are associated with birthweight and perinatal mortality,[20,21] we restricted our analysis to singleton live births and stillbirths of white non-Hispanic mothers at 37-44 weeks of gestation with birthweight of 2500 g or greater. A total of 5,983,409 births were included. Because we observed no differences in adverse birth outcomes between birthweights of 3500-3999 g and those of 4000-4499 g, we used 3500-4499 g as our reference category (2,754,223 infants [46.0%]), with 107,511 (1.8%) classified as high birthweight (HBW; birthweight 4500-4999 g) and 11,018 (0.2%) as very high birthweight (VHBW; birthweight of 5000 g or greater). The remaining category contained births between 2500 and 3499 g, comprising 3,110,657 infants (52.0%).

χ^2 tests for linear trend were used to compare proportions of demographic variables and maternal characteristics among the 4 birthweight groups, with 1-way analyses of variance used to compare gestational age. The rates of mortality (stillbirth, early neonatal [0-6 days], late neonatal [7-27 days], and postneonatal [28-364 days]), cause-specific mortality, and neonatal morbidity were calculated and compared among the birthweight groups. Unfortunately, the stillbirth data forwarded by the states to the NCHS do not include either the timing (antepartum vs intrapartum) or the cause of the stillbirths. Multiple logistic regression was used to estimate adjusted odds ratios and their 95% confidence intervals after controlling for maternal demographic and clinical variables. All data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

Table 1 shows the maternal demographic variables and clinical characteristics by birthweight category. Fetuses and infants in the HBW and VHBW categories were more likely than those of normal birthweight to be boys and of higher gestational age. Mothers of HBW and VHBW infants were more likely than those of normal birthweight infants to be married, older (35 years old or older), and multiparous. Larger proportions of mothers in the HBW and VHBW categories had a high educational level and diabetes, but lower proportions smoked during pregnancy.

As shown in Table 2, HBW was associated with higher perinatal mortality; an even larger increase in risk was observed for VHBW. Table 2 also shows that the majority of deaths among HBW and VHBW infants occurred in the early neonatal period. HBW and (especially) VHBW infants were more likely to experience stillbirth (adjusted odds ratio [OR] 2.7 [95% confidence interval (CI) 2.2 to 3.4] and 13.2 [95% CI, 9.8 to 17.7], respectively) and early neonatal death (adjusted OR 1.8 [95% CI, 1.3 to 2.4] and 6.4 [95% CI, 3.9 to 10.4]). VHBW in-