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Original article

Late-preterm birth and neonatal morbidities: population-level and within-family estimates

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ABSTRACT

Purpose: The objective of this study was to compare two salient neonatal outcomes—respiratory disorders and hyperbilirubinemia—between late-preterm (34–36 weeks) and full-term (37–41 weeks) singleton infants both at the population level and within families.

Methods: Analyses were based on natality data on all births in the state of New Jersey from 1996 to 2006 linked to newborn hospital discharge records. For population-level models, logistic regression analyses were conducted to estimate unadjusted and adjusted differences in outcomes by gestational age. For within-family analyses, unadjusted and adjusted logistic fixed-effects models were estimated with the latter including factors that differed across births to the same mother.

Results: Late-preterm birth increased the odds of a neonatal respiratory condition by more than fourfold (odds ratio, 4.08–4.53) and of neonatal hyperbilirubinemia by more than fivefold (odds ratio, 5.11–5.93) even when comparing births to the same mother and controlling for demographic and economic, behavioral, and obstetric factors that may have changed across pregnancies.

Conclusions: Based on population-level and within-family models, this study provides the strongest evidence to date that late-preterm birth is an important risk factor for adverse neonatal outcomes that other studies have found are associated with cognitive and behavioral disorders in childhood.

Introduction

Late-preterm infants, those born at 34 to 36 weeks of gestation, accounted for 9.1% of all births in the United States in 2006, up from 7.3% in 1990 [1]. Whereas 69% of all preterm births (<37 weeks) in 1990 were late preterm, the share increased to 72% in 2006. A National Institute of Child Health and Human Development workshop in 2005 brought attention to this large, growing, and understudied group and highlighted emerging findings that late-preterm birth is associated with a number of neonatal risks and complications, neonatal intensive care use, hospital readmissions, and infant mortality [2]. The rate of late-preterm birth declined somewhat since then, to 8.8% in 2008 [1], although it remains much higher than it was two decades ago.

Late-preterm birth has been linked to neonatal respiratory conditions and hyperbilirubinemia [2–4], both of which are not uncommon, often require substantial health care resources [5,6] and have been associated with childhood developmental impairments even when not severe [7–12]. However, preterm birth is strongly associated with socioeconomic status [13], and some of the "effects" of preterm birth, and of late-preterm birth in particular, may thus reflect unobserved confounding factors. For example, a recent study using nationally representative data from the United States found that mothers of children born late-preterm were more likely to be minority, low educated, unmarried, not coresiding with the father of the child, and living below poverty than mothers of full-term children [14].

The purpose of this study was to compare salient neonatal outcomes—respiratory conditions and hyperbilirubinemia—of late-preterm (34–36 weeks) and full-term (37–41 weeks) infants both at the population level and within families. The population-level analyses were conducted using a database on all births in New Jersey over an 11-year period. The within-family analyses allowed us to remove substantial confounding by socioeconomic status, genetics, and the mother's underlying physical health, but

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are based on a select sample. As far as we know, the effects of late-preterm birth, or preterm birth more generally, have not previously been investigated using a within-family research design.

Methods

Data

Analyses were based on data from the New Jersey Department of Health and Senior Services that included birth records for all births in the state of New Jersey from 1996 to 2006 (1,213,303 infants) linked to newborn hospital discharge records. The electronic birth certificate (EBC) records contained identifying information for each mother, as well as the date of her last live birth, which allowed us to match in-state births to the same mother during the observation period. The EBC contained data on the date and hospital of birth, demographic and economic factors, medical risk factors, prenatal cigarette smoking, prenatal care, obstetric procedures, complications of labor and delivery, and birth outcomes, as well as newborn diagnoses and interventions from the birth hospitalization. This research has been approved by the Institutional Review Boards of Rutgers Robert Wood Johnson Medical School and Columbia University.

The key exposure variable was late-preterm birth, conventionally defined as 34 to 36 completed weeks (34 0/7 to 36 6/7 weeks) of gestation, compared with full-term birth, defined as 37 to 41 completed weeks of gestation (37 0/7 to 41 6/7 weeks). We also consider gestational age in weeks. The EBC included a clinical assessment of gestational age, which according to the EBC coding manual (p. 83), measured the "development of the infant in weeks as judged by the clinician, using the best available information, (physical examination of the infant and/or ultrasound visualization)" [15]. The EBC also included information that allowed us to construct to a measure of gestational age based on the date of mother's last menstrual period, which we used to cross-check our results. In supplementary analyses, we considered whether the infant was small-for-gestational age (SGA; $<$10th percentile of birth weight for gestational age) and whether the infant was low birth weight ($<$2500 g).

We excluded multiple births ($n = 49{,}579$ infants) and infants with clinical gestational age less than 34 or more than 41 weeks ($n = 39{,}749$) or missing ($n = 2{,}169$), leaving a sample of 1,121,804 infants. Of those, 67,416 (6%) were late preterm and 1,054,804 were full term. In supplementary analyses, we excluded infants with congenital anomalies, specific diagnoses, and newborn hospital stays of less than 3 or 5 days. Mean gestational ages for the late-preterm and full-term groups were 35.4 and 39.2 weeks, respectively; 14.2% of the late-preterm infants were SGA compared with 8.6% of the full-term infants. Approximately one-third (35%) of the late-preterm infants and 2% of the full-term infants were low birth weight.

Outcome measures

The infant was coded as having had a respiratory condition if the discharge record indicated a respiratory-related diagnosis (bronchopulmonary dysplasia, meconium aspiration syndrome, pneumonia, air leak syndrome, home on oxygen, respiratory distress syndrome/hyaline membrane disease [RDS/HMD], transient tachypnea of newborn [TTN], persistent pulmonary hypertension and/or intervention [assisted ventilation, continuous positive airway pressure, surfactant therapy, and extracorporeal membrane oxygenation]). RDS/HMD and TTN, the only two respiratory conditions with adequate sample sizes for disaggregated analysis, were also analyzed separately. The infant was coded as having had hyperbilirubinemia if there was an indication of that diagnosis in the newborn discharge record. Of the 1,121,804 infants, 80,805 (7%) were coded as having a respiratory condition and 9384 (1%) were coded as having hyperbilirubinemia. In alternative models of hyperbilirubinemia, we used a more stringent outcome consisting of hyperbilirubinemia diagnosis plus phototherapy or exchange transfusion.

For the within-family analyses of neonatal respiratory conditions, we limited the sample to cases for which the mother had at least one infant with a respiratory condition and at least one infant without a respiratory condition during the observation period (76,730 infants born to 32,663 mothers). For the within-family analyses of neonatal hyperbilirubinemia, we limited the sample to cases for which the mother had at least one infant with hyperbilirubinemia and at least one infant without hyperbilirubinemia during the observation period (9431 infants born to 3941 mothers). These restrictions were required for estimating fixed-effects logistic regression models.

Control variables

Demographic and economic factors included the child's sex and the mother's age, marital status, parity, race/ethnicity, nativity, education, and Medicaid status. Behavioral factors included the trimester the mother initiated prenatal care and whether she smoked cigarettes during the pregnancy. Caesarian section delivery (separately for with and without labor trial) and induction of labor were also considered as possible confounding factors. Finally, we considered the array of medical risk factors and labor and delivery complications that are collected in birth records in the United States. Although some of these factors are potential confounders, many might mediate the effects of late-preterm birth so they were included in supplementary analyses rather than in the main models.

Statistical analyses

Stata version 13 statistical software (StataCorp LP, College Park, TX) was used to conduct the analyses. Potentially confounding demographic and economic, behavioral, and obstetric factors were compared by late-preterm versus full-term birth. For the population-level models, logistic regression analyses were conducted to estimate unadjusted and adjusted differences in outcomes by gestational age. Measures that differed significantly (based on chi-square tests) between late-preterm and full-term birth were included in adjusted models, along with indicators for hospital and year of birth. After dropping observations with missing data on covariates, the sample sizes for the logistic regression models of respiratory conditions and hyperbilirubinemia were 1,039,855 and 1,032,091, respectively. Standard errors were adjusted for clustering of births within families as some observations represented births to the same mother.

For the within-family analyses, unadjusted and adjusted logistic fixed-effects models were estimated using the xtlogit fe command. The adjusted logistic fixed-effects models included all of the covariates from Table 1 that were time varying (i.e., all factors other than race/ethnicity and nativity, for which the fixed-effects models implicitly controlled) plus year of the birth. Statistical significance of estimates was based on the Wald test.

Results

For 76% of the birth records indicating that the mother had a prior live birth on or after January 1, 1996, we were able to find the record for the previous birth. The other 24% of births were to mothers who had given birth in another state or whose records did not match for other reasons.

Compared with full-term infants, late-preterm infants were less likely to be female and more likely to have mothers who