OBSTETRICS

Risk factors for serious morbidity in term nonanomalous neonates

Janine E. Spain, MD; Methodius G. Tuuli, MD, MSCI; George A. Macones, MD, MSCE; Kimberly A. Roehl, MPH; Anthony O. Odibo, MD, MSCE; Alison G. Cahill, MD, MSCI

OBJECTIVE: The purpose of this study was to identify ante- and intrapartum risk factors for serious morbidity in term nonanomalous neonates.

STUDY DESIGN: We analyzed the first 5000 subjects within an ongoing prospective cohort study of consecutive term births from 2010-2012. The primary outcome was a composite of serious neonatal morbidity defined as ≥1 cases of hypoxic ischemic encephalopathy, meconium aspiration with pulmonary hypertension, requirement of hypothermia therapy, respiratory distress syndrome, seizures, sepsis or suspected sepsis, or death. We calculated odds ratios for the composite morbidity that is associated with ante- and intrapartum factors. Multivariable logistic regression was used to estimate adjusted odds ratios.

RESULTS: Of 5000 term nonanomalous births, 393 had the composite morbidity. Significant risk factors for morbidity were nulliparity, presence of meconium, first stage of labor >95th percentile, second stage of labor >95th percentile, pregestational diabetes mellitus, chronic hypertension, obesity, maternal intrapartum fever, and cesarean delivery. In contrast, induction of labor and gestational age ≥41 weeks were not associated with significant morbidity.

CONCLUSION: We identified several significant risk factors for serious morbidity in term nonanomalous neonates. Clinicians may use these risk factors to help anticipate the potential need for additional neonatal support at delivery.

Key words: neonatal morbidity, risk factor, term neonate

Cite this article as: Spain JE, Tuuli MG, Macones GA, et al. Risk factors for serious morbidity in term nonanomalous neonates. Am J Obstet Gynecol 2015;212:799.e1-7.

Approximately 5-18% of term gestational age (≥37 weeks) infants are admitted to the neonatal intensive care unit (NICU), which accounts for up to 40% of admissions to higher-level nurseries.[1-7] In addition to the use of limited resources and the financial burden on the health care system, these admissions frequently are unanticipated.

Previous studies have identified the most common diagnoses for NICU admission in term infants, which include congenital anomalies, followed by respiratory conditions, jaundice, hypoglycemia, and infection.[5,7] However, the vast majority of infants who are born at term are anatomically normal, and few studies have sought to identify ante- and intrapartum risk factors for these serious morbidities in term nonanomalous infants.[5]

The aim of our study was to identify risk factors for serious morbidity in term nonanomalous neonates. We hypothesized that there are specific identifiable ante- and intrapartum risk factors for serious morbidity in anatomically normal term infants. Identification of these factors will assist physicians to anticipate the need for additional neonatal support at delivery.

Materials and Methods

We analyzed the first 5000 subjects within an ongoing prospective cohort study from 2010-2012. This study included all births at term (≥37 weeks' gestational age) without major congenital anomalies. The parent database included all consecutive births at a single tertiary care hospital. Research assistants extracted the data from the medical records after delivery. The study was approved by the Washington University Human Research Protection Office.

The primary outcome was a composite neonatal morbidity defined by ≥1 of the following occurrences: hypoxic ischemic encephalopathy, meconium aspiration with pulmonary hypertension, requirement of hypothermia therapy, respiratory distress syndrome, seizures, sepsis or suspected sepsis, or neonatal death. Those infants with composite morbidity were compared with term neonates who did not have one of the composite neonatal outcomes or any other neonatal morbidity that required a higher level of nursery care.

Hypoxic-ischemic encephalopathy was defined by ≥1 of the following occurrences: (1) umbilical arterial pH <7.0, (2) base deficit −16, (3) need for respiratory support at 10 minutes of life, (4) 5-minute Apgar score <5 and (1) moderate-severe neonatal encephalopathy by National Institute of Child Health and Human Development criteria or (2) seizure activity.[8]

From the Department of Obstetrics and Gynecology, Washington University School of Medicine in St. Louis, St. Louis, MO.

Received Oct. 23, 2014; revised Dec. 19, 2014; accepted Jan. 22, 2015.

Supported in part by a Robert Wood Johnson Foundation Physician Faculty Scholar (A.G.C.).

The authors report no conflict of interest.

Presented in poster format at the 34th annual meeting of the Society for Maternal-Fetal Medicine, New Orleans, LA, Feb. 3-8, 2014.

Corresponding author: Janine E. Spain, MD. spainj@wudosis.wustl.edu

0002-9378/$36.00

http://dx.doi.org/10.1016/j.ajog.2015.01.028

Meconium aspiration with pulmonary hypertension was defined as respiratory distress (nasal flaring, subcostal and intercostal retractions, and need for supplemental oxygen to maintain oxygen saturations >95%) and transthoracic echocardiographic findings of elevated main pulmonary artery pressures (right-to-left shunting across the patent ductus arteriosus and atria, a flattened septum, and a tricuspid regurgitation jet). Respiratory distress syndrome included all neonates who required oxygen support after 6 hours of life or any need for mechanical ventilation. Suspected sepsis was diagnosed as a symptomatic neonate defined as ≥1 of the following occurrences: respiratory distress, temperature instability, apnea, lethargy, with or without abnormal complete blood count 6-12 hours after birth with leukopenia or leukocytosis with a ratio of immature cells of the neutrophilic series to total cells of the neutrophilic series >0.2, and/or positive blood culture. Suspected sepsis was included given that antibiotics are initiated empirically if there is a high clinical concern for neonatal infection because of associated risk for encephalopathy, seizures, cerebral palsy, and death.[9,10] Further, the sensitivity and specificity of blood cultures are poor for neonatal sepsis; thus, the inclusion of both suspected and confirmed sepsis cases includes those who required treatment for sepsis by either laboratory or clinical criteria and is most clinically relevant. The attending neonatologist confirmed all diagnoses.

Data were extracted from the maternal and neonatal medical records to obtain sociodemographic information, medical and antenatal history, and neonatal outcomes. The labor and delivery record was used to collect data on all intrapartum events and duration of each stage of labor. *Obesity* was defined as an admission body mass index (BMI) ≥30 kg/m^2. A maternal fever included maternal temperature ≥38.0°C during labor. The duration of the first stage of labor was started at the time at which a woman presented in labor or an induction of labor was begun and concluded when the woman reached 10 cm of cervical dilation. The second stage of labor was begun at 10 cm of cervical dilation and concluded with delivery of the infant. *Prolonged first or second stages of labor* were defined with the use of labor duration data from the patients in this cohort. Duration of >95th percentile was considered prolonged. Prolonged first stage of labor was defined as >13.75 hours for nulliparous women and >11 hours for multiparous women. Prolonged second stage of labor was defined as >3 hours for nulliparous women and >2 hours for multiparous women.

Baseline characteristics were compared between those with and without composite neonatal morbidity. Categoric variables were compared with the use of the χ^2 or Fisher exact test, as appropriate. Continuous variables were assessed for normality with the Kolmogorov-Smirnov test. Variables that were not normally distributed were compared with the Mann-Whitney *U* test, and normally distributed variables were compared with the Student *t* test.

TABLE 1
Baseline characteristics of women with and without neonatal morbidity composite

Variable	Morbidity composite	No morbidity composite	*P* value
n	393	4561	
Maternal age, y[a]	24.6 ± 6.2	25.6 ± 5.9	< .01
Advanced maternal age ≥35 y, n (%)	29 (7.4)	388 (8.5)	.51
Gestational age at delivery, wk[a]	39.0 ± 1.3	38.9 ± 1.2	.32
Maternal black race, n (%)	259 (65.9)	2965 (65.0)	.71
Body mass index, kg/m^2[a]	33.1 ± 7.1	31.9 ± 7.3	< .01
Preeclampsia, n (%)	47 (12.0)	429 (9.4)	.10
Gestational diabetes mellitus, n (%)	16 (4.1)	123 (2.7)	.15
Pregestational diabetes mellitus, n (%)	10 (2.5)	41 (0.9)	< .01
Nulliparous women, n (%)	257 (65.4)	1834 (40.2)	< .01
Previous cesarean, n (%)	45 (11.5)	383 (8.4)	.04
Labor type, n (%)			< .01
Spontaneous	76 (19.4)	1368 (30.0)	
Augmented	122 (31.0)	1223 (26.8)	
Induced	195 (49.6)	1970 (43.2)	
Prostaglandin use, n (%)	99 (25.2)	784 (17.2)	< .01
Foley bulb use, n (%)	60 (15.3)	415 (9.1)	< .01
Oxytocin use, n (%)	296 (75.3)	3006 (65.9)	< .01
Regional anesthesia, n (%)	371 (94.4)	4082 (89.5)	< .01
Birthweight, g[a]	3289 ± 531	3238 ± 453	.04
Birthweight >4000 g, n (%)	27 (6.9)	228 (5.0)	.12
Delivery, n (%)			
Vaginal	195 (49.6)	3653 (80.1)	< .01
Operative vaginal	31 (7.9)	242 (5.3)	.03
Cesarean	167 (42.5)	666 (14.6)	< .01
Maternal fever ≥38.0°C, n (%)	141 (36.0)	59 (1.3)	< .01

[a] Data are presented as mean ± SD.

Spain. Risk factors for term neonatal morbidity. Am J Obstet Gynecol 2015.