In-Hospital Mortality and Morbidity among Extremely Preterm Infants in Relation to Maternal Body Mass Index

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Abstract

Objective: To compare in-hospital survival and survival without major morbidities in extremely preterm infants in relation to maternal body mass index (BMI).

Methods: This retrospective cohort study included extremely preterm infants (gestational age 22\textsuperscript{0}/7 - 28\textsuperscript{6}/7 weeks). This study was conducted at National Institute of Child Health and Human Development Neonatal Research Network sites. Primary outcome was survival without any major morbidity.

Results: Maternal BMI data were available for 2415 infants. Survival without any major morbidity was not different between groups: 30.8% in the underweight/normal, 28.1% in the overweight, and 28.5% in the obese (P=.65). However, survival was lower in the obese group (76.5%) compared with overweight group (83.2%) (P=.02). Each unit increase in maternal BMI was associated with decreased odds of infant survival (P<.01).

Conclusion: Survival without any major morbidity was not associated with maternal obesity. An increase in maternal prepregnancy BMI was associated with decreased odds of infant survival.

Keywords

Obesity; body mass index; prematurity; mortality

INTRODUCTION

More than one-third of women between the ages of 20 and 39 years in the United States are obese.\textsuperscript{1} The overall obesity rate among all women increased from 33.2% in 2003-2004 to 37.9% in 2013-2014.\textsuperscript{1, 2} The United States’ Centers for Disease Control and Prevention reported data from 48 states on the prevalence of prepregnancy body mass index (BMI), categorized as underweight, normal weight, overweight, and obese.\textsuperscript{3} The overall prevalence of prepregnancy normal weight in 2015 was 45%, a decrease of 5% from 2011, with a corresponding increase in the overweight and obese categories. Nearly 25% of women were overweight and 25% of women were obese before pregnancy.\textsuperscript{3}
Overweight status and obesity in women before pregnancy is associated with maternal, fetal, and neonatal complications, including gestational diabetes, pregnancy-induced hypertension, preterm delivery, an increased risk of operative deliveries, stillbirth, macrosomia, fetal malformations, admission to the neonatal intensive care unit (NICU), and infant mortality. Most studies have examined associations between prepregnancy weight and outcomes of term infants. Maternal obesity has been associated with an increased risk of preterm delivery. Obesity may be a modifiable risk factor for improved maternal and neonatal outcomes.

The objective of this study was to compare the survival and survival without major morbidities of extremely preterm infants in relation to maternal BMI.

We hypothesized that survival and survival without morbidity would be lower among extremely preterm infants born to obese mothers compared with infants born to normal weight and overweight mothers.

**PATIENTS AND METHODS**

This was a retrospective study of prospectively collected data from the Generic Database Registry of the participating centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NICHD NRN). Extremely preterm infants (gestational age 220/7 to 286/7 weeks) born from January 2016 to June 2018 were eligible. Maternal data collected included race, age, marital status, hypertension, acute histologic chorioamnionitis, delivery mode, multiple births, prepregnancy weight by maternal recall or earliest first-trimester weight, education, and antenatal steroid administration. Data were collected until death, discharge, or 120 days, whichever occurred first and included birthweight, gestational age (GA), sex, small-for-gestational age (SGA) status defined as less than the 10th percentile for sex based on Alexander growth chart, Apgar scores, details of resuscitation in the delivery room, severe intracranial hemorrhage (ICH), cystic periventricular leukomalacia (cPVL), bronchopulmonary dysplasia (BPD; use of supplemental oxygen at 36 weeks’ postmenstrual age), stage 2 or greater necrotizing enterocolitis (NEC, modified Bell criteria), severe retinopathy of prematurity, late-onset sepsis, and survival until hospital discharge. Estimation of GA was recorded based on the following hierarchy: best Obstetric estimate followed by best Neonatologist’s estimate. Resuscitation in the delivery room was defined as receipt of chest compression or epinephrine. Severe ICH was defined as intraventricular hemorrhage with ventricular dilation or parenchymal hemorrhage (either unilateral or bilateral) noted on serial head ultrasonography performed before 28 days after birth. Cystic periventricular leukomalacia was defined as the presence of cystic echolucencies in the periventricular white matter on serial head ultrasonography performed before 36 weeks. The NRN Generic Database Registry was approved by the institutional review board at each site, with waiver of consent granted at all except 3 sites where written or oral parental consent was obtained.
Definitions of Weight Categories

The mother’s weight before pregnancy or the earliest weight during the first trimester was collected.

The BMI was calculated using prepregnancy or first-trimester weight in kilograms divided by height in meters squared. Mothers were classified as underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25–29.9 kg/m²), or obese (BMI ≥30 kg/m²).⁶

Statistical Analysis

The primary outcome was survival to hospital discharge or otherwise to 120 days of life without a major morbidity, defined as presence of any of the following: severe ICH, cPVL, late-onset sepsis, NEC (stage ≥2), BPD, or severe retinopathy of prematurity. Secondary outcomes were overall survival to discharge, as well as survival without the individual major morbidities. Survival is included as part of the primary and secondary outcomes to account for the difference in the occurrence of death rate in this high-risk population, that often occurs in the initial days after birth, before the outcome of interest can be assessed.¹² The rate of survival without major neonatal morbidity is expected to be 30% in the overall patient population.¹³ To detect a 6% difference for the primary outcome between infants born to obese mothers (27%) and infants born to normal/underweight mothers (33%), initial power analyses indicated that each group needed at least 915 infants for 80% power with 2-sided α of 0.05.

Continuous variables were described using mean with standard deviation or median with interquartile range and categorical variables using frequency and percentage. The characteristics of the mothers for whom prepregnancy or first-trimester weight were available were compared with those without availability of these data. The characteristics and outcomes of patients born to the mothers in the 3 groups (normal/underweight, overweight, and obese) were compared using the Student t test for continuous variables with normal distribution and the Mann-Whitney U test for variables without normal distribution. Because the rate of underweight mothers was expected to be very low, the underweight group was combined with the normal weight group a priori. A sensitivity analysis was conducted to determine if this grouping impacted our results. Categorical variables were compared using the Fisher exact test. The association between maternal weight group and outcomes was evaluated using logistic regression, adjusting for prespecified covariates of maternal race, socioeconomic status (maternal Medicaid insurance as a surrogate), GA, sex, SGA status, maternal hypertension, diabetes, antenatal steroids, and the random effect of center. Where the association was significant, pairwise comparisons (normal/underweight versus overweight, overweight versus obese, normal/underweight versus obese) were performed with Tukey-Kramer adjustments, and their corresponding odds ratios and 95% confidence intervals (CIs) reported. To explore the biologic plausibility of the mediating effects of preterm delivery or poor fetal growth, additional models were created that did not adjust for GA and SGA status. This additional modeling was performed on the primary outcome, as well as on each of the outcomes that showed significant overall differences by maternal weight group in the fully adjusted model. Secondary analyses evaluated the effect
of maternal BMI as a continuous variable on neonatal survival. Both linear and curvilinear BMI effects were tested using adjusted logistic regression.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) with a 2-sided α of 0.05.

RESULTS

Between January 2016 and March 2018, 3984 infants were born who were eligible for the study. Data on maternal BMI were available for 2415 (60.6%) infants; of these, 938 (38.9%) were born to underweight/normal weight mothers (85 underweight, 853 normal weight), 568 (23.5%) to overweight mothers, and 909 (37.6%) to obese mothers. Estimation of GA was recorded by the Obstetric estimate for 99% of subjects and by the Neonatologist’s estimate for remaining 1% subjects. The baseline characteristics comparing mothers for whom prepregnancy weight data were not available with those for whom data were available revealed that women without data were more likely to be of black race, unmarried, have lower educational achievement, and be on Medicaid insurance, and were less likely to be exposed to a complete course of antenatal steroids (Table 1). Obese mothers were older, more likely to be black, and have hypertensive disorder, diabetes, and histologic chorioamnionitis compared with normal/underweight and overweight mothers (Table 2a).

Infant characteristics at birth in relation to maternal prepregnancy BMI were compared (Table 2b). The primary outcome, survival without any major morbidity, was not different among the 3 groups: 30.8% in the normal/underweight group, 28.1% in the overweight group, and 28.5% in the obese group (P=.65, Table 3). The secondary outcome of overall survival was different among the 3 groups: 82.1% in the normal/underweight group, 83.2% in the overweight group, and 76.5% in the obese group (P=.02); the adjusted odds of survival among infants born to obese mothers was lower than for those born to overweight mothers (adjusted odds ratio [aOR]: 0.64, 95% CI: 0.43–0.95). Adjusted odds of survival among infants born to obese mothers was 0.72 (95% CI: 0.50–1.02) compared with those born to normal/underweight mothers. Survival without cPVL was different across the 3 weight groups: 78.6% in the normal weight/underweight group, 80.1% in the overweight group, and 72.7% in the obese group (P<.01); the adjusted odds of survival without cPVL among infants born to obese mothers were significantly lower compared with those born to overweight mothers (aOR: 0.63, 95% CI: 0.43–0.90). Survival without NEC was also different across the 3 weight groups: 77.2% in the normal weight/underweight group, 76.2% in the overweight group, and 70.9% in the obese group (P=.02); the adjusted odds of survival without NEC among infants born to obese mothers were significantly lower compared with those born to normal/underweight mothers (aOR: 0.71, 95% CI: 0.52–0.97).

No significant differences were found among the 3 weight groups in other morbidities. Sensitivity analyses removing infants born to underweight mothers did not impact the direction or significance of these findings.

When analyzed as a continuous variable, BMI was not associated with the primary outcome, survival without major morbidity. However, each unit increase in maternal BMI was associated with decreased odds of overall infant survival (aOR: 0.98, CI: 0.96–0.99, P<.01).
There was no evidence of a curvilinear relationship between BMI and survival. Figure 1 depicts this linear trend of the relationship between increasing maternal BMI and decreasing survival. For this figure, women were first grouped into finer BMI categories based on increments of 3 kg/m², starting from the lowest BMI value (14.9 kg/m²) in the population up to BMI greater than 50 kg/m²; the rate of survival was then plotted within each category.

Adjusted models indicated other factors independently associated with survival without major morbidity and mortality. Maternal hypertension (aOR: 0.76, 95% CI: 0.58–0.98), male sex (aOR: 0.76, 95% CI: 0.61–0.95), and SGA status (aOR: 0.26, 95% CI: 0.16–0.42) were associated with lower survival without major morbidities, whereas increase in each week of gestational age (aOR: 2.48, 95% CI: 2.27–2.71) was associated with higher survival without major morbidity (Figure 2a). Exposure to a complete course of antenatal steroids (aOR: 1.68, 95% CI: 1.30–2.18) and increasing week of gestation at birth (aOR: 2.12, 95% CI: 1.95–2.30) were associated with higher survival to hospital discharge, whereas SGA status (aOR: 0.21, 95% CI: 0.14–0.31) was associated with lower survival to hospital discharge (Figure 2b).

The results of additional modeling of survival without morbidity, and outcomes that showed significant adjusted differences by maternal weight group are noted on Table 4. In particular, the odds of survival were significantly lower for infants born to obese women compared with infants born to normal/underweight women (aOR: 0.64, 95% CI: 0.48–0.87) and compared with infants born to overweight women (aOR: 0.63, 95% CI: 0.45–0.88) in the model that did not adjust for GA and SGA status. The odds of survival remained significantly lower for infants born to obese women compared with infants born to overweight women after controlling for GA and SGA status. However, it was not significantly different for infants born to obese women compared with infants born to normal/underweight women (aOR: 0.72, 95% CI: 0.50–1.02) suggesting that the effect of maternal obesity on survival was partly mediated by poor fetal growth and risk of earlier delivery.

However, when the model is additionally adjusted for these birth factors, the relationship is no longer significant (aOR: 0.72, 95% CI: 0.50–1.02).

**DISCUSSION**

**Principal Findings**

This study had several clinically important findings: (1) a high prevalence of prepregnancy obesity (38%) and overweight status (24%) among mothers who delivered at extremely low gestations, (2) no significant association between maternal obesity or overweight status with survival without any major morbidity, and (3) a lower rate of survival to hospital discharge among extremely preterm infants born to obese women compared with normal weight and overweight women.

**Comparison of Results with Published Literature**

The rate of prepregnancy obesity (38%) in the current study is higher than the reported 25% rate of prepregnancy obesity among all women based on the United States’ Centers for
Disease Control and Prevention reported data from 48 states.\textsuperscript{3} We speculate that the difference in the prevalence of obese mothers in the current study may be due to a higher rate of preterm birth for obese mothers.

In a large population-based cohort study from Sweden (n=1,857,822), infant mortality was higher (5.8/1000) born to women with class 3 obesity (BMI \textgtr=40), as compared to 2.4/1000 noted among infants born to normal weight women (BMI 18.5–24.9).\textsuperscript{5} Based on a 2018 survey, the 5 states with the highest infant mortality rates in the United States are Mississippi (8.3%), Louisiana (7.6%), Arkansas (7.5%), South Carolina (7.2%) and West Virginia (7.1%), and the 5 states with the highest rates of obesity are Mississippi (39.5%), West Virginia (39.5%), Arkansas (37.1%), Louisiana (36.8%), and Kentucky (36.6%).\textsuperscript{14, 15}

A meta-analysis of 60 studies involving infants born at all gestational ages noted that infants of mothers who were overweight or obese were at increased risk of being stillborn, large for gestational age, and needing admission to NICU compared with infants born to mothers with normal prepregnancy weight\textsuperscript{7}; however, data on neonatal outcome among preterm infants in relation to maternal prepregnancy BMI are limited. Among infants born preterm, Carmichael and colleagues evaluated the risk of BPD in relation to maternal prepregnancy BMI among infants with a birthweight less than 1500 g or gestational age of 22 to 29 weeks from 2007 to 2011 using data from the California Quality Care Collaborative.\textsuperscript{16} They noted an increased risk of BPD among infants born to mothers with grade III obesity (BMI \textgtr=40.0 kg/m\textsuperscript{2}). However, no difference was noted for infants born to mothers who were overweight or had grade I (BMI 30.0–34.9 kg/m\textsuperscript{2}) or grade II (BMI 35.0–39.9 kg/m\textsuperscript{2}) obesity. The current study found no difference in survival without BPD (receipt of oxygen at 36 weeks’ postmenstrual age) in relation to maternal obesity or overweight status. Subgroup analysis comparing different grades of obesity and neonatal outcomes was not performed, and we did not evaluate survival without physiologic BPD. As a result, our definition of BPD may have overestimated the BPD prevalence in this population. Pai and colleagues evaluated the risk of ICH in relation to maternal prepregnancy BMI among infants born preterm (GA 22–32 weeks) from 2007 to 2011 using data from the California Quality Care Collaborative.\textsuperscript{17} The association between maternal obesity and neonatal ICH was not significant after controlling for the mediating effects of GA. Similar to Pai et al, we did not note any difference in rates of any or severe ICH among preterm infants born to obese, overweight, and normal/underweight mothers.

**Clinical Implications**

In the current study, we found no difference in the primary outcome of survival without any major morbidity in relation to maternal weight. However, the study may have been underpowered because of a lower (3%) difference in the primary outcome than the hypothesized 6% difference. Survival without cPVL and survival without NEC were lowest among infants born to obese mothers. There was no difference in survival without other individual morbidities among preterm infants born in the 3 groups. Extremely preterm infants born to obese mothers had lower survival. Maternal obesity has been previously reported to be associated with risk of preterm delivery.\textsuperscript{4}
The results from regression modeling with and without controlling for GA and SGA status revealed that GA and SGA status may potentially mediate the relationship between maternal obesity status and survival. No curvilinear relationships between BMI and mortality were detected; they either do not exist in the analysis population, or the power to detect them was inadequate. However, Figure 1 suggests that the relationship between increasing BMI and the rate of survival is approximately linear.

There is a plausible mechanism for the correlation between maternal obesity and fetal/neonatal deaths. Maternal obesity has been associated with a reduction in placental villous proliferation and apoptosis. Animal studies have noted that a long-term diet rich in fat is associated with an altered placental vasculature, reduced oxygenation of fetal tissues and an increased risk of fetal and neonatal deaths. Animal studies have shown an increase in proinflammatory cytokines and reactive oxygen species in the hypothalamus in response to a high-fat diet in mice. Obesity is associated with inflammatory and noninflammatory disturbances that may be associated with dysfunction or damage of the developing brain. Human studies demonstrate increased gliosis in the hypothalamus of obese individuals, as assessed by brain magnetic resonance imaging. Inflammation was noted to only partly explain the adverse outcomes in human studies. In the current study, the rate of histologic chorioamnionitis was higher in obese women (53.7%), as compared to normal/underweight (45.8%) and overweight women (50.9%). Components of maternal diet possibly contribute to a child’s brain dysfunction by noninflammatory damage to the developing brain. Other mechanisms may include hormonal changes, such as exposure to an increased concentration of leptin or insulin, or disruption of normal development of the serotonin system.

**Strengths and Limitations**

The strengths of this study include prospectively collected data on a recent cohort of patients using prespecified definitions for outcomes from multiple academic centers across the country. The effect of maternal BMI as a continuous variable on infant mortality was explored. The large sample size allowed for control of multiple potential confounders on neonatal outcomes. The use of BMI instead of just maternal weight is an advantage, because BMI is a valid proxy for adiposity. The correlation between maternal BMI and body fat was good, especially in early pregnancy.

The limitations of the study include the observational design of the study, which does not allow any causal inferences to be drawn. This was a study based on analyses of data collected not specifically to test the primary hypothesis of this study, therefore some potential confounders might not have been collected, introducing bias and limiting inferences on causal relationships. In addition, prepregnancy BMI was missing for 39% of the available population. The baseline characteristics of the mothers for whom prepregnancy weight data were not available compared with those for whom data were available were different. However, many potential confounders were controlled for, including maternal race, socioeconomic status, GA, sex, SGA status, maternal hypertension, diabetes, antenatal steroids, and the random effect of center in our adjusted analyses. Prepregnancy maternal weight may be confounded by socioeconomic status and diabetes before pregnancy. Another limitation is that in some cases, prepregnancy weight could be based on maternal recall,
the proportion of weight data collected by recall was unknown. However, maternal weight by recall was previously noted to correlate well with objective data, including weight check in the first trimester.28, 29 The NICHD NRN collects data from academic centers and may not completely represent the patient population in the whole country. The difference between outborn and inborn patients and the causes of death in relation to maternal obesity should be further explored. Randomized controlled trials have noted the efficacy of a gestational weight gain restriction program for obese women with benefits noted on women’s weight up to 6 years after intervention,30 and on their children’s BMI during the first 5 years of age.31

Research Implications

Future studies are needed to compare neurodevelopmental outcomes in relation to maternal prepregnancy weight status. The observed relationship between maternal obesity and adverse neonatal outcomes may have important clinical implications and should be tested in prospective studies focusing on the short-term morbidities as well as long-term neurodevelopmental outcome of infants in relation to the maternal prepregnancy body mass index.

CONCLUSIONS

Survival without any major morbidity was not associated with maternal BMI. An increase in maternal prepregnancy BMI was associated with decreased odds of infant survival. Preconception counseling and weight management for women may be beneficial to improve survival and lower certain morbidities among preterm infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

- aOR: adjusted odds ratio
- BMI: body mass index
- BPD: bronchopulmonary dysplasia
- CI: confidence interval
cPVL  cystic periventricular leukomalacia
GA     gestational age
ICH    intracranial hemorrhage
NEC    necrotizing enterocolitis
NICU   neonatal intensive care unit
SGA    small for gestational age

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Figure 1.
Infant survival by maternal body mass index. Number of infants is shown above each data point.
Figure 2.
A. Factors associated with survival to discharge without morbidities. Each OR and CI is jointly adjusted for the presence of all other covariates in the model, plus for the center as a random effect. BMI, body mass index; CI, confidence interval; OR, odds ratio; UW, underweight.
B. Factors associated with survival to discharge. Each OR and CI is jointly adjusted for the presence of all other covariates in the model, plus for the center as a random effect. BMI, body mass index; CI, confidence interval; OR, odds ratio; UW, underweight.
### Table 1

Maternal and Neonatal Characteristics of Subjects Born with and without Data on Prepregnancy or First-Trimester Maternal BMI

| Characteristic                              | No Maternal BMI Available N=1569 (39.4%) | Maternal BMI Available N=2415 (60.6%) | \( P \)  |
|---------------------------------------------|-----------------------------------------|----------------------------------------|---------|
| Maternal age (y)\(^d\)                      | 28.1 (6.1)                              | 29.0 (6.1)                             | 0.82    |
| Maternal race                               |                                        |                                        | <0.01   |
| Black                                       | 637 (41.4)                              | 834 (35.9)                             |         |
| White                                       | 817 (53.1)                              | 1281 (55.2)                            |         |
| Other                                       | 84 (5.5)                                | 206 (8.9)                              |         |
| Married maternal status                     | 665 (42.4)                              | 1160 (48.0)                            | <0.01   |
| Maternal education (> high school)          | 507 (46.1)                              | 1236 (59.7)                            | <0.01   |
| Medicaid insurance                          | 950 (60.1)                              | 1309 (54.3)                            | <0.01   |
| Maternal hypertension before pregnancy      | 235 (15.0)                              | 327 (13.6)                             | 0.32    |
| Hypertensive disorder of pregnancy          | 233 (14.9)                              | 345 (14.3)                             |         |
| Maternal diabetes before pregnancy          | 59 (3.8)                                | 111 (4.6)                              | 0.13    |
| Gestational diabetes                        | 53 (3.4)                                | 105 (4.4)                              |         |
| Histologic chorioamnionitis                 | 685 (48.6)                              | 1121 (50.0)                            | 0.43    |
| Singleton                                   | 1160 (74.0)                             | 1799 (74.5)                            | 0.74    |
| Cesarean delivery                           | 988 (63.2)                              | 1548 (64.2)                            | 0.57    |
| Complete course of antenatal steroids       | 942 (60.8)                              | 1612 (66.9)                            | <0.01   |
| Gestational age (wk)\(^d\)                  | 26.1 (1.9)                              | 26.1 (1.9)                             | 0.38    |
| Birth weight (g)\(^d\)                      | 825.5 (252.7)                           | 847.7 (262.4)                          | 0.10    |
| Small for gestational age                   | 151 (9.7)                               | 215 (8.9)                              | 0.47    |
| Male                                        | 794 (50.6)                              | 1258 (52.1)                            | 0.36    |

\(^d\) Mean (SD).

BMI, body mass index; SD, standard deviation.
| Characteristic                                      | Maternal BMI Categories                                                                 | P     |
|----------------------------------------------------|----------------------------------------------------------------------------------------|-------|
|                                                   | Normal/Underweight N=938 (38.9%)                                                       |       |
|                                                   | Maternal age (y)                                                                         | 27.9 (6.2) |
|                                                   | Maternal race                                                                            |       |
|                                                   | Black                                    290 (32.3)                               | 0.02  |
|                                                   | White                                    515 (57.4)                               |       |
|                                                   | Other                                    93 (10.4)                                |       |
|                                                   | Married maternal status                                                                 | 452 (48.2) |
|                                                   | Maternal education (> high school)                                                      | 458 (57.8) |
|                                                   | Medicaid insurance                                                                      | 493 (52.6) |
|                                                   | Maternal hypertension before pregnancy                                                  | 61 (6.5) |
|                                                   | Hypertensive disorder of pregnancy                                                      | 120 (12.8) |
|                                                   | Maternal diabetes before pregnancy                                                     | 13 (1.4) |
|                                                   | Gestational diabetes                                                                    | 20 (2.1) |
|                                                   | Histologic chorioamnionitis                                                             | 400 (45.8) |
|                                                   | Singleton                                                                              | 681 (72.6) |
|                                                   | Cesarean delivery                                                                       | 597 (63.7) |
|                                                   | Complete course of antenatal steroids                                                    | 626 (66.8) |
|                                                   | Mean (SD)                                |       |
|                                                   | Maternal age (y)                                                                         | 29.1 (5.8) |
|                                                   | Maternal race                                                                            | 197 (36.1) |
|                                                   | Black                                    306 (56.0)                               |       |
|                                                   | White                                    43 (7.9)                                 |       |
|                                                   | Married maternal status                                                                 | 275 (48.4) |
|                                                   | Maternal education (> high school)                                                      | 301 (62.1) |
|                                                   | Medicaid insurance                                                                      | 311 (54.9) |
|                                                   | Maternal hypertension before pregnancy                                                  | 59 (10.4) |
|                                                   | Hypertensive disorder of pregnancy                                                      | 83 (14.6) |
|                                                   | Maternal diabetes before pregnancy                                                     | 23 (4.1)  |
|                                                   | Gestational diabetes                                                                    | 23 (4.1)  |
|                                                   | Histologic chorioamnionitis                                                             | 270 (50.9) |
|                                                   | Singleton                                                                              | 439 (77.3) |
|                                                   | Cesarean delivery                                                                       | 369 (65.1) |
|                                                   | Complete course of antenatal steroids                                                    | 381 (67.1) |

*a* Mean (SD).

BMI, body mass index; SD, standard deviation.
Table 2b
Infant Characteristics at Birth by Maternal BMI

| Characteristic                                      | Normal/Underweight N= 938 (38.9%) | Overweight N=568 (23.5%) | Obese N=909 (37.6%) | P    |
|----------------------------------------------------|-----------------------------------|--------------------------|---------------------|------|
|                                                    | No (%) or Mean (SD)*              |                          |                     |      |
| Gestational age (wk)<sup>a</sup>                    | 26.3 (1.9)                        | 26.1 (1.8)               | 26.0 (1.9)          | <0.01|
| Sex, male                                          | 488 (52.0)                        | 305 (53.7)               | 465 (51.2)          | 0.64 |
| Apgar score 1 minute, median >4                    | 496 (52.9)                        | 306 (53.9)               | 442 (48.6)          | 0.08 |
| Apgar score 5 min, median >7                       | 512 (54.6)                        | 318 (56.0)               | 478 (52.6)          | 0.42 |
| Delivery room bag and mask ventilation             | 777 (82.8)                        | 460 (81.1)               | 729 (80.3)          | 0.36 |
| Delivery room CPAP                                 | 516 (55.1)                        | 298 (52.6)               | 450 (49.6)          | 0.06 |
| Delivery room endotracheal intubation              | 560 (59.8)                        | 357 (62.9)               | 587 (64.7)          | 0.09 |
| Delivery room chest compression                     | 60 (6.4)                          | 35 (6.2)                 | 54 (6.0)            | 0.92 |
| Delivery room epinephrine                          | 27 (2.9)                          | 19 (3.4)                 | 27 (3.0)            | 0.89 |
| Small for gestational age                          | 83 (8.9)                          | 54 (9.6)                 | 78 (8.6)            | 0.82 |
| Birth weight (g)<sup>a</sup>                       | 861.8 (258.9)                     | 844.7 (261.4)            | 833.4 (264.7)       | 0.07 |
| Birth length (cm)<sup>a</sup>                      | 33.5 (3.7)                        | 33.3 (3.6)               | 33.3 (3.6)          | 0.41 |
| Birth head circumference (cm)<sup>a</sup>          | 23.7 (2.4)                        | 23.6 (2.4)               | 23.5 (2.4)          | 0.07 |

<sup>a</sup> Mean (SD).

BMI, body mass index; CPAP, continuous positive airway pressure; SD, standard deviation.
## Table 3

Morbidity and Mortality by Maternal BMI with Logistic Regression Analysis and aOR (95% CI)

| Outcome                                                                 | Normal/Underweight, 938 (38.9%) | Overweight, 568 (23.5%) | Obese, 909 (37.6%) | \(p\) |
|-------------------------------------------------------------------------|---------------------------------|-------------------------|--------------------|-------|
| Survival without severe morbidities                                    | 284 (30.8)                      | 157 (28.1)              | 254 (28.5)         | 0.65  |
| Survival by discharge                                                  | 768 (82.1)                      | 470 (83.2)              | 693 (76.5)         | 0.02  |
| Resuscitation in the delivery room                                     | 64 (6.8)                        | 36 (6.4)                | 55 (6.1)           | 0.67  |
| Survival at discharge without severe ICH                               | 674 (72.2)                      | 409 (72.3)              | 616 (68.0)         | 0.29  |
| Survival at discharge without cPVL                                     | 736 (78.6)                      | 454 (80.1)              | 659 (72.7)         | <0.01 |
| Survival at discharge without BPD                                      | 366 (39.3)                      | 213 (37.7)              | 333 (36.8)         | 0.87  |
| Survival at discharge without medical or surgical NEC                  | 723 (77.2)                      | 433 (76.2)              | 644 (70.9)         | 0.02  |
| Survival at discharge without late-onset sepsis                        | 643 (68.6)                      | 375 (66.0)              | 580 (63.8)         | 0.65  |
| Survival at discharge without severe ROP                               | 662 (71.6)                      | 404 (72.3)              | 613 (67.4)         | 0.69  |
| Length of hospital stay in days among survivors\(\text{b}\)            | 107.5 (51.9)                    | 110.0 (54.6)            | 105.5 (46.7)       | 0.11  |
| Duration of oxygen support in days among survivors\(\text{c}\)         | 59.8 (41.1)                     | 63.6 (41.5)             | 60.5 (41.6)        | 0.63  |
| Duration of mechanical ventilation in days among survivors\(\text{d}\) | 20.0 (26.5)                     | 22.9 (29.2)             | 20.3 (27.1)        | 0.41  |

\(a\) Refers to overall significance among the 3 groups after adjustment for maternal race, socioeconomic status (maternal Medicaid insurance), maternal hypertension, maternal diabetes, gestational age, sex, small-for-gestational age status, and completion of antenatal steroid course as fixed effects; adjusted for center as a random effect.

\(b\) Mean (SD). Length of hospital stay was missing for 6.3% of surviving infants (5.1% underweight/normal, 7.0% overweight, 7.0% obese).

\(c\) Mean (SD). Duration of oxygen support was missing for 0.3% of surviving infants (0.5% underweight/normal, 0.0% overweight, 0.3% obese).

\(d\) Mean (SD). Duration of mechanical ventilation was missing for 0.9% of surviving infants (1.2% underweight/normal, 0.4% overweight, 0.9% obese).

BMI, body mass index; CI, confidence interval; cPVL, cystic periventricular leukomalacia; ICH, intracranial hemorrhage; NA, not applicable; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity.
Table 4
Morbidity and Mortality of Infants by Maternal BMI with Logistic Regression Analysis and aOR (95% CI)

| Outcome                                | Overweight vs Normal/Underweight | Obese vs Normal/Underweight | Obese vs Overweight | \( P \)   |
|----------------------------------------|----------------------------------|-----------------------------|---------------------|---------|
| Survival without severe neonatal morbidities |                                 |                             |                     | 0.14    |
| Model 1                                | NA                               | NA                          | NA                  |         |
| Model 2                                | NA                               | NA                          | NA                  | 0.09    |
| Model 3                                | NA                               | NA                          | NA                  | 0.65    |
| Survival by discharge                  |                                 |                             |                     | <0.01   |
| Model 1\(^a\)                          | 1.07 (0.77–1.49)                  | 0.71 (0.54–0.93)            | 0.66 (0.48–0.91)    | <0.01   |
| Model 2\(^b\)                          | 1.02 (0.72–1.45)                  | 0.64 (0.48–0.87)            | 0.63 (0.45–0.88)    | <0.01   |
| Model 3\(^c\)                          | 1.11 (0.74–1.66)                  | 0.72 (0.50, 1.02)           | 0.64 (0.43–0.95)    | 0.02    |
| Survival at discharge without PVL      |                                 |                             |                     |         |
| Model 1\(^a\)                          | 1.08 (0.79–1.48)                  | 0.72 (0.55–0.93)            | 0.66 (0.49–0.90)    | <0.01   |
| Model 2\(^b\)                          | 1.05 (0.76–1.45)                  | 0.65 (0.49–0.86)            | 0.62 (0.45–0.86)    | <0.01   |
| Model 3\(^c\)                          | 1.15 (0.80–1.67)                  | 0.72 (0.52–1.00)            | 0.63 (0.43–0.90)    | <0.01   |
| Survival at discharge without medical or surgical NEC | | | | |
| Model 1\(^a\)                          | 0.94 (0.70–1.27)                  | 0.71 (0.55–0.91)            | 0.75 (0.56–1.01)    | <0.01   |
| Model 2\(^b\)                          | 0.90 (0.66–1.23)                  | 0.65 (0.50–0.86)            | 0.72 (0.53–0.98)    | <0.01   |
| Model 3\(^c\)                          | 0.97 (0.68–1.37)                  | 0.71 (0.52–0.97)            | 0.74 (0.52–1.04)    | 0.02    |

For all models, when the overall test result was significant, pairwise comparisons were performed with Tukey-Kramer adjustments. \( \text{aOR} \), adjusted odds ratio; BMI, body mass index; CI, confidence interval; NA, not applicable; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia.

\(^a\)Model 1: \( P \) refers to overall significance among the 3 groups, adjusted only for the center as a random effect.

\(^b\)Model 2: \( P \) refers to overall significance among the 3 groups after further adjusting for maternal race, socioeconomic status (maternal Medicaid insurance), maternal hypertension, maternal diabetes, sex, and completion of antenatal steroids course as fixed effects.

\(^c\)Model 3: \( P \) refers to overall significance among the 3 groups after adjusting for all factors in model 2, plus birth factors of gestational age and small-for-gestational age status.