The Impact of Severe Maternal Morbidity on Very Preterm Infant Outcomes

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Objective To estimate the prevalence of severe maternal morbidity among very preterm births and determine its association with very preterm infant mortality and morbidity.

Study design This study used New York City Vital Statistics birth and death records linked with maternal and newborn discharge abstract data for live births between 2010 and 2014. We included 6901 infants without congenital anomalies born between $24^{0/7}$ and $32^{6/7}$ weeks of gestation. Severe maternal morbidity was identified as life-threatening conditions or life-saving procedures. Outcomes were first-year infant mortality, severe neonatal morbidity (bronchopulmonary dysplasia, severe necrotizing enterocolitis, stage 3-5 retinopathy of prematurity, and intraventricular hemorrhage grades 3-4), and a combined outcome of death or morbidity.

Results Twelve percent of very preterm live-born infants had a mother with severe maternal morbidity. Maternal and pregnancy characteristics associated with occurrence of severe maternal morbidity were multiparity, being non-Hispanic black, and preexisting health conditions, but gestational age and the percentage small for gestational age did not differ. Infants whose mothers experienced severe maternal morbidity had higher first-year mortality, 11.2% vs 7.7% without severe maternal morbidity, yielding a relative risk of 1.39 (95% CI: 1.14-1.70) after adjustment for maternal characteristics, preexisting comorbidities, pregnancy complications, and hospital factors. Severe neonatal morbidity was not associated with severe maternal morbidity.

Conclusions Severe maternal morbidity is an independent risk factor for mortality in the first year of life among very preterm infants after consideration of other maternal and pregnancy risk factors. *(J Pediatr 2019;215:56-63)*.

Severe maternal morbidity, defined as a life-threatening diagnosis or a lifesaving procedure during the delivery hospitalization.[1,2] occurs more frequently in very preterm than term deliveries. In high income countries, 1%-2% of women experience severe maternal morbidity during their delivery hospitalization, with an estimated 20% of cases occurring before 32 weeks of gestation.[3] There has been a significant focus on the life-threatening nature of severe maternal morbidity for moms, but no inquiry on how it impacts vulnerable very preterm babies. Very preterm babies account for over one-half of infant deaths and face high risks of morbidity and developmental impairment.[4-7]

Research on mothers and very preterm infants is often conducted in silos and, therefore, it is not known what percent of very preterm infants have a mother who experiences a severe morbid event. This information may be particularly relevant for very preterm infants because the context and events around birth, including the quality of obstetrical management, are determinant for their prognosis.[8-12] Suboptimal care during the delivery hospitalization has been shown to raise a mother's risks of severe maternal morbidity,[13,14] and this may extend to higher risks for her infant. Severe maternal morbidity could also be a marker for the severity of some pregnancy complications which have a negative impact on the infant.

Our goal was to estimate the prevalence of severe maternal morbidity among births before 32 weeks of gestation, to identify risk factors for co-occurrence of severe maternal morbidity in the setting of very preterm birth, and to investigate its association with risks of infant mortality and severe neonatal morbidity.

Methods

We used New York City Vital Statistics birth and death records linked with New York State discharge abstract data, The Statewide Planning and Research Cooperative System (SPARCS), for all live births in New York City hospitals in the years 2010 to 2014. The New York State Department of Health and Human Services linked the data using a probabilistic linking methodology, and more than 98% of all infant records were linked to vital statistics data and a further 98% of maternal discharge abstracts were linked with infant records. The linked

SPARCS	Statewide Planning and Research Cooperative System

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dataset included birth data, death data, and the infant's and mother's hospital discharge records for all infants born from 2010 to 2014 who were discharged by December 31, 2014, and all infant deaths from 2010 to 2015. Institutional Review Board approvals were obtained from the New York City Department of Health and Mental Hygiene, the New York State Department of Health, and the Icahn School of Medicine at Mount Sinai.

The study population included births without congenital anomalies between 24 and 32 weeks of gestation (6901 infants who were born to 6138 mothers). We focused on very preterm births, defined as births under 32 weeks[15] as these infants face highest risks of mortality and morbidity, and care quality in the perinatal period has been associated with their risks of mortality and morbidity.[8-12] We excluded births less than 24 weeks of gestational age and those with congenital anomalies because of their high risks of mortality and the possibility that death may have reflected a decision to abstain from active treatment. Cases with congenital anomalies were excluded based on diagnosis codes from the infant's SPARCS record, following previous studies.[16,17]

Our primary outcome variable was first year mortality, including deaths in-hospital and after discharge. We also investigated severe neonatal morbidity, defined by the presence on the infant birth hospital record of the *International Classification of Diseases, Ninth Revision* codes of any of the following diagnoses: bronchopulmonary dysplasia, necrotizing enterocolitis (unspecified, stage 2-3, laparotomy), retinopathy of prematurity (stage 3-5), intraventricular hemorrhage (grade 3-4), as in previous studies[18,19]; detailed codes are provided in **Table I** (available at www.jpeds.com). We created a composite variable of either first-year death or any neonatal morbidity during the delivery hospitalization. We assumed that children discharged home without these diagnoses were at very low risk of developing them after discharge.

We used a published algorithm to identify severe maternal morbidity, using diagnoses for life-threatening conditions and procedure codes for life-saving procedures defined by investigators from the Centers for Disease Control and Prevention.[20,21] The algorithm excludes severe maternal diagnoses for hospitalizations with a short length of stay to reduce misclassification associated with coding errors. A short length of stay is defined as less than the 90th percentile corresponding to ≤2 days for vaginal, ≤4 days for primary cesarean, and ≤3 days for repeat cesarean deliveries. However, length of stay reclassification is not applied to in-hospital maternal deaths, transfers, or delivery hospitalizations with severe complications identified by procedure codes.[20] We calculated in-hospital stay based on postpartum stay, as done by other researchers developing severe maternal morbidity indicators.[22] Because pregnant women with high-risk pregnancies can have long antenatal hospitalizations unrelated to severe maternal morbidity, postpartum stay is more relevant for our population. As this deviates from the published algorithm, we also computed severe maternal morbidity using total hospital stay and found an almost identical proportion of severe maternal morbidity cases.

Covariables included socioeconomic and clinical characteristics known to influence both maternal and infant outcomes that were available on the birth certificate, including self-identified race and ethnicity, maternal age, country of birth, multiple pregnancy, history of previous cesarean delivery, body mass index, and prenatal care. Maternal comorbidities were ascertained from the mother's SPARCS record as well as the birth certificate to maximize sensitivity of our measures.[23] We included medical risk factors that could lead to maternal morbidity, but were likely present on admission to the hospital (eg, diabetes, hypertension, disorders of placentation).[24,25] We also took into consideration newborn characteristics in our models, including gestational age, sex, and small for gestational age based on US birthweight charts.[26] We also described mode of delivery, but did not include it in our models as we did not have information on its timing with respect to severe maternal morbidity. Finally, we included hospital characteristics, including public/private ownership and nursery level.

Missing data were infrequent in this dataset; variables with the most missing data were the number of prenatal visits (3.9%), maternal prepregnancy body mass index (1.6%), and maternal educational level (0.8%).

Statistical Analyses

We first estimated the prevalence of severe maternal morbidity in our very preterm cohort, defined as the percent of newborns who had a mother with severe maternal morbidity. To assess risk factors for co-occurrence of severe maternal morbidity, we described the distribution of covariables among newborns with and without mothers with severe maternal morbidity and modeled adjusted risk ratios, considering demographic and social variables and pregnancy complications. To evaluate the impact of severe maternal morbidity on infant outcomes, we compared our outcomes based on severe maternal morbidity co-occurrence using χ^2 tests. We then estimated risk ratios, adjusting for maternal, infant, and hospital factors and taking into consideration clustering within hospitals and within multiple pairs.[27,28] Adjusted relative risks were derived using a modified Poisson regression model with robust SEs.[27,28] To describe risks of mortality over time, we constructed Kaplan-Meier survival curves, and survival estimates over the first 6 months of life were derived from the life table. Log-rank tests were used to compare survival. We also looked at the proportion of deaths occurring before and after discharge from hospital. We used SAS v 9.4 (SAS Institute, Cary, North Carolina)for all analyses.

Results

In our cohort of births between 24 and 32 weeks of gestation, 843 of 6901 (12.2%) of infants had a mother with a severe morbid event. Co-occurrence of severe maternal morbidity occurred more often among infants with older, multiparous, and non-Hispanic black mothers, as shown in **Table II**.

Other sociodemographic characteristics and prenatal care visits were not significantly different. Pregestational diabetes, hypertensive disorders and preeclampsia, and higher order multiple pregnancies were associated with severe maternal morbidity, and chorioamnionitis and gestational diabetes were similar in the 2 groups, and preterm premature rupture of membranes and precipitous labor were more common in preterm births without severe maternal morbidity. There were more cesarean deliveries among cases with severe maternal morbidity. The gestational age and percentage of small for gestational age infants did not differ by occurrence of severe maternal morbidity. There was also no difference in the distribution of severe maternal morbidity and nonsevere maternal morbidity cases in public vs private hospitals, but severe maternal morbidity cases occurred more often in hospitals with higher level nurseries.

In adjusted models (**Table III**), older maternal age, multiparity, non-Hispanic black race/ethnicity, and pregestational diabetes and hypertension were related to a higher likelihood of co-occurrence of severe maternal morbidity. Prepregnancy obesity was negatively related to the probability of co-occurrence of severe maternal morbidity.

First-year mortality was higher for infants with a mother who experienced severe maternal morbidity: 11.2% vs 7.7% when severe maternal morbidity did not occur ($P < .001$). A majority of deaths in both groups took place in the first week, but relative risks remained elevated after delivery: mortality in the first day of life was 2.5% vs 1.9% ($P = .004$) for children born to mothers with and without severe maternal morbidity and 6.8% vs 4.6% ($P = .004$) over the next 6 days, respectively, as reported in the **Figure**, which shows mortality risks over the first 6 months. Almost all first year deaths occurred within this time frame. The proportion of deaths that occurred during the neonatal hospitalization vs after discharge was similar: 92.9% of babies in the severe maternal morbidity group and 92.2 % in the group without severe maternal morbidity.

Adjusting for sociodemographic, clinical, and hospital factors reduced the relative risk of first year mortality associated with severe maternal morbidity from 1.47 (95% CI 1.15-1.84) to 1.39 (95% CI 1.14-1.70). Severe neonatal morbidity was not associated with the occurrence of severe maternal morbidity in unadjusted or adjusted models and severe maternal morbidity was not significant in the composite mortality and morbidity model (**Table IV**).

Discussion

Severe maternal morbidity occurred in 12% of very preterm live births and was associated with a 39% increased risk of infant death after adjustment for sociodemographic and clinical factors. These higher mortality risks were constant across the first 6 months of life. Severe maternal morbidity was unrelated to gestational age or growth restriction, the main prognostic factors for very preterm mortality. By identifying severe maternal morbidity as a risk factor for these infants, our study raises the possibility that quality initiatives targeting severe maternal morbidity could achieve reductions in their mortality.

Our results are consistent with a Canadian study that found higher mortality among infants admitted to a neonatal unit when mothers were also admitted to an intensive care unit,[29] but few studies have investigated the association between maternal morbidity and very preterm outcomes. The relatively high occurrence of severe maternal morbidity in our study is concordant with research showing that many cases of severe maternal morbidity are associated with very preterm delivery.[3] In addition, mortality rates are in line with those reported in other cohorts of nonanomalous live births between 24 and 32 weeks of gestation.[30,31]

Our results corroborate studies showing that older maternal age, being non-Hispanic black and hypertensive disorders are risk factors for severe maternal morbidity.[14,24] In contrast, maternal education, number of prenatal visits, gestational age, and growth restriction were not associated with severe maternal morbidity among very preterm births. Obesity was negatively associated with severe maternal morbidity risk, after adjustment for pregnancy complications such as hypertension and diabetes, which may reflect the high risk of spontaneous extremely preterm delivery among obese women.[32-34] Cesarean delivery was more common in severe maternal morbidity cases, as seen in other studies.[35,36]

Severe maternal morbidity did not affect risks of severe neonatal morbidity. If mortality risks are raised among the most vulnerable infants, survivors may be less likely to experience morbidity, giving the erroneous impression that morbidity risk is not impacted by severe maternal morbidity. Alternatively, severe maternal morbidity could truly have a lesser impact on morbidity risk; some studies have found that composite morbidity measures containing similar pathologies were less sensitive to perinatal management than mortality.[9,37] In addition, there may be an impact on other morbidities, such as sepsis, which affect risks of death,[38,39] but cannot be measured reliably with hospital discharge data.[40]

There are several explanations for the association between severe maternal morbidity and infant mortality. Quality of care is a determinant of adverse maternal as well as very preterm outcomes,[9,13] including in our prior research in New York City.[14,17] Higher risks for infants could be observed if poorly performing hospitals for mothers also performed poorly for babies, as suggested in a previous study which found a correlation between hospital performance for severe maternal morbidity and term newborn morbidity.[25] Future research on severe maternal morbidity and infant outcomes should include an expanded population of moderate preterm and term infants to evaluate whether these adverse effects are observed after the very preterm period.

Another explanation could be a negative impact of some maternal complications, such as preeclampsia or placental abruption, which increase risks for a severe maternal

Table II. Characteristics of live born very preterm newborns overall and by whether their mother had severe maternal morbidity

Characteristics	All newborns, n (%)	Mother without severe maternal morbidity, n (%)	Mother with severe maternal morbidity, n (%)	*P* value
Total	6901 (100)	6057 (87.8)	843 (12.2)	
Mother's age (y)				<.001
<20	369 (5.4)	339 (5.6)	30 (3.6)	
20-34	4620 (67.0)	41 056 (67.8)	515 (61.1)	
35-39	1400 (20.3)	1187 (19.6)	213 (25.3)	
40 or older	512 (7.4)	427 (7.0)	85 (9.1)	
Parity				<.001
Nulliparous	3060 (44.3)	2757 (45.5)	303 (35.9)	
Multiparous	3819 (55.3)	3288 (54.3)	531 (63.0)	
Mother's race				.008
Non-Hispanic black	2639 (38.2)	2274 (37.5)	365 (43.3)	
Hispanic	2089 (30.3)	1842 (30.4)	247 (29.3)	
Non-Hispanic white	1385 (20.1)	1241 (20.5)	144 (17.1)	
Asian	749 (10.9)	669 (11.0)	80 (9.5)	
Mother's education				.90
Less than high school	1557 (22.6)	1365 (22.5)	192 (22.8)	
High school	1608 (23.3)	1416 (23.4)	192 (22.8)	
Greater than high school	3682 (53.4)	3241 (53.5)	443 (52.6)	
Mother's insurance				.07
Governmental	4209 (61.0)	3665 (60.5)	544 (64.5)	
Commercial	2493 (36.1)	2214 (36.5)	279 (33.1)	
Uninsured	199 (2.9)	179 (3.0)	20 (2.4)	
Mother's prenatal visits				.9
0-5	1923 (27.9)	1682 (27.8)	241 (28.6)	
6-8	2006 (29.1)	1760 (29.1)	246 (29.3)	
9 plus	2717 (39.4)	2394 (39.5)	323 (38.3)	
Missing	255 (3.7)	222 (3.7)	33 (3.9)	
Smoked during pregnancy	270 (3.9)	238 (3.9)	32 (3.8)	.90
Prepregnancy body mass index				.55
Underweight (<18.5)	315 (4.6)	278 (4.6)	37 (4.5)	
Normal weight (18.5-24.9)	3078 (45.3)	2695 (45.1)	383 (46.8)	
Overweight (25.0-29.9)	1751 (25.8)	1536 (25.7)	215 (26.3)	
Obese (≥30)	1655 (24.3)	1472 (24.6)	183 (22.4)	
Plurality				
Singleton	5124 (74.3)	4506 (74.4)	618 (73.3)	.02
Twins	1580 (22.9)	1393 (23.0)	187 (22.2)	
Triplets or quadruplets	197 (2.9)	159 (2.6)	38 (4.5)	
Vaginal delivery	2118 (30.7)	2040 (33.7)	78 (9.2)	<.001
Cesarean delivery	4783 (69.3)	4018 (66.3)	765 (90.8)	<.001
Trial of labor	672 (9.7)	574 (9.5)	98 (11.6)	.001
Maternal complications				
Pregestational diabetes	185 (2.7)	140 (2.3)	45 (5.3)	<.001
Gestational diabetes	676 (9.8)	591 (9.8)	85 (10.1)	.76
Pregestational hypertension	592 (8.6)	472 (7.8)	120 (14.2)	<.001
Gestational hypertension	1749 (25.3)	1449 (23.9)	300 (35.6)	<.001
Preeclampsia	1243 (18.0)	1031 (17.0)	212 (25.2)	<.001
Chorioamnionitis	1197 (17.4)	1059 (17.5)	138 (16.4)	.42
Premature rupture of the membranes	2537 (36.8)	2331 (38.5)	206 (24.4)	<.001
Precipitous labor	316 (4.6)	300 (5.0)	16 (1.9)	<.001
Gestational age (wk)				
24-25	1014 (14.7)	899 (14.8)	115 (13.6)	.32
26-27	1283 (18.6)	1113 (18.4)	170 (20.2)	
28-29	1707 (24.7)	1487 (24.6)	220 (26.1)	
30-31	2897 (42.0)	2559 (42.2)	338 (40.1)	
Infant small for gestational age*	911 (13.2)	785 (13.0)	126 (15.0)	.11
Sex				
Female	3301 (47.8)	2871 (47.4)	430 (51.0)	.05
Male	3600 (52.2)	3187 (52.6)	413 (50.0)	
Hospital characteristics				
Public	1364 (19.8)	1181 (19.5)	183 (21.7)	.13
Private	5537 (80.2)	4877 (80.5)	660 (78.3)	
Nursery level				.002
2	235 (3.4)	218 (3.6)	17 (2.0)	
3	3585 (52.0)	3177 (52.4)	408 (48.4)	
4	3081 (44.7)	2663 (44.0)	418 (50.0)	

*Birthweight <10th percentile of US birthweight charts.[26]

Table III. Characteristics associated with having a mother with severe maternal morbidity for very preterm newborns

Characteristics	Unadjusted risk ratios with 95% CI	Adjusted risk ratios, with 95% CI*
Mother's age (y)		
<20	0.72 (0.50-1.03)	0.79 (0.54-1.14)
20-34	Ref	Ref
35-39	1.34 (1.17-1.57)	1.29 (1.11-1.51)
40 or older	1.46 (1.17-1.83)	1.41 (1.12-1.78)
Parity		
Nulliparous	Ref	Ref
Multiparous	1.40 (1.23-1.60)	1.30 (1.13-1.50)
Mother's race		
Non-Hispanic black	1.33 (1.11-1.59)	1.27 (1.04-1.54)
Hispanic	1.14 (0.94-1.38)	1.13 (0.92-1.39)
Non-Hispanic white	Ref	Ref
Asian	1.03 (0.79-1.33)	1.00 (0.77-1.31)
Mother's education		
Less than high school	1.03 (0.88-1.20)	0.97 (0.81-1.17)
High school	0.99 (0.85-1.16)	0.94 (0.79-1.11)
Greater than high school	Ref	Ref
Mother's insurance		
Governmental	1.15 (1.01-1.32)	1.16 (0.98-1.37)
Commercial	Ref	Ref
Uninsured	0.90 (0.58-1.38)	0.92 (0.58-1.45)
Mother's prenatal visits		
0-5	1.05 (0.90-1.23)	1.02 (0.87-1.21)
6-8	1.03 (0.88-1.21)	1.01 (0.87-1.18)
9 plus	Ref	Ref
Smoked during pregnancy	0.97 (0.70-1.35)	1.01 (0.72-1.40)
Body mass index		
Underweight (<18.5)	0.92 (0.67-1.26)	1.02 (0.74-1.40)
Normal weight (18.5-24.9)	Ref	Ref
Overweight (25.0-29.9)	0.96 (0.82-1.12)	0.86 (0.73-1.01)
Obese (≥30)	0.86 (0.73-1.02)	0.72 (0.60-0.85)
Multiple pregnancy	1.06 (0.91-1.21)	1.05 (0.90-1.23)
Maternal complications		
Pregestational diabetes	2.05 (1.57-2.66)	1.76 (1.34-2.31)
Gestational diabetes	1.03 (0.83-1.27)	1.00 (0.80-1.25)
Pregestational hypertension	1.77 (1.49-2.10)	1.29 (1.05-1.58)
Gestational hypertension	1.63 (1.42-1.85)	1.20 (0.95-1.52)
Preeclampsia	1.53 (1.32-1.76)	1.14 (0.90-1.46)
Chorioamnionitis	0.93 (0.79-1.11)	1.08 (0.90-1.29)
Premature rupture of the membranes	0.56 (0.48-0.65)	0.60 (0.51-0.71)
Precipitous labor	0.40 (0.25- 0.65)	0.45 (0.28- 0.73)
Newborn characteristics		
Gestational age (wk)		
24-25	0.97 (0.80-1.19)	1.15 (0.93-1.42)
26-27	1.14 (0.96-1.35)	1.20 (1.00-1.43)
28-29	1.10 (0.94-1.29)	1.14 (0.97-1.34)
30-31	Ref	Ref
Small for gestational age†	1.15 (0.97-1.38)	0.89 (0.74-1.07)
Sex		
Female	Ref	Ref
Male	0.88 (0.77-1.00)	0.93 (0.82-1.05)
Hospital characteristics		
Public	1.13 (0.97-1.31)	1.08 (0.91-1.29)
Private	Ref	
Nursery level		
2	Ref	
3	1.57 (0.99-2.51)	1.53 (0.94-2.49)
4	1.88 (1.18-2.99)	1.88 (1.16-3.06)

*Adjusted for all variables in table.
†<10th percentile of US birthweight charts.[26]

morbidity event and are also at the origin of the preterm birth. However, although these complications are risk factors for poor outcome in general population studies,[41,42] research on very preterm infants has not shown that they increase mortality risks,[43] although abruption may be related to neonatal morbidity.[44] It is possible, nonetheless, that severe maternal morbidity may be a marker of the severity of some complications which are poorly captured by available data on comorbidities.

Our study calls attention to the relevance of a research framework based on the mother-child dyad. This paradigm could have broader application. For instance, severe maternal

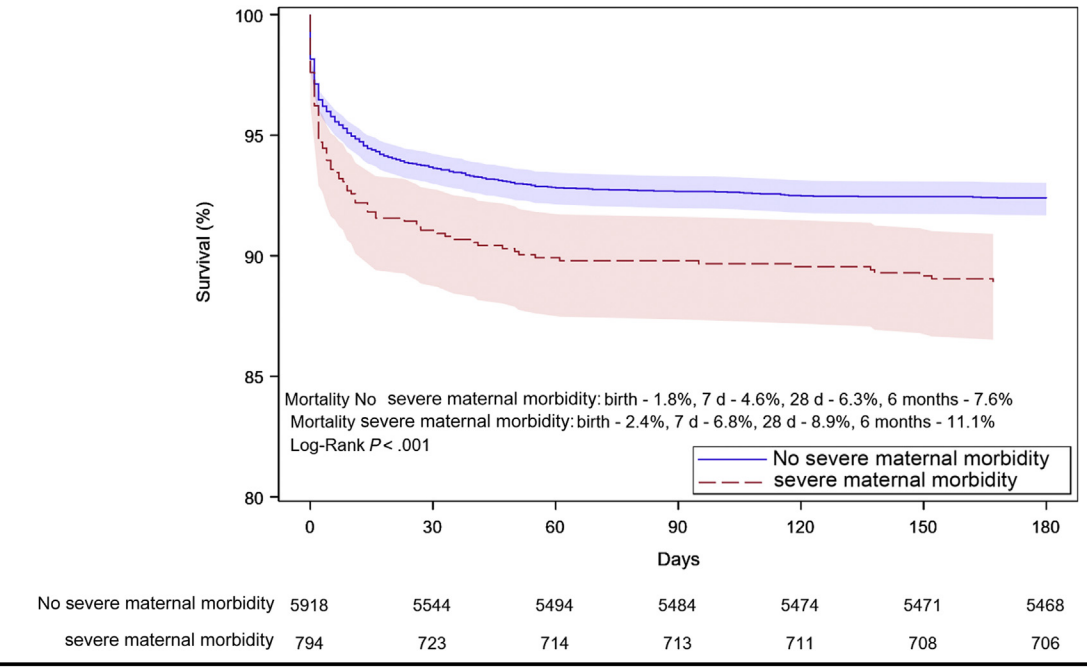

Figure. Infant survival over the first 6 months of life by occurrence of severe maternal morbidity.

morbidity may have longer-term effects on very preterm children's health and development. It is negatively associated with breastfeeding,[45] which requires initiation and frequent milk expression soon after delivery, and leads to longer maternal hospitalization, often in a different facility,[29] which could affect the process of bonding with the newborn. More broadly, mothers who experience severe maternal morbidity may be at increased risk for postpartum depression or suffer from other health sequelae which could impact the mother-baby relationship.[46,47] There is some evidence that maternal depression and anxiety are related to adverse developmental outcomes for children born very preterm.[48] Furthermore, child outcomes may be associated with maternal risks of severe maternal morbidity or with maternal recovery and resilience after severe maternal morbidity, as suggested in the previously cited Canadian study, where the mother's risks of death in the intensive care unit was higher when her infant was admitted to a neonatal intensive care unit.[29]

This study's strengths are its population-based design, use of variables from hospital discharge and vital statistics, linkage of maternal and newborn data, the large sample enabling investigation of 2 uncommon outcomes, and consideration of clustering within hospitals and multiple pairs. Because we had data on timing of death, we were able to compare changes in mortality risks over time; however, information on timing was not available for neonatal or maternal morbidities. Other limitations include the exclusion of stillbirths. Given that severe maternal morbidity may affect risks of intrapartum death, adding stillbirths could lead to a strengthening of the association between severe maternal morbidity and mortality. Further, coding errors for diagnoses and procedures are of concern when using hospital discharge and birth certificate data,[49] although using both sources improves the sensitivity of data on maternal comorbidities.[23] Finally, it was not possible to differentiate between maternal and fetal indications for delivery.

Severe maternal morbidity occurred in over 1 in 10 very preterm deliveries and was a risk factor for infant death, but not severe neonatal morbidity, after adjusting for other known prognostic factors. Further investigation is needed to understand the causes of this excess mortality risk to develop strategies to improve perinatal management. These results should encourage researchers to include data on maternal outcomes related to childbirth in research network databases and cohort studies of very preterm infants. ■

Table IV. Impact of occurrence of severe maternal morbidity on very preterm outcomes

Neonatal outcomes	Mother without severe maternal morbidity n (%)	Mother with severe maternal morbidity n (%)	*P* value	Unadjusted risk ratio	95% CI	Adjusted risk ratio*	95% CI
1 y mortality	462 (7.8)	91 (11.4)	<.001	1.47	1.17-1.83	1.39	1.14-1.70
Severe neonatal morbidity	1294 (21.9)	178 (22.4)	.75	1.02	0.87-1.20	0.97	0.85-1.11
Composite death or morbidity	1615 (27.3)	249 (31.3)	.02	1.15	1.04-1.31	1.10	0.99-1.22

*Adjusted for variables in Table II and controlling for clustering patients within the hospital of delivery and multiples.

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50 Years Ago in *The Journal of Pediatrics*

Why Patients Don't Follow Medical Advice: A Study of Children on Long-Term Antistreptococcal Prophylaxis

Gordis L, Markowitz M, Lilienfeld AM. J Pediatr 1969;75:957-68.

Gordis et al describe a cohort study of children with a history of rheumatic fever who, in collaboration with school nurses, were followed with weekly randomly scheduled urine specimens to determine compliance with recommended oral penicillin prophylaxis. To identify risk factors for noncompliance, the authors examined a cohort of 111 African American children with complete data. Correlations with demographic and medical factors, rheumatic fever and penicillin knowledge, family structure, and cultural and attitudinal factors were examined. Adolescents and female children were found to be less compliant, whereas hospitalization for rheumatic heart disease and parental involvement at any age (as indicated by accompanying their child to the clinic) were associated with increased treatment adherence. Importantly, there was no correlation with parental income, education, or occupation, or living in a single parent home. The authors recommended intensive follow-up efforts be directed at patients with multiple risk factors for noncompliance.

Today, acute rheumatic fever and rheumatic heart disease are rare in the developed world but remain high in developing regions.[1] Studies in areas of high prevalence have determined that lack of access to medical care (eg, lack of insurance coverage or long distance to health facilities) contribute to poor adherence,[2,3] factors notably not studied by Gordis et al. In addition, in a population-based investigation conducted in New Caledonia, recommendations included both individual-level interventions (eg, increasing patient education), and system-level solutions (eg, an appointed nurse to coordinate a registry system).[2] This modern focus on system-level interventions to influence individual health highlights the evolving understanding of the importance of social and institutional determinants of health over the last 5 decades.

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Table I. Severe neonatal morbidity *International Classification of Diseases, Ninth Revision* diagnosis and procedure codes

Outcomes	Subgroup	ICD-9 code
BPD		770.7
NEC		
	NEC_unspec	777.5
	NEC_stage2	777.52
	NEC_stage3	777.53
	Laparotomy	456, 4561, 4562, 4563, 457, 4571, 4572, 4573, 4574, 4575, 4576, 4579, 458, 459, 4590, 4591, 4592,4593, 4594, 4595, 460, 4601, 4602, 4603, 4604, 4605, 461, 4610, 4611, 4613, 4614, 462, 4620, 4621, 4622, 4623, 4624, 463, 4631, 4632, 4639, 464, 4640, 4641, 4642, 4643, 468, 4680, 4681, 4682, 4685, 4686, 4687, 541, 541,5411, 5412, 5419
ROP		
	ROP_stage3	362.25
	ROP_stage4	362.26
	ROP_stage5	362.27
	ROP_surg	142, 1421, 1422, 1423, 1424, 1425, 1426, 1427, 1429, 1434, 144, 1441, 1449, 145, 1451, 1452, 1453, 1454, 1455, 1459
IVH		
	IVH_grade3	772.13
	IVH_grade4	772.14

BPD, Bronchopulmonary Dysplasia; *ICD-9*, International Classification of Diseases, Ninth Revision; *IVH*, intraventricular hemorrhage; *NEC*, Necrotizing enterocolitis; *ROP*, Retinopathy of prematurity.